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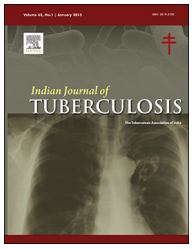

Editorial

TB care in Private Sector: Much more needed

Even though India's Revised National Tuberculosis Control Program (RNTCP) has been widely acknowledged as a successful public health program, only about 50% of Tuberculosis (TB) patients get diagnosed in the public sector, while the rest are diagnosed in the largely unregulated private sector. During 2015, out of estimated global annual incidence of 9.6 million TB cases, 2.2 million TB cases were estimated to have occurred in India. The TB control programme notified 1.2 million cases leaving behind 1 million cases undetected.[1]

In the private sector, a patient goes through multiple channels before getting a correct diagnosis and this may take from weeks to months during which he/she continues to transmit the disease.[2] Therefore, getting an early and accurate TB test in the private sector is crucial for breaking this chain of transmission and reducing the risk of drug resistance.

Hence, understanding the amount of tuberculosis managed by the private sector in India is crucial to understanding the true burden of the disease in the country, and also helping in planning for government intervention in the private sector. In the absence of quality surveillance data on privately treated patients, commercial drug sales data offer an empirical foundation for disease burden estimation.[3]

Non-standardized practices in the private sector, lack of supervision for ensuring treatment adherence have increased treatment interruptions and subsequent drug resistance among TB patients in the country. Timely notification gives an opportunity to support private sector for better practices in terms of standards TB care which include helping the patients to get right diagnosis, treatment, follow-up, contact tracing, chemoprophylaxis and facilities of social support systems.

RNTCP has made tremendous efforts in accelerating notification of TB cases from the private sector in recent past by taking few concentrated and special initiatives, *vis-a-vis*, placing TB notification advertisement in news bulletins, constituting state level TB notification committees to oversee the progress of TB notification efforts in all states, direct one to one sensitization of private practitioners and laboratories for TB notification by the state TB notification teams and giving hassle free direct web-login to the registered private providers for direct TB notification in NIKSHAY. "NIKSHAY" is a case-based web online application under RNTCP for monitoring of TB program and TB surveillance. This programme is determined to move with Digital India campaign and aspiring to use ICT advancements to enhance its surveillance system through e-NIKSHAY.

Patient Centric Approach has also been advocated for management of TB cases. Mobile health (mHealth)-based tools such as smartphone apps have been suggested as tools to support TB control efforts (e.g., identification, contact tracing, case management including patient support).[4] For instance, smartphone mobile apps that had an alert/reminder function (eCompliance, eDetection, and MDR-TB Clinic) were developed for health care workers to display reports of expected appointments or pending questionnaires needed during home visits.[4]

Another worth mentioning initiative taken is TB precision treatment which includes optimized drug exposure in relation to drug susceptibility testing. The factors affecting treatment success depends on genetic makeup, environmental factors and lifestyle of subjects. Ahead of World Tuberculosis Day on March 24 this year the government has launched a new drug called Bedaquiline to specifically treat multi-drug resistant TB which is one of such examples.[5]

Strong government stewardship creates an opportunity to manage PPs and align their practices to public health programmes. However a top-down strategy may fail if the interests of the PPs are not considered in planning and implementing PPM. With the initiative came funding commitment as well as direct guidance on the conditions for PP involvement. Treatment success for new smear-positive cases treated by PPs was close to WHO targets and as good as in the NTP in Delhi. Successful PPM projects often use a common set of basic intervention components, including training, strengthened referral and information systems and strengthened supervision and monitoring.[6]

Government of India has brought together multiple stakeholders to increase patient access and affordability to rapid, accurate, and WHO endorsed tests to diagnose TB in the Indian private sector. Projects, Initiative for Promoting Affordable & Quality Tuberculosis Testing (IPAQT) and Demand Generation and Notification Efforts (DENOTE) were implemented in this direction. Delhi Medical Association (DMA) acted as a link between the PPs and RNTCP (public sector). RNTCP had an overall responsibility to govern the project and supervise the activities of DMA. PPs were trained to diagnose and manage TB according to RNTCP guidelines under the supervision of DMA.[7]

Rapid point of care diagnostic tests such as GeneXpert, have the capability of diagnosing TB in less than 2 h were

implemented in field camps. As of May 2016, over 3,00,000 tests being already conducted, with approximately 70,000 patients being positively diagnosed with TB in these camps.

Laboratories in the private sector deliver majority of diagnostics services and are therefore a major source of information for epidemiological surveillance. Therefore an objective needs to be implemented to facilitate linkages and collaboration between private laboratories and public health systems through process improvements and eventual recommendations for policy change. As a part of this initiative a team of 15 field representatives collaborated with 23 quality-assured private laboratories in major cities to understand data recording practices of laboratories and their collection centers. Field team also liaised with RNTCP on behalf of partner labs for strengthening linkage to care by adding provisions for data transfer in the absence of an automated system.[2]

Some of the findings from recent studies enlightens implications for tuberculosis strategy in India. First, the vast disorganized private health-care sector poses major challenges to tuberculosis control. India's RNTCP has committed to providing free, high-quality tuberculosis care to patients in the private sector.[8] Second, there is urgent need for further strengthening of tuberculosis surveillance in the private sector. Although there has been increasing notification of tuberculosis cases by the private sector to public health authorities, these accounted in 2014 for 106 414 patients.[9]

Third, methods for estimating the tuberculosis burden should be complemented by independent approaches generating primary data. In addition to the surveillance needs, a national prevalence survey would provide direct evidence for the numbers of patients receiving treatment in the private sector.

Although it might be tempting to hold India's large informal health sector responsible for the observed high usage of tuberculosis drugs, recent work from India, using standardized patients, reveals that anti-tuberculosis drugs are rarely dispensed by pharmacists, informal providers, and practitioners of alternative medical systems.[10,11]

The private sector is massive, heterogeneous, and growing. In spite of mandatory notification, many patients are still not notified to the RNTCP. Two decades of attempts to improve collaboration between the public and private sectors, have not yet worked except in few innovative pilots. The existing TB surveillance system lacks the capacity to count the large pool of privately diagnosed and treated TB cases, and what is not measured is unlikely to be improved.

Reaching to TB patients seeking care in private sector and bringing them under the surveillance is an enormous challenge. Recently, the programme has taken an initiative to engage private practitioners at a large scale by providing free anti-TB drugs and Information & Communication Technology support to encourage TB notification from private sectors with good results.

Moreover, while timely diagnosis of TB is important, it is extremely important to seek proper care and treatment post-diagnosis of TB. While National Tuberculosis Control Programme initiatives such as IPAQT have brought down the cost of WHO-endorsed diagnostic tests and increased access and pilot projects such as DENOTE have increased the notification rates (Clinton Health access initiative. TB care in Indian Private Sector: 2016).

In future, even though early diagnosis of TB is critical in reducing the transmission of TB, understanding the patient journey post-diagnosis is important to design policy guidelines and treatment protocols. Efforts for detailing up to the level of detailing for TB patients, experience of treatment initiation need to be incorporated in the Indian private sector. More studies need to be initiated in combination with existing and improved sources of data, could help to build a truly comprehensive picture of the management of tuberculosis in India.

REFERENCES

1. World Health Organization. *Global Tuberculosis Control. WHO report.* 2016 http://www.who.int/tb/publications/global_report/en/.
2. Kapoor S, Raman A, Satyanarayana S. How did the TB Patients reach DOTS services in Delhi? A study of patient treatment seeking behavior. *PLoS ONE.* 2012;7(8):e42458. http://dx.doi.org/10.1371/journal.pone.0042458.
3. Arinaminpathy N, Batra D, Khaparde S, et al. The number of privately treated tuberculosis cases in India: an estimation from drug sales data. *Lancet Infect Dis.* 2016;16:1255–1260.
4. Iribarren SJ, Schnall R, Stone PW, Carballo-Diéguez A. Smartphone applications to support tuberculosis prevention and treatment: review and evaluation. *JMIR Mhealth Uhealth.* 2016;4(2):e25. http://dx.doi.org/10.2196/mhealth.5022.
5. Guidelines for Use of Bedaquiline in RNTCP PMDT in India. http://www.tbcindia.nic.in/showfile.php?lid=3246.
6. Lönnroth K, Uplekar M, Arora VK, et al. Public-private mix for improved TB control – what makes it work? *Bull World Health Organ.* 2004;82:580–586.
7. Arora VK, Lonnroth K, Sarin R. Improved case detection of tuberculosis through a public-private partnership. *Indian J Chest Dis Allied Sci.* 2004;46:133–136.
8. Sachdeva KS, Dewan P, Kumar A, Satyanarayana S. New vision for Revised National Tuberculosis Control Programme (RNTCP): universal access—"reaching the un-reached". *Indian J Med Res.* 2012;135:690–694.
9. Central TB Division, RNTCP Status Report 2015. Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India. http://www.tbcindia.gov.in/.
10. Das J, Kwan A, Daniels B, et al. Use of standardised patients to assess quality of tuberculosis care: a pilot, cross-sectional study. *Lancet Infect Dis.* 2015;15:1305–1313.
11. Satyanarayana S, Kwan A, Daniels B, et al. Use of standardised patients to assess antibiotic dispensing for tuberculosis by pharmacies in urban India: a cross-sectional study. *Lancet Infect Dis.* 2016;16:1261–1268.

K.K. Chopra[a,b,*]
[a]*Director, New Delhi Tuberculosis Centre, New Delhi, India*
[b]*Associate Executive Editor, Indian Journal of Tuberculosis, India*

V.K. Arora[a,b]
[a]*Vice Chairman (P&R), TB Association of India, India*
[b]*Executive Editor, Indian Journal of Tuberculosis, India*

**Corresponding author at*: New Delhi Tuberculosis Centre, New Delhi, India. Tel.: +91 9811547066
E-mail address: chopra_drkk@yahoo.co.in (K.K. Chopra)

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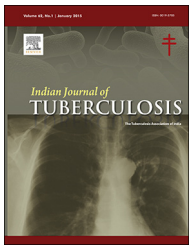

Original Article

Abdominal tuberculosis: A retrospective analysis of 45 cases

Suruchi Shreshtha [a,*], *Deepak Ghuliani* [b]

[a] *Assistant Professor, General Surgery, Dr Baba Saheb Ambedkar Medical College & Hospital, Delhi, India*
[b] *Associate Professor, General Surgery, Maulana Azad Medfical College, Delhi, India*

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ABSTRACT

Abdominal tuberculosis is defined as infection of the peritoneum, hollow or solid abdominal organs with *Mycobacterium tuberculosis*. The peritoneum and the ileocaecal region are the most likely sites of infection and are involved in the majority of the cases by haematogenous spread or through swallowing of infected sputum from primary pulmonary tuberculosis. Pulmonary tuberculosis is apparent in less than half of the patients. Patients usually present with abdominal pain, and the cause is usually identified through a combination of radiologic, endoscopic, microbiologic, histologic and molecular techniques. Anti-microbial treatment is the same as for pulmonary tuberculosis. Surgery is occasionally required.

1. Introduction

Tuberculosis (TB) is the deadliest communicable disease worldwide and has been declared as a global emergency by the World Health Organization.[1] Its estimated prevalence was 9 million with 3.17 million annual incidence in 2013. South-East Asia and Western Pacific regions represented 56% of the global TB burden, with India itself sheltering one-fourth of the cases.[2] The global mortality due to TB was 1.5 million in 2013, with India accounting for approximately 550,000 deaths each year.

Extra-pulmonary organ involvement of TB is approximately 10–15% in the patients without human immunodeficiency virus (HIV).[3] Its prevalence is on the rise as a result of increasing prevalence of acquired immunodeficiency syndrome (AIDS) and primary resistance to anti-tubercular drugs.[4] Similarly, atypical presentations and atypical extra-pulmonary forms of TB are also increasing. Among the extra-pulmonary TB patients, 11–16% of the patients have abdominal TB. Among the patients with active TB, before the advent of specific anti-tubercular drugs, the incidence of abdominal TB was 55–90% and has now regressed to 25% after the development of specific drugs.[5]

Abdominal TB can involve any part of the gastrointestinal tract (GIT) from mouth to anus, peritoneum and the pancreatobiliary system. It has varied presentation, often masquerading as other common and rare diseases,[6] particularly inflammatory bowel disease, colonic malignancy or gastrointestinal infections.[1] In the present retrospective study, the clinical, laboratory and radiological features of abdominal TB were analyzed.

2. Aim

The aim of this study was to evaluate the demographics, clinical presentation, management and outcome in the patients with abdominal TB.

* *Corresponding author at*: Dr Baba Saheb Ambedkar Medical College & Hospital, Delhi.
E-mail addresses: suruchishreshtha@yahoo.com (S. Shreshtha), drdeepakghuliani@gmail.com (D. Ghuliani).
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3. Methods

The case records of 45 patients with discharge diagnosis of abdominal TB managed in General Surgery department at Lok Nayak Hopsital from April 2014 to March 2015 were reviewed. Complete physical examination, medical and family history, erythrocyte sedimentation rate (ESR), routine biochemical tests, Mantoux skin test and chest X-ray were performed in all the patients. Abdominal ultrasonography (USG), microbiological examination (sputum, ascites and pus), barium study, abdominal computed tomography (CT) or laparotomy was performed when indicated.

Diagnosis of abdominal TB was based upon (1) a positive acid-fast bacilli (AFB) smear or culture, (2) histopathology showing granulomatous inflammation (with or without caseation), (3) radiological features compatible with TB on barium study, ultrasound or CT scan of the abdomen, (4) intraoperative findings suggestive of TB and (5) patients with a high index of clinical suspicion and negative diagnostic workup but showed a good response to therapeutic trial of anti-TB medicines.

Patient characteristics, demographics, laboratory reports, radiological and surgical findings, response to anti-tubercular treatment and surgical procedure performed were also evaluated. All patients received four-drug regimens (streptomycin or ethambutol, rifampicin, pyrazinamide and isoniazid) for 6 months.

3.1. *Statistical analysis*

The SPSS 12 standard version was used for data analyses. Descriptive analysis was done for demographic, clinical and radiographic features and results are presented as mean $\pm$ standard deviation (SD) and percentages for continuous variable and number and percentage for categorical variable. All p-values were two sided and considered as statistically significant if $p < 0.05$.

4. Results

Abdominal TB affects individuals in third and fourth decades of life.[7] The median age of the patients (30 females and 15 males) was 25 years (range 15–75 years). Majority of the patients were from the low socio-economic group (93%) and were females (66.6%). The most frequent symptoms (Table 1) were abdominal pain (97%), constipation (45.5%) and weight loss (36%). The mean duration of symptoms showed great variation ranging from one day to 2 years. Only 11 patients (25%) had concomitant fever, compared to 35.7% in the study by Hu et al.[8] Peritoneal signs were noted in 50% of the patients, while partial and complete bowel obstruction was seen in 18 (40%) and 12 (26.3%) patients, respectively.

Majority of the patients had anaemia (average haemoglobin – 9.2 g/dl), raised ESR (average ESR – 42 mm/h) and hypoalbuminaemia similar to the study by Baloch et al.[9] and Uygur-Bayramiçli et al.[10] Mantoux skin test was positive in only 12 (26.3%) patients.

Table 1 – Characteristics of abdominal tuberculosis patients (n = 45) of mean age.

Patient characteristic	n	%
Male	15	33.3
Female	30	66.6
Past history of TB	6	13.3
Family history of TB	8	17.7
Associated pulmonary TB	11	25
Abdominal pain	44	97
Fever	11	25
Weight loss	16	36
Vomiting	39	86.6
Ascites	19	43
Constipation	21	46.6
Diarrhoea	5	11
Partial bowel obstruction	18	40
Acute intestinal obstruction	12	26
Perforation	10	22

The diagnosis of abdominal TB was confirmed (Table 2) on the basis of intraoperative findings in 19 patients (42%), ultrasound in 18 (40%), histopathology in 14 (31%), CT abdomen in 6 (13.3%), microbiology in 4 (8.8%) and adenosine deaminase (ADA) in 3 (6.6%) patients. Three patients (6.6%) were diagnosed by a positive response to anti-tuberculous treatment.

The most common abdominal USG findings were ascites (43%) and ileocaecal thickening (16%). Ascitic fluid analysis had exudative fluid, with only one patient staining positive for AFB on BacTec test. The majority of patients in this review had bowel involvement (49%), with peritoneal involvement in 14 (36%) and lymph node disease in 6 (15%) patients. This is in agreement with other reviews on abdominal TB in which intestinal type of abdominal TB ranged from 50 to 78% of the patients.[10]

22 patients (50%) required urgent surgical exploration, which revealed ileal strictures in 5 (12.8%), dense inter-bowel adhesions and cocoon in 8 (20%), ileocaecal mass in 2 (5.1%) and intestinal perforation in 9 (23%) patients. 14 patients required stoma, while 4 patients (18.2%) were managed with resection anastomosis and two patients (9%) required adhesiolysis only. The results are in comparison to a study conducted by Baloch et al.[9] in which resection anastomosis was performed in 30% of the patients. Out of 44 patients, 33 (75%) patients were considered to have primary intestinal TB and 11 (25%) patients had secondary intestinal TB.

Table 2 – Diagnostic yield of various investigations in patients with abdominal tuberculosis.

Investigation	n (patients in whom investigations were performed)	Yield of diagnostic test n/%
Barium meal follow through	21	18/85.7
Ultrasound	29	24/83
CT scan abdomen	7	6/86
Histopathology	19	14/73.6
Ascitic fluid ADA	8	3/37.5
Mantoux skin test	45	12/26.3

5. Discussion

Abdominal TB denotes involvement of GIT (65–78%), peritoneum, lymph nodes and solid organs, i.e. liver, spleen and pancreas. Predominant site of involvement by abdominal TB was intestinal in 39 (88.6%) patients, which has also been seen in other studies (50–78%).[10–14] The majority of the patients (49%) with intestinal TB in this review had ileocaecal involvement, as seen in other series.[1,15] The suggested cause is increased physiological stasis, increased rate of fluid and electrolyte absorption, minimal digestion and abundant lymphoid tissue.[16,17] The frequency of bowel involvement reduces away from the ileocaecal region. The lesions may be ulcerative, hypertrophic and stricturous or a combination of the three.[18,19] Ulcerative and stricturous lesions are usually seen in the small intestine. Colonic and ileocaecal lesions are ulcerohypertrophic. Peritoneal disease may be of the following types: wet type with ascites, dry type with adhesions or fibrotic type with omental thickening and loculated ascites.[20] In the literature, the incidence of peritoneal TB is around 43%.[17]

Mycobacterium tuberculosis reaches the GIT via (i) haematogenous spread from the pulmonary focus in childhood, with later reactivation; (ii) ingestion of bacilli in sputum from active lung focus; (iii) direct spread from adjacent organs; and (iv) through lymphatics from infected nodes and fallopian tubes.[3] The earlier belief that most cases are due to reactivation of quiescent foci is being challenged with a recent study using DNA fingerprinting showing that 40% cases are due to reinfection.[21]

Majority of the patients (93%) in this study belonged to poor socio-economic class, 3rd decade and were females, as seen in other studies.[9,22–25] In developing countries, poor nutritional status, poverty, overcrowding, illiteracy and limited access to health care facilities have been implicated to contribute to TB, pulmonary as well as extra-pulmonary.[22,24] In comparison, in the developed world, TB accompanies HIV, ageing and transglobal migration.[3,26] The median age of the patients was 25 years (range 15–75 years), similar to study by Baloch et al.[9] (mean age of 35.6 years) while in contrast with Hu et al.[8] (57% patients older than 60 years).

The clinical presentation of abdominal TB can be acute, chronic and acute on chronic or an incidental finding on laparotomy for unrelated causes. The duration of symptoms ranged from 1 day to 2 years similar to other studies.[9–11] The most frequent symptoms were abdominal pain (97%), constipation (45.5%) and weight loss (36%) as in other studies.[8–11] Abdominal pain, varying from 70 to 95%,[9,10] can be either colicky due to luminal compromise, or dull and continuous when the mesenteric lymph nodes are involved. Mid abdominal colicky pain representing intermittent small bowel obstruction is seen in 90–100% of the patients.[26] Ulcerative type of intestinal TB often presents with chronic diarrhoea and malabsorption, while stricturous type presents with recurrent intestinal obstruction as obstipation, vomiting, abdominal distension and colicky pain abdomen. Other features were fever, abdominal distension, anorexia and weakness. The prevalence of such symptoms varies from 30 to 80% in the literature[12,27] with the most common being fever, ranging from 40 to 70%.[28]

Abdominal examination may reveal no abnormality or a doughy feel, ascites, lump abdomen or visible peristalsis with dilated bowel loops. A well-defined, firm, usually mobile mass is often (63%) palpable in the right lower quadrant of the abdomen. Associated lymphadenopathy may also give rise to one or more lumps, which may be mobile (mesenteric nodes) or fixed (para-aortic or illiac nodes).[15]

Paustian[16] in 1964 stated that one or more of the following four criteria must be fulfilled to diagnose abdominal TB: (i) histological evidence of tubercles with caseation necrosis; (ii) typical gross description of operative findings with mesenteric nodes histological evidence of TB; (iii) animal inoculation or culture of suspected tissue resulting in growth of *M. tuberculosis*; and (iv) histological demonstration of AFB in a lesion. Three diagnostic stages have been evaluated in the diagnosis of abdominal TB. The first two stages, i.e. clinical evaluation and radiologic examination (usg, barium studies and CT abdomen), give indirect evidence of the disease. The third stage includes the invasive techniques (laparoscopy) to achieve direct evidence. However, the diagnosis of TB has its own difficulties since it often mimics other diseases clinically[29] as well as radiologically.[18]

Features suggestive of active pulmonary TB on chest X-rays were found in 9 (20.5%) patients as in a study by Sharma and Bhatia,[20] compared to 64% patients in a study by Uygur-Bayramiçli et al.[10] Plain X-rays of abdomen revealed distended loops of bowel and air fluid level in 80% of the cases. It may also show enteroliths (proximal to obstruction.), evidence of obstruction (dilated bowel loops with multiple air fluid levels), ascites, perforation or intussusceptions. Pneumoperitoneum on X-rays is detected in only 50% of the cases.[30]

5.1. *USG*

Ultrasound is very useful for imaging peritoneal TB. It may show (i) intra-abdominal fluid – free or loculated; (ii) ''club sandwich'' sign due to interloop ascites; (iii) lymphadenopathy (mesenteric, peri-pancreatic, periportal and para-aortic groups); (iv) bowel wall thickening (15 mm or more),[19] especially involving ileocaecal region; and (v) pseudokidney sign suggests involvement of the ileocaecal region, which is pulled up to a sub-hepatic position.[6] Mesenteric thickening, with enhanced mesenteric echogenicity along with lymphadenopathy, is the characteristic sonographic feature of early abdominal TB.[17,19] Abdominal USG performed on 29 patients showed ascites in 19 (43%) patients, abdominal mass in 13 (29.5%) patients and lymphadenopathy in 12 (29.5%) patients compared to ascites in 79% and enlarged lymph nodes in 35% of the patients by Uygur-Bayramiçli et al.[10]

5.2. *Barium studies*

Many studies[9–11] have documented barium meal follow through (BMFT) as the most used diagnostic investigation, demonstrating bowel lesions such as multiple strictures and distended caecum or terminal ileum in 80–90% of the cases. Other features of TB on barium study are rapid intestinal transit; barium hypersegmentation, precipitation, flocculation and dilution; thickened intestinal folds; luminal stenosis with smooth but stiff contours, multiple strictures with segmental

dilatation of bowel loops or/and fixity and matting of bowel loops.[6] In this study, BMFT helped diagnose 18 (41%) patients with suspected intestinal TB. Findings included dilated bowel loops, strictures, deformed and pulled up caecum and bowel wall thickening. The most common area of involvement in this study was distal ileum (51%) similar to the study by Baloch et al.[9]

Barium enema may be useful for ileocaecal disease. It may show[32] (i) early spasm and oedema of the ileocaecal valve, thickening of ileocaecal valve and/or wide gaping of the valve with narrowing of the terminal ileum (''Fleischner'' or ''inverted umbrella sign'')[33]; (ii) Fold thickening and contour irregularity of the terminal ileum; (iii) ''Conical caecum'', shrunken in size and pulled out of the iliac fossa[32]; (iv) loss of normal ileocaecal angle and dilated terminal ileum with retracted, fibrosed caecum (''goose neck deformity''); (v) ''Purse string stenosis'' – localized stenosis opposite the ileocaecal valve with a rounded off smooth caecum and a dilated terminal ileum; (vi) ''Stierlin's sign'' – narrowing of the terminal ileum with rapid empyting into a shortened, rigid or obliterated caecum; (vii) ''String sign.''

5.3. *CT scan*

The findings on CT suggestive of abdominal TB are ascites, thickened peritoneum and enhancing peritoneal nodules, circumferential caecal and terminal ileal thickening with proximal dilatation, adherent loops, regional nodes and mesenteric thickening. Tubercular ascitic fluid is of high attenuation value (25–45 HU)[34] due to its high protein content. Mesenteric involvement (patchy or diffuse increase in density, mesenteric stranding and stellate appearance) and presence of macronodules (>5 mm in diameter), omental cake appearance, thin omental line (fibrous wall covering the infiltrated omentum), peritoneal or extra-peritoneal masses with low-density centres and calcification and splenomegaly or splenic calcification have been seen more commonly with peritoneal tuberculous.[35] In TB, the mesenteric, mesenteric root, celiac, porta hepatis and peri-pancreatic nodes are characteristically involved, reflecting the lymphatic drainage of the small bowel.[36] Lymph nodes may show four patterns of contrast enhancement computed tomography – peripheral rim, non-homogenous, homogenous enhancement and homogenous non-enhancement.[37] Complications of perforation, abscess and obstruction are also seen. Thus abdominal CT findings appear to provide more objective data about the disease than other radiological methods.[10]

Abdominal CT was performed on 7 of these patients who presented with abnormal findings in USG. Ascites in 5 (73%), mesenteric thickening in 4 (57%), iloeceacal thickening in 4 (57%), abdominal lymphadenopathy in 5 (73%) and omental involvement in 3 (42.8%) patients were observed as important CT findings. Only one (14%) patient had completely normal CT examination.

5.4. *Ascitic fluid examination*

Ascitic fluid examination reveals straw coloured fluid with high protein (>3 g/dl), serum ascitis albumin gradient <1.1 g/dl, cells >1000/mm^3 with predominantly lymphocytes (>70%)[3] and ADA levels >33 U/l.[10,39] AFB stain was positive in <3% of the cases. A positive culture is obtained in <20% of the cases, and it takes 6–8 weeks for the mycobacterial colonies to appear. Carera et al.[33] in their study achieved 83% culture positivity on culturing 1 litre of ascitic fluid after centrifugation.

5.5. *Laparoscopic findings*

Laparoscopy is another useful investigation, especially in doubtful cases. It can help diagnose up to 87–92% cases of peritoneal TB.[38] The findings may be as follows: (i) thickened peritoneum with 4–5 mm tubercles on parietal peritoneum, omentum, liver or spleen; (ii) thickened peritoneum without tubercles and (iii) fibro-adhesive peritonitis. Bhargawa et al.[26] in their study of 87 patients found that gross appearance is 95% accurate, compared to histology or culture. In this series, no laparoscopy was performed due to logistic issues.

5.6. *Immunological tests*

The conventional techniques used in diagnosing TB like AFB smear microscopy lack sensitivity (53.3%) and the gold standard (specificity was 100%) culture test takes time. Since abdominal TB is paucibacillary, the yield of organisms is low (under 50%)[14] and characteristic histological changes are taken as diagnostic. Also getting a tissue for histology may not always be possible. Tuberculin test may be positive but cannot differentiate between active and inactive disease. In comparison, multiplex polymerase chain reaction (PCR) test has a much higher sensitivity of 93.7% and a specificity of 97.3% in AFB smear positive samples.[11]

5.7. *Laparotomy*

In the absence of any positive laboratory and radiologic tests, the diagnosis is often established by obtaining a surgical specimen. Nevertheless, exploratory laparotomy has been suggested in cases suspected of abdominal carcinomatosis without definite diagnosis.[41] Tubercular perforations are usually single and proximal to a stricture.[14]

5.8. *Empirical*

In the present series, in 3 (7%) patients with suggestive history but negative workup, therapeutic trial of anti-TB drugs therapy (ATT) was the basis of diagnosis. In the literature, up to 40% of the patients are diagnosed after therapeutic trial of anti-TB drugs.[14]

5.9. *Pathology*

The gross pathology is characterized by transverse ulcers, fibrosis, thickening and stricturing of the bowel wall, enlarged and matted mesenteric lymph nodes, omental thickening and peritoneal tubercles.[6] Tuberculous granulomas are initially formed in the mucosa or the Peyer's patches in the bowel, often just beneath the ulcer bed, mainly in the sub-mucosa. Characteristic granulomas may be seen only in the mesenteric lymph nodes, especially in the patients who have taken anti-tubercular therapy. The reverse, i.e., the presence of

granulomas in the intestine and no granulomas in the draining lymph nodes is rare.[42] Tubercular ulcers are relatively superficial, single or multiple, do not penetrate beyond the muscularis and intervening mucosa is usually uninvolved.[43] Cicatricial healing of these ulcers and occlusive arterial changes contribute to strictures.[14] In long-standing lesions, there may be variable degree of fibrosis of the bowel wall, which extends from submucosa into the muscularis. As already described by Hoon et al., lesions in bowel may be ulcerative, ulcerohyperplastic and hyperplastic varieties.[42] The peritoneum is thick, hyperaemic, with loss of lustre and is studded with tubercles.[14]

Common histological features on biopsy specimen were the presence of non-caseating granuloma in 12 (63%) with central caseation in 2 (9.5%) patients and inflammation only in 9 (42.7%) compared to 14 (68%) patients; central caseation was in 25% cases and chronic inflammatory infiltration in 7% of the patients.[10]

5.10. *Management*

The recommended treatment for abdominal TB is anti-TB therapy for a minimum of 6 months.[7] A randomized comparison of 6 months chemotherapy with 12 months course by Balasubramanian et al.[44] at Chennai demonstrated cure rate of 99% and 94%, respectively. Surgical intervention may also be required to establish the diagnosis if medical treatment fails or to treat complications of abdominal TB.[7] In the present study, most of the patients required urgent surgical intervention, i.e. 56.4% in comparison to 80% of the patients in a study by Baloch et al.[9] Some reports suggest successful treatment of obstructing intestinal lesions with ATT alone.[45] In a study by Uygur-Bayramiçli et al.,[10] 76% of the patients responded to medical treatment alone while 17% of the patients required additional surgical intervention. Though patients usually report improvement in systemic symptoms in a few weeks, relief of intestinal symptoms may require a much longer period. Strictures are treated by strictureplasty[46] or resection anastomosis, perforations by ileostomy or resection and anastomosis.[9] Predictors of need for surgery were long strictures (>12 cm) and multiple areas of involvement.[47] Three patients died during the course of anti-tuberculous therapy. The major cause of death in these patients was due to concomitant sepsis and septic shock instead of TB itself. The overall crude mortality rate was 7.6% compared to 21.4%[8] and 14.8% in the study by Chen et al.[41] A possible reason for higher mortality among operated patients may be due to late presentation and pre-existing complications like malnutrition, perforation and sepsis. Advanced age, delay in initiating therapy and underlying cirrhosis have been associated with higher mortality rates.[48,49]

5.11. *Limitations of the study*

One of the limitations in this study is the retrospective nature of the data set, but it does not interfere with the objective of the study. Secondly, all tests were not done in every patient because each test is not indicated in every case. The other limitation was inability to confirm the diagnosis either by culture of AFB or PCR in all cases. In conclusion, abdominal TB is a complex disease and has diverse symptomatology that is non-specific. Tissue diagnosis is mandatory for appropriate management but it is invasive, expensive and unfortunately not always conclusive either. A high index of clinical suspicion is required along with the help of multiple adjuvant diagnostic tools for diagnosis of ATB. Until the time when we have a specific test for diagnosis of abdominal TB, this remains a challenge for physician.

6. Conclusion

The findings of the present study confirm earlier reports on prevalence of abdominal TB among lower socio-economic and female population, the difficulties of diagnosis including non-specific clinical features, unhelpful laboratory tests, negative results with tuberculin skin tests and Ziehl–Neelsen staining and false-negative ultrasound, CT scans, bacteriological test and histopathological test. Thus, no single test is adequate for diagnosis of abdominal TB in all patients.

In conclusion, extreme vigilance in the patients with unexplained abdominal conditions is the key to the successful diagnosis of abdominal TB. Early diagnosis, early anti-tuberculous therapy and surgical treatment of the associated complications are essential for survival.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Sood R. Diagnosis of abdominal tuberculosis: role of imaging. *J Indian Acad Clin Med*. 2001;2(3):170–176.
2. World Health Organisation. *Global Tuberculosis Report*. 2014.
3. Horvath KD, Whelan RL. Intestinal tuberculosis: return of an old disease. *Am J Gastroenterol*. 1998;93:692–696.
4. Kahana LM. The modern face of tuberculosis. *Can J Surg*. 1986;29:393–394.
5. Wang HS, Chen WS, Su WJ, et al. The changing pattern of intestinal tuberculosis: 30 years' experience. *Int J Tuberc Lung Dis*. 1998;2:569–574.
6. Peda Veerraju E. Abdominal tuberculosis. In: Satya Sri S, ed. In: *Textbook of Pulmonary and Extrapulmonary Tuberculosis* 3rd ed. New Delhi: Interprint; 1998:250–252.
7. Lazarus AA, Thilagar B. Abdominal tuberculosis. *Dis Mon*. 2007;53:32–38.
8. Hu M-L, Lee C-H, Kuo C-M, et al. Abdominal tuberculosis: analysis of clinical features and outcome of adult patients in southern Taiwan. *Chang Gung Med J*. 2009;32(5):509–515.
9. Baloch NA, Anees S, Baber M, et al. Abdominal tuberculosis: a review of 68 cases. *J Surg Pak*. 2002;7:12–14.
10. Uygur-Bayramiçli O, Dabak G, Dabak R. A clinical dilemma: abdominal tuberculosis. *World J Gastroenterol*. 2003;9(5):1098–1101.
11. Chong VH. Differences in patient profiles of abdominal and pulmonary tuberculosis: a comparative study. *Med J Malays*. 2011;66(4):318–321.
12. Ramesh J, Banait GS, Ormerod LP. Abdominal tuberculosis in a district general hospital: a retrospective review of 86 cases. *QJM*. 2008;101:189–195.

13. Chou CH, Ho MW, Ho CM, et al. Abdominal tuberculosis in adult: 10-year experience in a teaching hospital in central Taiwan. *J Microbiol Immunol Infect.* 2010;43:395–400.
14. Kapoor VK. Abdominal tuberculosis. *Postgrad Med J.* 1998;74:459–467.
15. Bhansali SK. Abdominal tuberculosis. Experiences with 300 cases. *Am J Gastroenterol.* 1977;67:324–337.
16. Paustian FF, Tuberculosis of the intestine. 2nd ed. Bockus HL, ed. *Gastroenterology*. vol. 11. Philadelphia: W.B. Saunders, Co.; 1964: 311.
17. Kedar RP, Shah PP, Shivde RS, et al. Sonographic findings in gastrointestinal and peritoneal tuberculosis. *Clin Radiol.* 1994;49:24–29.
18. Talwar BS, Talwar R, Chowdhary B, et al. Abdominal tuberculosis in children: an Indian experience. *J Trop Pediatr.* 2000;46:368–370.
19. Jain R, Sawhney S, Bhargava DK, et al. Diagnosis of abdominal tuberculosis: sonographic findings in patients with early disease. *AJR.* 1995;165:1391–1395.
20. Sharma MP, Bhatia V. Abdominal tuberculosis. *Indian J Med Res.* 2004;120:305–315.
21. Vij JC, Malhotra V, Choudhary V, et al. A clinicopathological study of abdominal tuberculosis. *Indian J Tuberc.* 1992;39: 213–220.
22. Khan R, Abid S, Jafri W, et al. Diagnostic dilemma of abdominal tuberculosis in non-HIV patients: an ongoing challenge for physicians. *World J Gastroenterol.* 2006;12 (39):6371–6375.
23. Shehzad R, Osman L, Abid KJ, et al. Epidemiology, clinical presentation and site of involvement in abdominal tuberculosis – a retrospective study. *Ann King Edward Med Coll.* 1999;5:228–229.
24. Ayaz M, Rathore MA, Afzal MF, et al. Changing trends in abdominal tuberculosis. *Pak J Surg.* 1996;12:186–187.
25. Baloch N, Tufail M, Durrani K, et al. Abdominal tuberculosis: a varied presentation. *Pak J Med Res.* 1993;32:259–262.
26. Bhargawa DK, Tandon HD, Chawla TC, et al. Diagnosis of ileocecal and colonic tuberculosis by colonoscopy. *Gastrointest Endosc.* 1985;31:68–70.
27. Tandon RK, Sarin SK, Bose SL, et al. A clinico-radiological reappraisal of intestinal tuberculosischanging profile. *Gastroenterol Jpn.* 1986;21:17–22.
28. Muneef MA, Memish Z, Mahmoud SA, et al. Tuberculosis in the belly: a review of forty-six cases involving the gastrointestinal tract and peritoneum. *Scand J Gastroenterol.* 2001;36:528–532.
29. Misra SP, Misra V, Dwivedi M, et al. Colonic tuberculosis: clinical features, endoscopic appearance and management. *J Gastroenterol Hepatol.* 1999;14:723–729.
30. Ranjan P, Ghoshal UC, Aggarwal R, et al. Etiological spectrum spsoradic malabsorption syndrome in Northern Indian adults at a tertiary hospital. *Indian J Gastreoenterol.* 2004;23:94–98.
32. Kapoor VK, Chattopadhyay TK, Sharma LK. Radiology of abdominal tuberculosis. *Australas Radiol.* 1988;32: 365–367.
33. Carera GF, Young S, Lewicki AM. Intestinal tuberculosis. *Gastrointest Radiol.* 1976;1:147–155.
34. Suri S, Gupta S, Suri R. Computed tomography in abdominal tuberculosis – pictorial review. *Br J Radiol.* 1999;72:92–98.
35. Ha HK, Jung HL, Lee MS, et al. CT differentiation of tuberculous peritonitis and peritoneal carcinomatosis. *AJR.* 1996;167:743–748.
36. Gulati MS, Sarma D, Paul SB. CT appearances in abdominal tuberculosis. A pictorial assay. *Clin Imaging.* 1999;23:51–59.
37. Pombo F, Rodriguez E, Mato J, et al. Patterns of contrast enhancement of tuberculous lymph nodes demonstrated by computed tomography. *Clin Radiol.* 1992;46:13–17.
38. Sanai FM, Bzeizi KI. Systematic review: tuberculous peritonitis – presenting features, diagnostic strategies and treatment. *Aliment Pharmacol Ther.* 2005;22:685–700.
39. Dwivedi M, Misra SP, Misra V, et al. Value of adenosine deaminase estimation in the diagnosis of tubercuous ascites. *Am J Gastroenterol.* 1990;85:1123–1125.
41. Chen YM, Lee PY, Perng RP. Abdominal tuberculosis in Taiwan: a report from Veterans' General Hospital, Taipei. *Tuber Lung Dis.* 1995;76:35–38.
42. Hoon JR, Dockerty MB, Pemberton J. Ileocaecal tuberculosis including a comparison of this disease with non-specific regional enterocolitis and noncaseous tuberculated enterocolitis. *Int Abstr Surg.* 1950;91:417–440.
43. Tandon HD, Prakash A. Pathology of intestinal tuberculosis and its distinction from Crohn's disease. *Gut.* 1972;13: 260–269.
44. Balasubramanian R, Nagarajan M, Balambal R, et al. Randomised controlled clinical trial of short course chemotherapy in abdominal tuberculosis: a five-year report. *Int J Tuberc Lung Dis.* 1997;1:44–51.
45. Balasubramanian R, Ramachandran R, Joseph P, et al. Interim results of a clinical study of abdominal tuberculosis. *Indian J Tuberc.* 1989;36:117–121.
46. Pujari BD. Modified surgical procedures in intestinal tuberculosis. *Br J Surg.* 1979;66:180–181.
47. Anand BS, Nanda R, Sachdev GK. Response of tuberculous stricture to antituberculous treatment. *Gut.* 1988;29:62–69.
48. Mehta JB, Dutt A, Harvill L, et al. Epidemiology of extrapulmonary tuberculosis. A comparative analysis with pre-AIDS era. *Chest.* 1991;99:1134–1138.
49. Chow KM, Chow VC, Hung LC, et al. Tuberculous peritonitis-associated mortality is high among patients waiting for the results of mycobacterial cultures of ascitic fluid samples. *Clin Infect Dis.* 2002;35:409–413.

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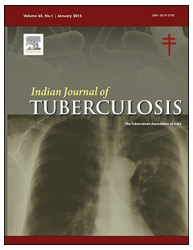

Original Article

Periodontal status of tuberculosis patients – Is there a two-way link?

Anamika Sharma [a], *Harshita Garg* [b,*], *Shivi Khattri* [a], *Shatakshi Sharma* [b]

[a] *Department of Periodontology, Subharti Dental College and Hospital, NH-58, Subhartipuram, Delhi-Haridwar Bypass Road, Meerut, India*
[b] *Postgraduate Student, Department of Periodontology, Subharti Dental College and Hospital, NH-58, Subhartipuram, Delhi-Haridwar Bypass Road, Meerut, India*

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ABSTRACT

Background: The influence of systemic disorders on periodontal tissues is well established. Amongst various chronic debilitating diseases, tuberculosis (TB) is one of the major health problems in most developing countries. Although it has a definite affinity for the lungs, it can affect any part of the body including the oral cavity. TB and periodontitis are the two distinct disease processes. But environmental and biological factors play a key role in etiopathogenesis of both the diseases. These factors alter tissue microenvironment leading to cascade of untoward events.

Aim: To assess and compare the periodontal status of TB patients with that of non-TB subjects.

Materials and methods: 50 subjects were recruited and divided into 2 groups. Group A consisted of subjects suffering from TB serving as Test group while group B included non-TB subjects serving as Control group.

Statistical analysis: Unpaired *t*-test was used.

Results and conclusion: Statistically significant difference in probing pocket depth and bleeding on probing was found between groups A and B, with the difference being higher in group A subjects, thus concluding that periodontal status might be linked with TB.

1. Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis, is a chronic infectious granulomatous disease that is communicable and usually associated with foci of diseases elsewhere in the body. It is described as a major health problem across the world and is considered as the king of diseases in Vedas and has been mentioned in 600 BC by Sushruta and Chakra.[1]

Over 95% of TB deaths occurs in lower and middle income countries, and it is a major cause of death among women aged between 15 and 44 years. In 2014, an estimated 1 million children became ill with TB and 140,000 children died of TB.[2]

Depending upon the organ system involved, it is classified as pulmonary or extra-pulmonary, with pulmonary TB being the most common form. However, the disease can also occur in the skin, lymph nodes, bones, kidneys and in the oral cavity.[3]

* *Corresponding author.*
E-mail address: drharshi1518@gmail.com (H. Garg).

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Due to the introduction of effective chemotherapy, oral tuberculous lesions account for less than one percent of extra-pulmonary cases. It can be primary or secondary. Primary lesions are extremely rare. It generally occurs in younger adults and mostly involves gingiva. In contrast, secondary oral TB is more common, accounts for approximately 0.005–1.5% of the total cases, and is seen mostly in older adults.[4] Intra-oral sites frequently involved are tongue, palate, lips, alveolar mucosa and jaw bones.[5] TB in the oro-facial region may manifest in various forms like tuberculous ulcer and tuberculous gingivitis. This secondary infection of oral tissues can result from either haematogenous or lymphatic spread or from auto-inoculation by the infected sputum.[6]

Systemic factors modify periodontitis principally through their effects on normal immune and inflammatory mechanisms, and thus periodontal disease has been associated with a number of systemic diseases. Frequent focal and prolonged remission with reduced exacerbation has been observed in periodontitis patients suffering from pulmonary TB compared with patients without TB. In a study,[7] it was established that focal pulmonary inflammation causes infectious excessive load violations in microbiocenosis and activation of pro-inflammatory cytokines (Interleukin 1, 3 and Tumor necrosis factor-alpha (TNF-α)) in the fluid of periodontal pockets, thus increasing the frequency and prolonging the exacerbation of periodontitis.

Therefore, this study was conducted to assess the various clinical parameters of periodontal health among the patients who reported at the TB & Chest Department, Subharti Medical Hospital and comparing them with non-TB subjects.

2. Materials and methods

This cross-sectional study involved the joint collaboration of the Department of General medicine, Subharti Medical College and Hospital and Department of Periodontology, Subharti Dental College and Hospital, Swami Vivekananda Subharti University (SVSU), Meerut, Uttar Pradesh. The study was approved by the institutional review board, SVSU. The study population included a total of 50 subjects from whom written informed consent was obtained, and they were divided into 2 groups. Group A involved 35 subjects suffering from TB serving as Test group and group B included 15 systemically healthy subjects serving as Control.

The subjects excluded from the study were patients on corticosteroids within 4 weeks prior to the application of the study; subjects who had undergone any surgical intervention 6 months prior to the study; smoking or use of any tobacco products; alcohol or drug abuse as defined by criteria in Diagnostic and Statistical Manual of Mental Disorders[8]; and pregnant or lactating females.

3. Clinical examination

1. A detailed medical and dental history was recorded.
2. All the enrolled participants underwent detailed oral examination.
3. The severity of periodontal disease was clinically measured using the following indices – Plaque index (PI), pocket probing depth (PPD), clinical attachment level (CAL) and oral hygiene index simplified (OHIS), gingival index (GI), bleeding on probing (BOP) and missing teeth.
4. CAL and PPD were measured using UNC-15 probe.
5. All the clinical measurements were recorded by a single trained examiner to avoid inter-examiner bias.

4. Results

Periodontal status of a total of 50 individuals was examined and the data obtained were tabulated and subjected to statistical analysis. The values were represented in percentage (%) and mean ± standard deviation. The significance between two means (group I and II) was tested using the Student's *t*-test. *P* values <0.005 was considered statistically significant.

The mean of GI, OHIS, PPD, CAL, BOP and number of missing teeth among the two groups are summarised in Table 1 and Fig. 1. In both the groups (group I and group II), the difference in mean values of CAL, GI and OHIS were comparable and not statistically significant.

Inter-group comparison of mean PI and missing teeth showed no statistical significant difference. However, significant positive correlation was found in PPD (3.08 ± 0.466 and 2.56 ± 0.493 in group I and II, respectively) (Fig. 2) and BOP (0.763 ± 0.149 and 0.642 ± 0.222 in group I and II, respectively) (Fig. 3) with *P* value ≤0.005 (Table 1).

5. Discussion

Influence of systemic conditions on the periodontium has long been recognised and supported by scientific evidence.[1] These

Table 1 – Comparison of clinical variables between different study groups.

Variables	Group A Mean value ± SD	Group B Mean value ± SD	*P* value
Gingival index (GI)	1.60 ± 0.39	1.62 ± 0.44	0.901
OHIS	3.03 ± 0.898	2.54 ± 0.946	0.101
Probing depth (PD) (mm)	3.08 ± 0.466	2.56 ± 0.493	0.001
Plaque index (PI)	1.828 ± 0.534	1.584 ± 0.504	0.148
Missing teeth	4.6 ± 0.689	2.07 ± 0.463	0.018
CAL (mm)	3.88 ± 0.772	3.44 ± 0.831	0.089
BOP (%)	0.763 ± 0.149	0.642 ± 0.222	0.001

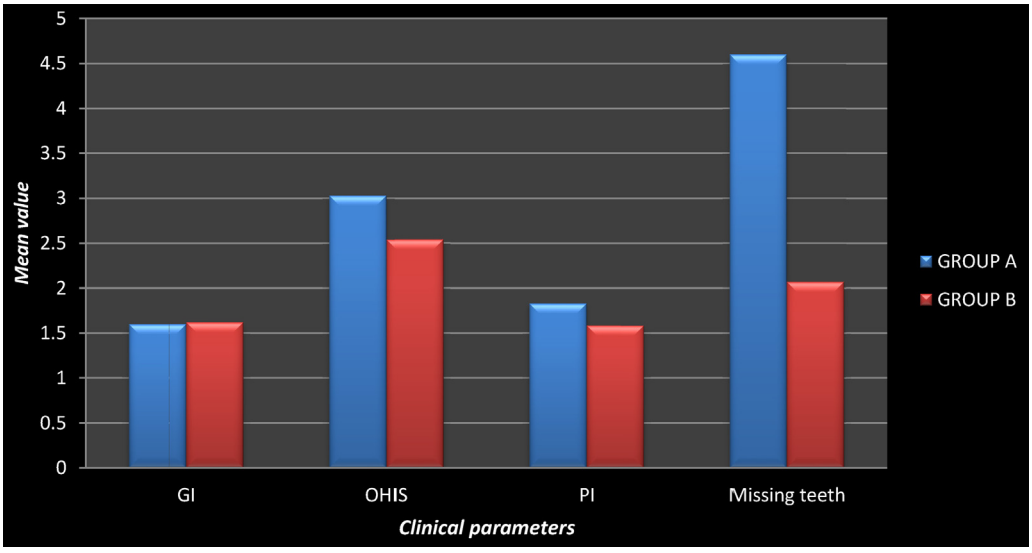

Fig. 1 – Comparison of variables (GI, OHIS, PI and missing teeth) in group I and group II.

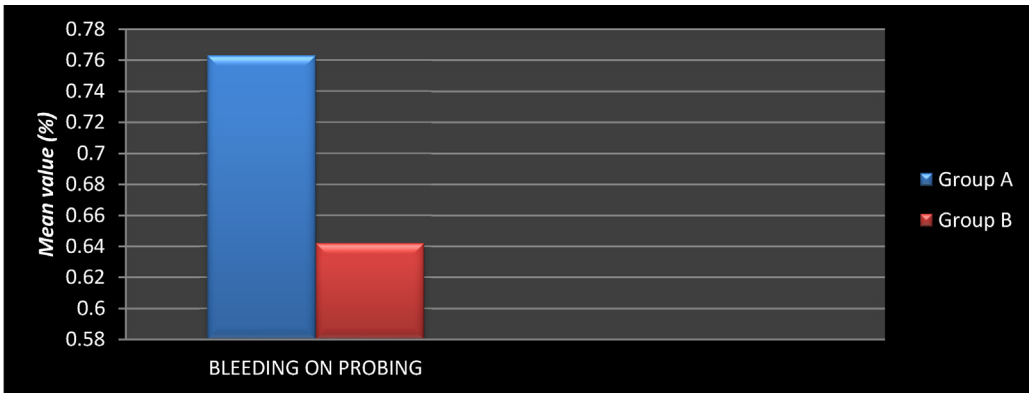

Fig. 2 – Inter-group comparison of bleeding on probing (BOP).

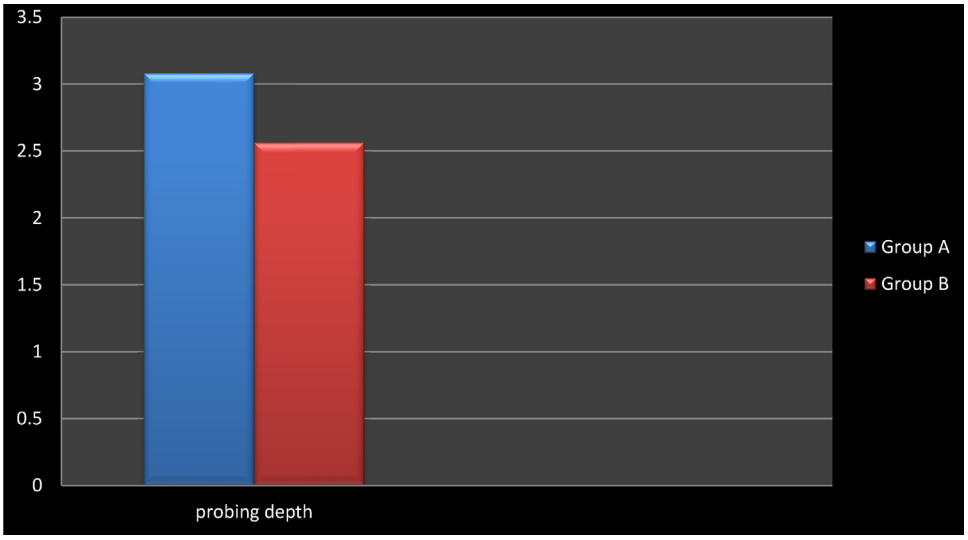

Fig. 3 – Inter-group comparison of probing depth.

have been attributable to the inflammatory nature of periodontitis. Periodontal disease not only affects periodontal tissues, but also exerts systemic effect by altering homeostatic mechanisms of the human body, including lipid peroxidation process, microcirculation, immune mechanisms and cytokine network.[9,10]

A number of studies has been proposed earlier showing the association of periodontal disease with various systemic conditions such as diabetes mellitus,[11,12] coronary artery diseases,[13,14] stroke[15] and respiratory diseases.[16] However, studies showing the link between TB and periodontitis are very few.

This study was done to assess the periodontal status of the subjects with TB. It was found that these subjects had a worsened periodontal status when compared to the non-TB subjects. The reason for this might be due to lack of maintenance of proper oral hygiene and less access to dental care due to poor systemic health of such individuals.

Some studies[7,17–19] showed a positive correlation between TB and periodontitis. According to these studies, endogenous intoxication and an imbalance in the lipid peroxidation system occurs in the patients with focal pulmonary TB.[7] These are among the main factors in the development of more frequent and prolonged recurrence of periodontitis leading to increase in periodontal pockets along with worsening of local inflammatory response and activation of pro-inflammatory cytokines.[17] Similarly, a study was conducted in which the patients suffering from TB received immuno-modulators and significant reduction was found in the local inflammation and microbial load in periodontal pocket, thus showing that there might be a link between TB and periodontal disease.[18] A study by Aluru et al.[19] is in accordance with this study, which concluded that TB-infected patients are much prone to periodontal infections, which might be due to their immuno-compromised condition. On the other hand, few studies[20,21] are in disagreement with the present finding where no significant difference was observed in periodontal status and duration of illness and it was concluded that TB status of the patient did not influence the periodontal status.

6. Conclusion

It can be concluded that TB might influence the periodontal status of individuals by depressing the immune mechanism, and thus may affect the periodontium negatively.

7. Limitations and future directions

This study paves a way for future studies that may investigate the more definitive mechanism linking periodontitis and TB. In addition, selective sampling of subjects included may not truly represent the trends in the community as a whole. Therefore, larger sample size is required for more direct correlation.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Hasan S, Khan AM. *Proceedings of the World Medical Conference; Tuberculosis – A Common Disease with Uncommon Oral Features Report of Two Cases with Detailed Review of Literature*. 2011; 156–166. ISBN: 978-1-61804-036-7.
2. Palakuru SK, Lakshman VK, Bhat KG. Microbiological analysis of oral samples for detection of *Mycobacterium tuberculosis* by nested polymerase chain reaction in tuberculosis patients with periodontitis. *Dent Res J*. 2012;9 (6):688–693.
3. Topazian RG, Goldberg MH. *Oral and Maxillofacial Infections*. 2nd ed. WB Saunders Co.; 1987:413.
4. Mani NJ. Tuberculosis initially diagnosed by asymptomatic oral lesions. Report of three cases. *J Oral Med*. 1985;40: 39–42.
5. Prabhu SR, Sengupta SK. Bacterial infections due to mycobacteria A. tuberculosis. In: Prabhu SR, Wilson DF, Daftary DK, Johnson NW, eds. In: *Oral Diseases in the Tropics*. Oxford Medical Publications, Oxford University Press; 1993 :195–202.
6. Greenberg MS, Glick M. *Burkitts Oral Medicine Diagnosis and Treatment*. 10th ed. New York: BC Decker Inc.; 2003.
7. Alexandrova E. *The Effectiveness of Treatment of Periodontitis in Patients with Focal Pulmonary Tuberculosis*. DisserCat-Scientific Electronic Library; 2014. Available from: Google% 20Translate.html.
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Available from http://dsm.psychiatryonline.org/doi/book/10.1176/appi.books.9780890425596.
9. Sorokin. The AA status of oral health in patients with acute enteric infections/AA Sorokin: Materials II Annual All-Russian Congress on Infectious Diseases, Moscow, 29–31 March 2010, g.-S. 300-301.
10. Loos BG. Systemic markers of inflammation in periodontitis. *J Periodontol*. 2005;76(11 suppl):2106–2115.
11. Teng YT, Taylor GW, Scannapieco F, et al. Periodontal health and systemic disorders. *J Can Dent Assoc*. 2002;68:188–192.
12. Bluher M, Fasshauer M, Tonjes A, Kratzsch J, Schon MR, Paschke R. Association of interleukin-6, C-reactive protein, interleukin-10 and adiponectin plasma concentrations with measures of obesity, insulin sensitivity and glucose metabolism. *Exp Clin Endocrinol Diabetes*. 2005;113:534–537.
13. Hung HC, Willett W, Merchant A, Rosner BA, Acherio A, Joshipura KJ. Oral health and peripheral arterial disease. *Circulation*. 2003;107:1152–1157.
14. Elter JR, Champagne CME, Offenbacher S, Beck JD. Relationship of periodontal disease and tooth loss to prevalence of coronary heart disease. *J Periodontol*. 2004;75:782–790.
15. Sfyroeras GS, Roussas N, Saleptsis VG, Argyriou C, Giannoukas AD. Association between periodontal disease and stroke. *J Vasc Surg*. 2012;55:1178–1184.
16. Prasanna SJ. Causal relationship between periodontitis and chronic obstructive pulmonary disease. *J Indian Soc Periodontol*. 2011;15(4):359–365.
17. Sharma A, Nagtilak S, Khattak BP, Singh G, Bano T. Alteration in salivary proteins following non-surgical periodontal therapy in generalised chronic periodontitis subjects. *Int J Pharm Biol Sci*. 2015;6(1):306–314.
18. Martinez AB, Mattila R, Font RG, Meurman JH. Immunomodulatory drugs: oral and systemic adverse effects. *Med Oral Patol Oral Cir Buccal*. 2014;19(1):24–31.
19. Aluru S, Ismail SM, Kishore Kumar A, Chiranjeevi T, Bhaskar M, Rao P. Enumeration of anerobic periodontal pathogen from tuberculosis and chronic periodontitis patients by

paper points and curettes: CFU based evaluation. *IJOMAS*. 2014;1(1).
20. Javali MA, Patil V, Ayesha H. Periodontal disease as the initial oral manifestation of abdominal tuberculosis. *Dent Res J*. 2012;9(5):634–637.
21. Anjum S, Reddy PP, Monica M, Praveen BH. Oral health status of the patients with tuberculosis at the Govt TB and chest diseases Hospital, Andhra Pradesh, India. *Int J Dent Clin*. 2010;2(4):12–15.

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Original Article

Pattern of socio-economic and health aspects among TB patients and controls

A.K. Kapoor [a,*], Vijit Deepani [b], Meenal Dhall [c], Satwanti Kapoor [a]

[a] Professor, Department of Anthropology, University of Delhi, Delhi 110007, India
[b] UGC-NET JRF, Department of Anthropology, University of Delhi, Delhi 110007, India
[c] Assistant Professor, Department of Anthropology, University of Delhi, Delhi 110007, India

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ABSTRACT

Background: Socio-economic and health-related factors have a significant impact on tuberculosis (TB) incidence among population residing in resource-scare settings.
Objective: To evaluate the pattern of socio-economic and health-related factors among TB patients and control in Delhi, India.
Methods: The present cross-sectional study was performed among 893 TB patients (or cases) and 333 healthy disease-free controls. The data for the present study was obtained from several district TB centres in north, west and south Delhi. The collected data was edited, coded and statistical analysed with the help of SPSS 20.0 version.
Results: Illiteracy and primary education were significant risk factors being associated with a TB. Rented housing condition had an odds ratio (OR) of 1.4 (95% confidence interval [CI]: 1.09–1.89) compared to owned housing condition. 3–5 individuals per room were 3 times more likely to be associated with a case of TB (95% CI: 2.49–4.41). Migrant individuals were 13 times more likely to be associated with a case of TB (95% CI: 8.77–19.78) in comparison to settled population. Daily consumption of non-vegetarian food also significantly contributed to case of TB with an OR of 3.4 (95% CI: 2.51–4.72). Loss of appetite and family TB served as significant health-related factors associated with TB risk.
Conclusion: Lower educational status, rented household, individuals per room (as a measure of overcrowding) and migratory status served as prominent risk factors for TB disease. Preference and frequency of non-vegetarian food being consumed, night sweating, weight loss, loss of appetite, earlier TB and family TB were principle health-related risk factors associated with TB disease.

1. Introduction

Tuberculosis (TB) is a major health problem and leading cause of mortality, primarily in countries characterised with poor socio-economic backgrounds[1] and resource scarcity. Though India is the second-most populous country in the world, one fourth of the global incident TB cases occur in India annually.[2]

Socio-economic determinants influence individuals' health behaviours, access to healthcare resources, degree of exposure

* *Corresponding author*. Tel.: +91 9910544142.
E-mail address: anupkapoor46@rediffmail.com (A.K. Kapoor).
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to certain diseases and environmental factors.[3] Prevalence of TB is determined by individuals' income status, and has a negative impact on human and economic productivity.[4]

Rapid urbanisation gives birth to ideal conditions for TB epidemics to prosper, unless guarded by good urban planning, social reforms, environmental protection and a well-coordinated urban health care system.[5] TB incidence is generally higher in urban settings in comparison to rural areas.[6] Exposure to some TB risk factors such as smoking, alcohol abuse, unsafe sex and unhealthy diet may maximise when absolute poverty declines at the same time as rapid socio-cultural transitions lead to altered health behaviour patterns.[5] The potential increment in risk increase due to assemblage of TB risk factors is often further enhanced by fragmented health care systems in urban areas, and poor health care access among urban slum dwellers.[6]

The drivers of the epidemic and social determinants of TB need to be addressed to reduce TB incidence.[7] These comprise co-morbidities (such as human immunodeficiency virus [HIV] and diabetes), substance use (such as alcohol and tobacco) and the social and economic conditions that impel both the course of the TB epidemic and exposure to these risk factors.[7]

The aim of the present study was to evaluate the pattern of socio-economic and health-related factors among TB patients and control in Delhi, India.

2. Materials and methods

2.1. Study design and data collection

The present study was a cross-sectional study. It was conducted among adult TB patients (which included both pulmonary TB [PTB] and extra-pulmonary TB [EPTB] cases) and healthy disease-free control subjects from Delhi, India. Data of TB patients was obtained from 12 TB district centres and hospitals of north, west and south Delhi.

2.2. Participants

The study comprised of 983 adult TB patients (which included 632 PTB cases and 351 EPTB cases) and 333 healthy disease-free control subjects. The age of the subjects ranged from 15 to 80 years. Controls were healthy subjects devoid of the disease history. Controls were matched with cases for age. The TB cases selected were patients who had been taking TB medicine on regular basis as confirmed from doctors at their respective TB centres. The subjects were unrelated to each other. The present study was performed on heterogeneous population.

2.3. Selection criteria

Only those subjects who took their medicines on regular basis as confirmed by the doctors and/or health workers and also followed the dietary norms as advised by doctors were selected for the present study. Only new cases of PTB were taken. None of the HIV +ve patients were retained in the sample. Exclusion criteria for the controls were as follows: previous anti-TB treatment, any form of disease and HIV +ve as confirmed by the doctors.

2.4. Ethical consent

A well-informed written consent from the subjects for their willingness to participate in the present study was taken before the collection of data. The study was approved by the Institutional Ethics Committee of the Department of Anthropology, University of Delhi, India.

2.5. Variables

Socio-economic factors included marital status, age at marriage, educational status, profession, house ownership, number of individuals per room, family type, earning members in household, family income, personal income, mode of commuting (transportation) and migratory status. Health-related factors included food habits, frequency of non-vegetarian food, health status perception, health problems, type of medicine system preferred, smoking, alcohol consumption, Bacillus Calmette–Guérin (BCG) vaccination, night sweats, fever, weight loss, loss of appetite, earlier TB and family TB (family member suffering from TB).

2.6. Statistical analysis

The collected data was edited, coded and statistically analysed with the help of SPSS 20.0 version. Multinomial regression analysis was conducted to identify the significant risk factors associated with development of TB (through odds ratio [OR]).

3. Results

Out of 1316 subjects consulted, 983 were patients (or cases) and 333 were controls. The sex distribution among patients was 57% male and 43% females while among controls it was 52% males and 48% females.

Distribution of subjects according to socio-economic status and health-related factors and crude ORs between case and controls for socio-economic and health-related factors showing association with TB are listed in Tables 1 and 2 respectively.

Table 1 exhibits that majority of cases (23.7%) had received only primary education. Majority of controls (33.3%) were graduates or post-graduates. Most of TB patients (63%) had household ownership. Number of individuals per room is a crucial indicator of overcrowding. This parameter exhibits that most of TB cases (64.6%) resided with 3–5 individuals per room. Majority of controls (43.8%) lived with less than 3 individuals per room. Most of TB cases (83.9%) had less than 3 earning members in their household. Most of TB cases (53.4%) had family income Rs. 10,000 and above. Similarly, most of the healthy controls (40.5%) had family income Rs. 10,000 and above.

Marital status and age at marriage did not show association to development TB risk. Illiteracy and primary education were approximately 2 times (95% confidence interval [CI]: 1.65–3.41) and 4 times (95% CI: 8.77–19.78) respectively being associated with a TB. Government job and unemployment resulted in 68% (OR = 0.32, 95% CI: 0.17–0.60) and 59% (OR= 0.41, 95% CI: 8.77–19.78) less chances of developing TB risk in relation to reference category. Rented housing condition had an OR of

Table 1 – Association of socio-economic factors with TB.

Variables	Cases N = 983 (%)	Controls N = 333 (%)	[a]Exp(B)	CI (95%)
Marital status				
Married	573 (58.3)	212 (63.7)	0.79	0.61–1.02
Unmarried	405 (41.2)	118 (35.4)	RC	
Age at marriage				
21 and below	375 (38.1)	145 (43.5)	0.72	0.50–1.02
22 and above	206 (21.0)	57 (17.1)	RC	
Educational status				
Illiterate	226 (23.0)	71 (21.3)	**2.37**	1.65–3.41
Literate	110 (11.2)	12 (3.6)	**6.83**	3.58–13.01
Primary	233 (23.7)	42 (12.6)	**4.13**	2.74–6.23
High. sec.	141 (14.3)	65 (19.5)	**1.62**	1.10–2.37
Sr. Sec.	124 (12.6)	30 (9.0)	**3.08**	1.93–4.92
Graduate (+postgraduate)	149 (15.2)	111 (33.3)	RC	
Profession				
Govt. job	23 (2.3)	23 (6.9)	**0.32**	0.17–0.60
Pvt. job	300 (30.5)	85 (25.5)	1.12	0.78–1.60
Self employed	160 (16.3)	32 (9.6)	1.60	0.99–2.51
House wife	237 (24.1)	80 (24.0)	0.94	0.65–1.35
Unemployed	26 (2.6)	20 (6.0)	**0.41**	0.22–0.78
Any other	237 (24.1)	75 (22.5)	RC	
House ownership				
Rented	353 (35.9)	94 (28.2)	**1.44**	1.09–1.89
Own	619 (63.0)	237 (71.2)	RC	
Individuals per room				
3–5	635 (64.6)	112 (33.6)	**3.31**	2.49–4.41
6–7	83 (8.4)	48 (14.4)	1.01	0.67–1.52
8+	13 (1.3)	14 (4.2)	0.54	0.25–1.19
<3	250 (25.4)	146 (43.8)	RC	
Family type				
Nuclear	686 (69.8)	248 (74.5)	**0.68**	0.51–0.91
Joint (+extended)	297 (30.2)	73 (21.9)	RC	
Earning members				
≥3	158 (16.1)	37 (11.1)	1.45	0.99–2.12
<3	825 (83.9)	280 (84.1)	RC	
Family income p.m. (Rs.)				
10,000 and below	458 (46.6)	111 (33.3)	1.06	0.80–1.40
10,001 and above	525 (53.4)	135 (40.5)	RC	
Personal income p.m. (Rs.)				
10,000 and below	392 (39.9)	127 (38.1)	1.12	0.74–1.68
10,001 and above	116 (11.8)	42 (12.6)	RC	
Migration				
Migrated	538 (54.7)	28 (8.4)	**13.17**	8.77–19.78
Settled	445 (45.3)	305 (91.6)	RC	
Transportation				
Public	612 (62.3)	167 (50.2)	1.02	0.77–1.34
Private	371 (32.7)	103 (30.9)	RC	

TB, tuberculosis; Exp(B), crude odds ratio (OR); CI, confidence interval; RC, reference category; High. Sec., higher secondary; Sr. Sec., senior secondary; Govt. job, government job; Pvt. job, private job; p.m., per month; Rs., rupees.
The numeric values in bold are indicative of either being risk or protective factors for TB.
[a] Univariate analysis performed on variables.

1.4 (95% CI: 1.09–1.89) compared to owned housing condition. 3–5 individuals per room were 3 times more likely to be associated with a case of TB (95% CI: 2.49–4.41). Nuclear family condition was significantly associated with not being a case of TB. Number of earning members per household, Family Income and Mode of transport were not significantly associated with a case of TB. Migrant individuals were 13 times more likely to be associated with a case of TB (95% CI: 8.77–19.78) in comparison to settled population.

Table 2 shows that 85.6% TB cases preferred non-vegetarian food. Out of total TB cases, 55.1% TB cases consumed non-vegetarian food daily. Majority of healthy controls (41.7%) consumed non-vegetarian food occasionally. Majority of TB patients did not smoke (76.1%) and consume alcohol (78.6%). Most of TB patients (64.9%) were BCG vaccinated. Most of the TB patients (50.9%) experienced weight loss. Night sweating was absent in most of TB cases (79.0%). Family TB was absent in majority of TB cases (68.7%).

Non-vegetarian food was 3 times more likely to be associated with a case of TB (95% CI: 2.47–4.38). Daily consumption of Non-vegetarian food also significantly contributed to case of TB with an OR of 3.4 (95% CI: 2.51–4.72).

Table 2 – Association of health-related factors with TB.

Variables	Cases N = 983 (%)	Controls N = 333 (%)	[a]Exp(B)	CI (95%)
Food habit				
Non-veg.	841 (85.6)	214 (64.3)	**3.30**	2.47–4.38
Veg.	142 (14.4)	119 (35.7)	RC	
Freq. of non-veg.				
Daily	542 (55.1)	74 (22.2)	**3.44**	2.51–4.72
Occasionally	296 (30.1)	139 (41.7)	RC	
Health status perception				
Poor	9 (0.9)	16 (4.8)	**0.14**	0.06–0.33
Average	258 (26.2)	133 (39.9)	**0.50**	0.38–0.65
Good	716 (72.8)	184 (55.3)	RC	
Health problem				
Gastric trouble	36 (3.7)	23 (6.9)	**0.22**	0.13–0.39
Diabetes	24 (2.4)	14 (4.2)	**0.24**	0.12–0.48
Respiratory problem	37 (3.8)	9 (2.7)	0.58	0.27–1.24
Any other	160 (16.3)	184 (55.3)	**0.12**	0.09–0.17
Absent	726 (73.9)	103 (30.9)	RC	
Med. Sys. Pref.				
Allopathic	980 (99.7)	306 (81.9)	**26.69**	8.00–89.00
Any other	3 (0.3)	25 (7.5)	RC	
Smoking				
Yes	235 (23.9)	67 (20.1)	1.23	0.91–1.67
No	748 (76.1)	263 (79.0)	RC	
Alcohol				
Yes	210 (21.4)	69 (20.7)	1.03	0.76–1.40
No	773 (78.6)	261 (78.4)	RC	
BCG vaccination				
Yes	638 (64.9)	250 (75.1)	**0.61**	0.46–0.81
No	345 (35.1)	83 (24.9)	RC	
Night sweat				
Yes	206 (21.0)	19 (5.7)	**4.38**	2.70–7.14
No	777 (79.0)	314 (94.3)	RC	
Fever				
Yes	505 (51.4)	18 (5.4)	**18.49**	11.31–30.21
No	478 (48.6)	315 (94.6)	RC	
Weight loss				
Yes	500 (50.9)	19 (5.7)	**17.11**	10.59–27.64
No	483 (49.1)	314 (94.3)	RC	
Loss of appetite				
Yes	519 (52.8)	21 (6.3)	**16.62**	10.50–26.3
No	464 (47.2)	312 (93.7)	RC	
Earlier TB				
Yes	319 (32.5)	20 (6.0)	**7.52**	4.69–12.05
No	664 (67.5)	313 (94.0)	RC	
Family TB				
Yes	308 (31.3)	39 (11.7)	**3.40**	2.40–4.93
No	675 (68.7)	294 (88.3)	RC	

TB, tuberculosis; Exp(B), crude odds ratio (OR); CI, confidence interval; RC, reference category; non-veg., non-vegetarian; veg., vegetarian; Freq., frequency; Med. Sys. Pref., medicine system preferred; BCG, Bacillus Calmette–Guérin vaccine.
The numeric values in bold are indicative of either being risk or protective factors for TB.
[a] Univariate analysis performed on variables.

Average health status was significantly associated with not being a case of TB. Various health problems such as gastric trouble, diabetes and others (hypertension, body pain, etc.) did not contribute to development of TB case. Instead, they acted as protective factors for TB. Smoking and alcohol consumption were not associated with TB risk. Fever, weight loss and loss of appetite were significant factors associated with TB risk. Cases with earlier manifestation of TB were 7 times more likely to be associated with TB infection (95% CI: 4.69–12.05).

4. Discussion

It has been established that socio-economic status of a population is an important indicator of prevalence, diagnosis and treatment of TB.[8] The association between TB and poverty is governed by overcrowding, poorly ventilated housing, malnutrition, smoking, stress, social deprivation and poor social capita.[9] The present study also exhibits similarities with the study.

The present study suggested that illiteracy and primary education had strong effects on developing TB cases. Higher educational status probably reflected increased awareness and hence better diagnosis of disease. Poor socio-economic status with its attendant poor education is related with poor knowledge of TB, risks of infection and dissemination and with inadequate and/or delayed availability of health care.[10]

Unemployment and government job served as protective factors for a case of TB. Number of individuals per room as a measure of overcrowding showed a significant association with a case of TB. Over-crowding increases the risk of disease transmission.[11,12] Overcrowding, by decreasing the degree of air space that is shared, results in increased exposure to *Mycobacterium tuberculosis*.[10] Nuclear family served as a protective factor for a case of TB.

Migration showed strong association to development TB risk in the present study. Migration elevates the risks of transmission of infectious diseases such as TB, particularly if migrants originated in high prevalent countries.[9] Mobile communities gather in peri-urban areas where their neighbours live in similar deprived conditions characterised by absence of proper education, overcrowding, malnutrition, unhygienic living conditions, poor health care access and poor treatment compliance leading to high TB morbidity in these communities.[9]

Shetty et al.[13] conducted matched case–control study in Bangalore, India to evaluate potential socio-demographic risk factors for TB and found that TB was associated with low education level, kitchen type and diabetes, reflecting the complex interaction between non-communicable disease, urbanisation and a changing economic climate in Bangalore.

Odone et al.[14] conducted a prospective cohort study of index TB patients and their household contacts in Lima and found that patients with higher socio-economic status had a 3-fold increased risk of transmitted resistance compared to those with lower socio-economic status when acquired resistance served as the baseline and quality of housing mediated most of the impact of socio-economic status.

Non-vegetarian food and frequency of non-vegetarian food being consumed as a measure of dietary pattern showed strong association for TB risk. A study[15] of TB in south London among Asian immigrants from the Indian subcontinent concluded that a vegetarian diet is an independent risk factor for TB in immigrant Asians. In the present study, it was found that health problems such as gastric trouble, diabetes and any other (hypertension, body pain, etc.) acted as a protective factors for a case of TB. In a study conducted to determine diabetes prevalence among a cohort of TB cases registered under Revised National Tuberculosis Control Program in selected TB units in Tamil Nadu, it was found that diabetes mellitus risk was higher among PTB, especially sputum positive, than non-PTB.[16]

The present study showed no effect of smoking and alcohol consumption on development of TB risk in multivariate analysis. Tobacco smoking was demonstrated as a risk factor for men with TB in an age-matched case control study from South India[17]; whether this association was controlled by other socio-economic or demographic factors is not exhibited. In another study, it was found that passive smoking is associated with development of childhood TB.[18] The present study showed that weight loss and loss of appetite served as significant health-related risk factors for TB development.

5. Conclusion

The present study concluded that lower educational status, rented household, individuals per room and migratory status served as prominent risk factors for TB disease. Preference and frequency of non-vegetarian food being consumed, night sweating, weight loss, loss of appetite, earlier TB and family TB were key health-related risk factors associated with TB disease. Hence, the present study provides crucial information on the current status of TB, and the findings will aid to frame new strategies for clinical practice in communities where the prevalence of TB is still high and resources are scarce.

Conflicts of interest

The authors have none to declare.

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REFERENCES

1. Maartens G, Wilkinson RJ. Tuberculosis. *Lancet*. 2007;370:2030–2043.
2. Directorate General of Health Services. *TB India 2016: Revised National TB Control Programme Annual Status Report*. Tuberculosis Control India; 2016 http://www.tbcindia.nic.in/showfile.php?lid=3180 [accessed June 2016].
3. Ghose B, Zhaohui C, Zhifei H. Understanding the social determinants of TB and HIV in South Asia. *PeerJ PrePr*. 2014;2:e579v1.
4. Benatar SR, Upshur R. Tuberculosis and poverty: what could (and should) be done? *Int J Tuberc Lung Dis*. 2010;14(10):1215–1221.
5. Kjellström T, Mercado S, Sattherhwaite D, McGranaham G, Friel S, Havemann K. *Our Cities, Our Health, Our Future: Acting on Social Determinants for Health Equity in Urban Settings. Report to the WHO Commission on Social Determinants of Health from the Knowledge Network on Urban Settings*. Kobe: World Health Organization Kobe Centre; 2007.
6. Lönnroth K, Zignol M, Uplekar M. Controlling TB in large metropolitan settings. In: Raviglione M, ed. In: *TB: A Comprehensive International Approach*. New York: Informa Healthcare; 2006.
7. Rasanathan K, Sivasankara Kurup A, Jaramillo E, Lönnroth K. The social determinants of health: key to global

tuberculosis control. *Int J Tuberc Lung Dis*. 2011;15(suppl 2): S30–S36.
8. Kaulagekar A, Radkar A. Social status makes a difference: tuberculosis scenario during national family health survey-2. *Indian J Tuberc*. 2007;54:17–23.
9. Figueroa-Munoz JI, Ramon-Pardo P. Tuberculosis control in vulnerable groups. *Bull World Health Organ*. 2008;86 (September (9)):733–735.
10. Gupta D, Das K, Balamughesh T, Aggarwal N, Jindal SK. Role of socio-economic factors in tuberculosis prevalence. *Indian J Tuberc*. 2004;51(1):27–32.
11. Mangtani P, Jolley DJ, Watson JM, Rodrigues LC. Socioeconomic deprivation and notification rates for tuberculosis in London during 1982–91. *BMJ*. 1995;310 (6985):963–966.
12. Druncker EP, Alcabes W, Bosworth W, Sckell B. Childhood tuberculosis in the Bronx, New York. *Lancet*. 1994;343: 1482–1485.
13. Shetty N, Shemko M, Vaz M, D'souza G. An epidemiological evaluation of risk factors for tuberculosis in South India: a matched case control study. *Int J Tuberc Lung Dis*. 2006;10:80–86.
14. Odone A, Calderon R, Becerra MC, et al. Acquired and transmitted multidrug resistant tuberculosis: the role of social determinants. *PLOS ONE*. 2016;11(1).
15. Strachan DP, Powell KJ, Thaker A, Millard FJ, Maxwell JD. Vegetarian diet as a risk factor for tuberculosis in immigrant south London Asians. *Thorax*. 1995;50(2):175–180.
16. Viswanathan V, Kumpatla S, Aravindalochanan V, et al. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. *PLoS ONE*. 2012;7:e41367.
17. Kolappan C, Gopi PG. Tobacco smoking and pulmonary tuberculosis. *Thorax*. 2002;57:964–966.
18. Patra S, Sharma S, Behera D. Passive smoking, indoor air pollution and childhood tuberculosis: a case control study. *Indian J Tuberc*. 2012;59:151–155.

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Original Article

Prevalence & pattern of respiratory diseases including Tuberculosis in elderly in Ghaziabad – Delhi – NCR

Sonisha Gupta [a,*], *Vijay Arora* [b], *O.P. Sharma* [c], *L. Satyanarayana* [d], *Atul Kumar Gupta* [e]

[a] *Associate Professor, Department of Tuberculosis & Respiratory Diseases, Santosh Medical College & Hospital, Ghaziabad, India*
[b] *Santosh University, Ghaziabad, India*
[c] *Geriatric Society of India, K-49, 2nd Floor, Green Park Main, New Delhi, Delhi 110016, India*
[d] *ICPO, ICMR, India*
[e] *Department of Surgery, Santosh Medical College & Hospital, Ghaziabad, India*

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ABSTRACT

Elderly population is continuously increasing all over the world including India. Old age is associated with significant prevalence of chronic illnesses. Population based study to find prevalence & pattern of respiratory diseases in elderly in India is difficult to find. Present study was done in an urban locality of Ghaziabad inhabited mainly by low socio – economic status population. Two part questionnaire was used as main tool. Through part one 1522 elderly were screened for respiratory disease. Respiratory disease was confirmed & diagnosed by part two of questionnaire, physical examination & necessary investigations. Prevalence of respiratory diseases was 18.8% in this study. Prevalence of respiratory diseases was almost double in elderly males as compared to females. COPD was most prevalent respiratory disease followed by Bronchial asthma.

1. Introduction

The size of India's older adult population is greater than the total population of many developed and developing countries. World old age population was 784 million in 2011. India's old population (83 million) accounts for 10% of world's old age population in 2011. According to World Health Statistics 2011, India's old age population comprises 7% of the nation's total population (1.2 billion). Following the trend in rest of the world, in India also, the share and size of elderly population are increasing over time. Over the next four decades, India's demographic structure is expected to shift dramatically from a young to an ageing population. It is expected to increase up to 12% by 2026 (173 million) and by 2050 expected to increase to 316 million (approx. 20%).[1]

Although ageing population is a sign of progress in social, economic, and healthcare fields it also poses challenge of meeting growing demand for providing geriatric healthcare services. The human ageing process affects multiple organs and tissues with progressive deterioration of their functions.[2] This leads to decreased functional reserve of organ systems. The lungs can lose more than 40% of their capacity over time.[3] This decreased functional capacity along with weakened immune defences makes organs and thus the subject more vulnerable to various diseases. Old age is characterized by one

* *Corresponding author*. Tel.: +1 8527214794.
E-mail address: sonishagupta@gmail.com (S. Gupta).
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or more chronic diseases. In industrialized countries as well as India chronic diseases are the leading cause of morbidity and mortality among elderly.

Very few population-based studies to determine prevalence of chronic respiratory diseases for elderly's in India have been done.[4–6] In our search, we were unable to find any study on prevalence and pattern of chronic respiratory diseases in elderly. Present study was undertaken to determine the same in a low socio-economic locality in urban area of national capital region (NCR).

2. Material and Methodology

This cross-sectional study was carried out in Nandgram, Ghaziabad. Nandgram is a locality in Ghaziabad city with more than 10,000 houses inhabited mainly by lower middle class families. People aged 60 years and above residing in the area were included. Total sample size of 1500 was taken. Elderly people unwilling to be part of study or unable to answer questionnaires because of inability to speak or altered orientation or other reasons were excluded. Predesigned, pretested questionnaire was used as a tool.

Questionnaire had 2 parts. First part included socio-demographic characteristics and self-reported co-morbidities. Medical records of patients were seen. Information related to chronic diseases other than respiratory system was recorded based on their report of investigation done by their physician/doctor. This first part screened out suspected respiratory cases. Three health care workers were trained for this purpose.

These elderly with suspected respiratory disease were asked part two of questionnaire. This questionnaire was aimed to find the type of respiratory disease. Questionnaire was developed using various international standard questionnaires for respiratory diseases.[7–10] Patient underwent post-bronchodialator reversibility testing to differentiate between bronchial asthma and chronic obstructive pulmonary disease (COPD). If increase of forced expiratory volume 1 (FEV1) $>$ 12% or $>$200 ml increase from pre-brochodialator value, then it was considered bronchial asthma. Asthma was the only possible diagnosis when FEV1/forced vital capacity (FVC) $\geq$ 0.7and If post-bronchodialator FEV1/FVC $<$ 0.7 persists then it was considered classified as COPD according to GOLD guidelines. Patients with additional symptoms and signs (e.g., haemoptysis, weight loss, fever, sign of bronchiectasis and other structural lung disease) were suggested an alternative pulmonary diagnosis, and they underwent further investigations along with screening questionnaire as mentioned above to establish diagnosis.

General examination and respiratory system examination were carried out. Pulomonary function test (PFT) was performed. Other necessary investigations to make a diagnosis were done if required. For acute illness recall period was one month while for chronic illness it was one year.

3. Results

A total of 1522 cases were recorded. Through part 1 questionnaire, 367 elderly with suspected respiratory disease were screened out. These suspected cases were called for second step which included administration of part 2 of questionnaire, general physical and respiratory system examination, PFT and other investigations as required. Out of 367 suspected cases, 29 (7.9%) dropped out and 56 (15.2%) turned out non-respiratory. 282 cases were diagnosed as respiratory cases.

Out of total 1522 cases, 666 (43.7%) were males and 856 (56.2%) were females. Mean age of respondents was 64.5 years. Prevalence of co-morbidity among elderly males was 96% (640/666) and among elderly females it was 98.2% (841/856). In overall 1522 cases, mean number of co-morbidities was 1.71 per respondent. In total 1493 cases were analysed as 29 cases (19 males and 10 females) dropped out.

Prevalence of respiratory diseases was 18.8% (282/1493) in this study. Prevalence of respiratory disease was almost double in males (26.1% – 169/647) as compared to females (13.1% – 113/846) (Table 1). Mean age of respiratory patients was 64.9 years (Table 2).

COPD was the most prevalent respiratory disease constituting 56.4% (159/282) of all respiratory patients. Overall prevalence of COPD in our study was 10.6% (159/1493). Prevalence among elderly males was higher (16.0% – 104/647) than females (6.5% – 55/846). Elderly patients who had COPD alone were 126/282 (44.7%). Mean age among them was 66 years. Significant number of COPD patients (33/159, i.e., 20.7%) had another respiratory co-morbidities, with pulmonary tuberculosis being the most common co-morbidity affecting 16 patients. Among all COPD cases 10.1% (16/159)

Table 1 – Prevalence of respiratory diseases.

Disease	Number overall (*n* –1493)	Prevalence (%) Overall	Number male (*n* – 647)	Prevalence (%) Male	Number female (*n* – 846)	Prevalence (%) Female
Respiratory	282	18.9	169	26.1	113	13.3
COPD	159	10.6	104	16.0	55	6.5
COPD alone	126	8.43	81	12.5	45	5.3
Bronchial asthma	57	3.8	24	3.7	33	3.9
Bronchial asthma alone	32	2.14	14	2.16	18	2.12
Overlap syndrome	28	1.87	9	1.39	19	2.24
TB	34	2.3	24	3.7	10	1.2
Bronchiectasis	15	1	10	1.5	5	0.6
ILD	8	0.5	5	0.8	3	0.35

Respiratory diseases were more prevalent in males (males – 26.1% vs females – 13.3%).

Table 2 – Pattern of respiratory diseases.

Diseases	No.	(%)	Mean age (yeas)	Smokers no.	Smokers (%)	Non-smokers no.	Non-smokers (%)	Bio-mass exp.	(%)
COPD (T)	159	56.4	66.0	135	84.9	24	15.1	46	29.0
BA (T)	57	20.2	64	5	8.8	52	91.2	13	22.8
Overlap syndrome	28	9.92	64.4	4	14.2	24	85.7	11	39.3
Pulm. TB	34	12	65.4	18	52.9	16	47	4	11.7
Bronchiect.	15	5.3	65.4	8	53.3	7	46.7	3	20
ILD	8	2.8	62	5	62.5	3	37.5	2	25
								4	66.7

COPD is the most prevalent respiratory disease followed by bronchial asthma. Significant number of elderly had COPD-bronchial asthma overlap syndrome (*n* – 28, 9.92%).

patients had tuberculosis, 2.5% (4/159) had bronchiectasis, 1.25% (2/159) had OSA. One patient each (1/159 – 0.62%) of COPD had Interstitial lung disease (ILD) and lung cancer.

Smokers among all COPD patients were 84.9% (135/159). Bidi was the most common addiction, being used by 91 smokers, followed by cigarette (39) and hukka (17). Many of them were using more than one smoking agents. Out of 24 non-smokers among COPD patients, 21 had history of exposure to biomass fuel. Thus making only 3 elderly with COPD having no history of smoking or biomass fuel. Among the 126 patients who had COPD alone, 13 (10.3%) were diabetic, 34 (26.9%) hypertensive, 10 (7.9%) cardiac and 54 (42.8%) had joint pain.

Bronchial asthma was the 2nd most prevalent respiratory diagnosis affecting 57/282 (20.2%) of all respiratory elderly patients. Mean age was 64 years. Only 13 (22.8%) patients had history of exposure to biomass fuel and 5 (8.8%) were smokers. A large number of patients with bronchial asthma had (44% – 25/57) allergic rhinitis. 3.5% (2/57) had tuberculosis, 1.75% (1/57) had bronchiectasis and 5.3% (3/57) had maxillary sinusitis. Elderly patients who had bronchial asthma alone account for 32/282 (11.34%). Among these 32 bronchial asthma patient, 6 (18.75%) were diabetic, 8 (25%) were hypertensive, 3 (9.4%) were cardiac, 15 (46.9%) had joint pain.

Prevalence of overlap-syndrome was 28/1493 (1.87%) in elderly population. Number of males were 9(1.39%) and females were 19 (2.24%). Mean-age was 64.4 years. Respective number of smokers among them were 4 and 17, who had a history of exposure to biomass fuel. Among these patients 10 (35.7%) were diabetic, 16 (57.1%) hypertensive, 6 (21.4%) had cardiac problem and 17 (60.7%) joint pain.

Pulmonary tuberculosis was seen among 34 (12.0%) of all respiratory elderly patients with mean-age of 65.4 years. Among 34 patients of tuberculosis, 47% (16/34) had COPD, 5.9% (2/34) bronchial asthma, and 2.9% (1/34) had bronchiectasis along with it. There was only 2.9% (1/34) case of miliary tuberculosis and 11.7% (4/34) cases of pleural effusion and 2.9% (1/34) had abdominal tuberculosis. Many elderly with tuberculosis also had non-respiratory co-morbidity. 2 (14.3%) were diabetic, 2 (14.3%) were hypertensive, 1 (7.14%) patient had cardiac problem and 6 (42.9%) had joint problem.

Bronchiectasis was prevalent in 5.3% (15/282) of all respiratory patients with mean-age of 65.4 years. Among these 15 patients, 8 (53.3%) were smokers, 3 (20%) had biomass fuel exposure and 1 (6.7%) had occupational exposure. Among all these 15 bronchiectasis, 26.6% (4/15) of patients was associated with COPD, 6.6% (1/15) was associated with pulmonary tuberculosis, and 6.6% (1/15) had bronchial asthma along with bronchiectasis, 60% (9/15) had no association with other respiratory diseases. Elderly patients who had bronchiectasis alone account for 3.19% (9/282) of all respiratory cases.

There were only 8 patients of ILD which accounted for 2.8% of all respiratory patients. Mean-age among ILD was 62 years. Smokers among ILD were 5 (62.5%) and 2 (25%) had biomass exposure and 6 (75%) had occupational exposure. Among these 8 patients, 87.5% (7/8) had no association with other respiratory diseases. Only one patient had (12.5%) COPD.

Only 4 patients had lung cancer, which account for 1.41% (4/282) of all respiratory patients. Half of them were smokers and three of them were exposed to biomass fuel. There were no occupational exposure among them. It was seen that 75% (3/4) of all lung cancer had no association with other respiratory diseases and 25% (1/4) had association with COPD.

4. Discussion

Respiratory diseases are a major cause of morbidity and mortality in elderly. Prevalence of respiratory diseases in our study is 18.5%.

There is wide variation in prevalence of respiratory diseases reported in literature. An important reason for this wide variation is due to the methodology adopted. Studies about morbidity profile of elderly have noted respiratory illness either as self reported illness or self reported symptom, i.e., cough or breathlessness. Further studies noting self reported respiratory illness have reported only one or two illnesses (COPD, asthma or tuberculosis). They also differ regarding sample population, as some studies are community-based, other hospital-based and some other based on special groups, i.e., old age homes.

A study on the health care for the rural aged in Madurai district, Tamil Nadu reported that of the 1910 elderly screened, 16% had respiratory problem.[11] One study among elderly in urban slum of Pune reported 5% prevalence of respiratory illness.[12] An ICMR study reported 10% prevalence of respiratory ailments.[13]

Respiratory disorders are among leading causes of mortality in elderly. According to Government of India Statistics, respiratory disorders account for 10% mortality while infections including tuberculosis account for another 10%.[14]

Comparatively higher prevalence of respiratory disease in our study could be due to the fact that study population was taken from a low socio economic urban locality in urban area of NCR. As high as 90.1% of sample population belonged to lower middle or lower socio-economic status. Various studies have reported relationship between low socio-economic status and respiratory diseases.[15,16] Another probable reason could be high pollution level in NCR.

Prevalence of respiratory disease was almost double in males (26.1% – 169/647) as compared to females (13.1% – 113/847). It is consistent with geriatric homes-based study in Ahmedabad, India which also had higher prevalence of respiratory disorder among males as compared to females (11% vs 8%).[17] A study conducted in village of Tamil Nadu by Bayapareddy et al. also reported higher respiratory morbidity among elderly males (14.5%) as compared to females (11.2%).[18]

Higher prevalence of respiratory diseases in males is attributed to the differential rates of smoking and occupational exposure between the two genders. According to national sample survey 50th round survey, around 52% males and 13% of females were tobacco users.[19] According to national family health survey-2 (98–99) 39% elderly males were smokers while for elderly females this figure was only 6%.[20]

COPD is the fourth leading cause of death in the world. By 2030, the disease is expected to be the third leading cause of death worldwide.[21]

There is wide variation in prevalence of COPD reported in various studies from India and abroad. Besides geographical differences in prevalence they are also due to difference in methodology used to make diagnosis. While most of epidemiological studies have used questionnaire based diagnosis others have used spirometry based diagnosis. The global prevalence of physiologically defined chronic obstructive pulmonary disease (COPD) in adults aged ≥40 years is approximately 9–10%.[22]

Prevalence of COPD in Indian adult males in studies has ranged from 1.9% to 8.1%. For females it is lower ranging from 1.2% to 4.6%.[4,23–26] Gender differential in prevalence of COPD can be attributed to difference in risk behaviour between males and females as already discussed. Even among COPD patients in our study while 97.1% (101/104) males were smokers only 61.8% (34/55) females had history of smoking. In Indian females exposure to bio-mass fuel is an important cause of COPD. In our study 42 females out of 46 with COPD had history of exposure to bio-mass fuel for cooking.

Very few studies on prevalence of COPD in Indian elderly are available. A Dibrugarh study reported 7.5% prevalence of COPD in elderly.[27] It also showed higher prevalence in males (8.8%) as compared to females (5.4%), which is consistent with our study. Another study published in Lancet (2009) showed prevalence of COPD in elderly from 1.8% (urban) to 7.6% (rural).[28] According to a 2008 East Delhi study, age above 50 years is a significant risk factor. Individuals between 51 and 69 years of age were nearly three times, while those above 70 years were six times more likely to have chronic respiratory symptoms.[29]

Patients with COPD had higher co-morbidity rate (100%) than overall sample population (97%). Number of co-morbidities per person was also higher in COPD patients (2.14 vs 1.71). It has been observed in the ECLIPSE study that co-morbidities were significantly higher in patients with COPD than in smokers and never smokers.[30] Co-morbidities associated with COPD are cardiovascular disorders (coronary artery disease and chronic heart failure), hypertension, metabolic diseases (diabetes mellitus, metabolic syndrome and obesity), and bone disease (osteoporosis and osteopenia).[31] Multiple factors are responsible for increased co-morbidities in patients with COPD. Ageing, smoking, air pollution are common risk factors for many co-morbidities. Besides these poor nutrition, use of glucocorticoids for treatment of COPD, increased levels of pro-inflammatory cytokines, hypoxaemia low testosterone levels in patients with COPD are also responsible.

Relationship between COPD and exposure to smoke is universally agreed. In Indian females exposure to biomass fuel is also a significant risk factor as seen in our study. Various studies have documented it.[32,33]

In the past, asthma was considered mainly as a childhood disease; however, recent studies have indicated that asthma is highly frequent in the elderly population with its prevalence ranging from 4.5% to 12.7%.[34] Padda et al. (1998) reported that bronchial asthma was found in 12.61% cases.[35] Another study found bronchial asthma in 17.92% of the elderly persons.[36] In our study it was 2nd most common respiratory illness after COPD. According to Murthy and Sastry elderly constitute majority of cases of chronic asthma in India. They estimated prevalence in elderly in urban areas rising from 8.27% in 1996 to 8.75% in 2016.[37]

In our study almost 10% (28/282) patients with respiratory illness had COPD-asthma overlap syndrome. Other studies have also suggested that some patients suffer from both asthma and COPD, and that they represent an important clinical population with peculiar characteristics.[38,39] They have worse health related quality of life and more frequent exacerbations. According to an Italian study this syndrome is more prevalent in elderly.[40]

In present study tuberculosis was 3rd most common respiratory illness after COPD and asthma. Elderly are more vulnerable to tuberculosis. It may be due to compromised immunity resulting from increased co-morbidity, multiple chronic illnesses (e.g., diabetes or chronic lung disease) and age-related immune-senescence.[41] Significant number (19/34 – 55.9%) of patients with Tuberculosis had associated respiratory illness (16/34 – 47% COPD, 2/34 – 5.9% asthma, 1/34 – 2.9% bronchiectasis). This finding is consistent with another study of author on Himachal Pradesh elderly in which 64% elderly with Tuberculosis had associated COPD.[42] Presence of another respiratory illness alters clinical presentation leading to late diagnosis.

ILD, a heterogeneous group of disorders, is characterized by diffuse involvement of pulmonary parenchyma with variable degree of lung fibrosis.[43] They diminish the lung's capacity for alveolar gas diffusion. Regarding prevalence of ILD in India, very few, single centre studies only are available.[44–46] The prevalence of idiopathic pulmonary fibrosis in the US has been estimated as 14.0–27.9 cases/100,000.[47] In our study 8 patients were found to be having ILD; males (5) were being more than females (3). Prevalence of lung cancer was 0.27% (4/1493) in our study. For rare diseases such as ILD and lung cancer, sample size of 1500 is too small to comment on prevalence.

5. Conclusion

Globally, as well as in India, demographic structure is changing. Continuously increasing geriatric population is making it imperative to understand peculiar health problems of this population. Respiratory disorders are an important cause of morbidity and mortality amongst elderly. COPD is the most common respiratory morbidity followed by asthma and tuberculosis. COPD/asthma overlap syndrome is another peculiar problem of this age group. Another peculiar feature of this age group is frequently associated respiratory and non-respiratory co-morbidities. Associated respiratory co-morbidity alters the clinical presentation thus making correct diagnosis more difficult. Associated co-morbidities also have implications for more careful and individualized treatment approach.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. WHO. *World Health Statistics*. 2011. http://www.who.int/whosis/whostat/2011.
2. Bowling A, Dieppe P. What is successful ageing and who should define it? *BMJ*. 2005;331:1548–1551.
3. Harik-Khan RI, Wise RA, Fozard JL. Determinants of maximal inspiratory pressure. The Baltimore longitudinal study of aging. *Am J Respir Crit Care Med*. 1998;158:1459–1464.
4. Radha TG, Gupta CK, Singh A, Mathur N. Chronic bronchitis in an urban locality of New Delhi – an epidemiological survey. *Indian J Med Res*. 1977;66:273–285.
5. Qureshi KA. Domestic smoke pollution and prevalence of chronic bronchitis-asthma in a rural area of Kashmir. *Indian J Chest Dis Allied Sci*. 1994;36:61–72.
6. Akhtar MA, Latif PA. Prevalence of chronic bronchitis in urban population of Kashmir. *J Indian Med Assoc*. 1999;97:365–369.
7. Alaska Tuberculosis Program Manual Forms – Alaska Department of Health and Social Services. dhss.alaska.gov/dph/Epi/id/Documents/01-Internal/TB_Forms.pdf Last accessed May 2016.
8. Bai J, Peat JK, Berry G, Guy B, Woolcock AJ. Modified questionnaires of shortened version of the IUATLD (International Union Against Tuberculosis and lung diseases). *Chest*. 1998;114:1343–1348.
9. Modified COPD Population Screener T.M. (COPD-PS). www.copd.org Last accessed May 2016.
10. Modified Questionnaires UCSF Medical Center ILD Clinic. University of California, San Francisco. http://www.ucsf.edu Last accessed May 2016.
11. Venkoba Rao A. *Health Care of Rural Aged*. New Delhi: Indian Council of Medical Research; 1990:10.
12. Pandve HT, Deshmukh P. Health survey among elderly population residing in an urban slum of Pune city. *J Indian Acad Geriatr*. 2010;6(1):5–8.
13. Khokhar A, Mehra M. Life style and morbidity profile of geriatric population in an urban community of Delhi. *Indian J Med Sci*. 2001;55:609–615.
14. Guha R. Morbidity related epidemiological determinants in Indian aged – an overview. In: Ramachandran CR, Shah B, eds. In: *Public Health Implications of Ageing in India*. New Delhi: Indian Council of Medical Research; 1994.
15. Viegi G, Scognamiglio A, Baldacci S, Pistelli F, Carrozzi L. Epidemiology of chronic obstructive pulmonary disease. *Respiration*. 2001;68:4–19.
16. Bigoniya P, Shukla A, Iram H, Iram F. Study on prevalence of respiratory disease in urban population of Bhopal city. *AJPRHC*. 2012;4(2):52–62.
17. Banker K, Prajapati B, Kedia G. Study of health profile of residents of Geriatric home in Ahmedabad district. *Natl J Community Med*. 2011;2(3):378–382.
18. Piramanayagam A, Bayapareddy N, Pallavi M, Madhavi E, Nagarjuna reddy N, Radhakrishna L. A cross sectional study of the morbidity pattern among the elderly people South India. *Int J Med Res Health Sci*. 2013;2(3):372–379.
19. National Sample Survey Organization. Survey results on consumption of tobacco in India: NSS 50th round (1993–94). *Sarvekshana*. 1998;74:259–387.
20. Rani M, Bonu S, Jha P, Nguyen SN, Jamjoum L. Tobacco use in India: prevalence and predictors of smoking and chewing in a national cross sectional household survey. *Tobacco Control*. 2003;12(e4):1–8.
21. World Health Statistics 2008. www.who.int/respiratory/copd/ Last accessed May 2016.
22. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J*. 2006;28:523–532.
23. Singh H. Certain clinical and epidemiological patterns of chronic obstructive lung disease as seen in Northern India. *Indian J Chest Dis*. 1964;6:183–194.
24. Viswanathan R. Epidemiology of chronic bronchitis: morbidity survey in Patna urban area. *Indian J Med Res*. 1966;54:105–111.
25. Thiruvengadam KV, Raghava TP, Bhardwaj KV. Survey of prevalence of chronic bronchitis in Madras city. In: Viswanathan R, Jaggi OP, eds. In: *Advances in Chronic Obstructive Lung Disease*. Delhi: Asthma and Bronchitis Foundation of India; 1977:59–66.
26. Ray D, Abel R, Selvaraj KG. A 5-yr prospective epidemiological study of chronic obstructive pulmonary disease in rural South India. *Indian J Med Res*. 1995;101:238–244.
27. Medhi GK, Hazarika NC, Borah PK, Mahanta J. Health problems and disability of elderly individuals in two population groups from same geographical location. *J Assoc Physicians India*. 2006;54:539–544.
28. Sousa RM, Ferri CP, Acosta D, et al. Contribution of chronic diseases to disability in elderly people in countries with low and middle incomes: a 10/66 Dementia Research Group population-based survey. *Lancet*. 2009;374:1821–1830.
29. Chhabra P, Sharma G, Kannan AT. Prevalence of respiratory disease and associated factors in an urban area of Delhi. *Indian J Community Med*. 2008;33(4):229–232.
30. Agusti A, Calverley PM, Celli B, et al. Characterisation of COPD heterogeneity in the ECLIPSE cohort. *Respir Res*. 2010;11:122–136.
31. Vijayan VK. Chronic obstructive pulmonary disease. *Indian J Med Res*. 2013;137:251–269.
32. Mahesh PA, Jayaraj BS, Prahlad ST, et al. Validation of a structured questionnaire for COPD and prevalence of COPD in rural area of Mysore: a pilot study. *Lung India*. 2009;26:63–69.
33. Jindal SK, Aggarwal AN, Chaudhry K, et al. A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoking and environmental tobacco smoke exposure. *Indian J Chest Dis Allied Sci*. 2006;48:23–29.

34. Yáñez A, Cho S-H, Soriano JB, et al. Asthma in the elderly: what we know and what we have yet to know. *World Allergy Organ J*. 2014;7:8.
35. Padda AS, Mohan V, Singh J, Deepti SS, Singh G, Dhillon HS. Health profile of aged persons in urban and rural field practice areas of medical college, Amritsar. *Indian J Community Med*. 1998;23(2):72–76.
36. Makwana NR, Shah VR, Kalpesh G, Sudha Y. Health problems in geriatrics – a cross sectional study. *JPBMS*. 2012;20(16):1–4.
37. Murthy KJR, Sastry JG. Economic burden of asthma. In: *NCMH Background Papers. Burden of Disease in India*. 2005; 251–258.
38. Hersh CP, Jacobsen FL, Gill R, Silverman EK. Computed tomography phenotypes in severe, early-onset chronic obstructive pulmonary disease. *COPD*. 2007;4:331–337.
39. Viegi G, Matteelli G, Angino A, et al. The proportional Venn diagram of obstructive lung disease in the Italian general population. *Chest*. 2004;126(4):1093–1101.
40. de Marco R, Pesce G, Marcon A, et al. The coexistence of asthma and chronic obstructive pulmonary disease (COPD): prevalence and risk factors in young, middle-aged and elderly people from the general population. *PLOS ONE*. 2013;8(5):e62985.
41. Negin J, Abimbola S, Marais BJ. Tuberculosis among older adults – time to take notice. *Int J Infect Dis*. 2015;32:135–137.
42. Arora VK, Bedi RS. Geriatric tuberculosis in Himachal Pradesh – a clinico-radiological profile. *JAPI*. 1989;37(3):205–206.
43. Raghu G. Interstitial lung disease. In: Goldman L, Schafer AI, eds. In: *Cecil Medicine* 24th ed. Philadelphia: W.B. Saunders; 2011:556–566.
44. Maheshwari U, Gupta D, Aggarwal AN, Jindal SK. Spectrum and diagnosis of idiopathic pulmonary fibrosis. *Indian J Chest Dis Allied Sci*. 2004;46:23–26.
45. Sharma SK, Pande JN, Verma K, Guleria JS. Bronchoalveolar fluid (BALF) analysis in interstitial lung diseases: a 7 years experience. *Indian J Chest Dis Allied Sci*. 1989;31:187–196.
46. Subhash HS, Ashwin I, Solomon SK, David T, Cherian AM, Thomas K. A comparative study on idiopathic pulmonary fibrosis and secondary diffuse parenchymal lung disease. *Indian J Med Sci*. 2004;58:185–190.
47. Nalysnyk L, Cid-Ruzafa J, Rotella P, Esser D. Incidence and prevalence of idiopathic pulmonary fibrosis: review of the literature. *Eur Respir Rev*. 2012;21:355–361.

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Original Article

Association of ABO blood group polymorphism and tuberculosis: A study on Bengalee Hindu caste population, West Bengal, India

S. Ganguly [a], P. Sarkar [b], D. Chatterjee [c], A.R. Bandyopadhyay [d,*]

[a] Research Student, Department of Anthropology, University College of Science, Technology & Agriculture, University of Calcutta, 35, Ballygunge Circular Road, Kolkata 700019, India

[b] UGC (NET), Junior Research Fellow, University College of Science, Technology & Agriculture, University of Calcutta, 35, Ballygunge Circular Road, Kolkata 700019, India

[c] Assistant Professor, Department of Anthropology, University College of Science, Technology & Agriculture, University of Calcutta, 35, Ballygunge Circular Road, Kolkata 700019, India

[d] Professor, Department of Anthropology, University College of Science, Technology & Agriculture, University of Calcutta, 35, Ballygunge Circular Road, Kolkata 700019, India

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ABSTRACT

Tuberculosis (TB) is an infectious disease commonly caused by the bacillus mycobacterium and worldwide estimation demonstrated that more than 8.6 million people are infected by TB. Many of the previous studies reported the association between TB and ABO blood group polymorphism. In this context, the objective of the present study is to understand the association of ABO blood group polymorphism and TB in Bengalee Hindu caste population. The present study consists of 100 clinically diagnosed TB patients and 100 apparently healthy individuals with no previous history of TB from the same population of the same area. The distribution of ABO phenotypes demonstrated significant ($p < 0.05$) excess of AB blood group in TB patients and significant ($p < 0.05$) decrease of O blood group in controls. Logistic regression analysis revealed that individuals with non O blood group have 1.97 times (95% CI 1.04–3.75) greater chance of developing TB than individuals with O blood group.

1. Introduction

Pulmonary tuberculosis (TB) is an infectious disease caused by the bacillus mycobacterium.[1] TB affects commonly the lungs (pulmonary TB). Apart of this, it is responsible for maximum mortality throughout the world, especially in developing countries[1] and in Indian context, infectious disease like TB is the single major communicable disease.[2] The susceptibility of TB creates major public health burden which has been identified as High Burden Country (HBC) cause of 10,000 cases per year in India.[2]

ABO and Rhesus blood groups were found to be most clinically important in transfusion practice. The association

* Corresponding author.
E-mail addresses: arup.cu@gmail.com, abanthro@caluniv.ac.in (A.R. Bandyopadhyay).
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between blood group and viral infectious disease including malaria, cholera and small pox was demonstrated in subsequent studies.[3] The association between ABO blood group polymorphism and TB has been reported in various studies.[4]

Since the distribution of ABO blood group varies among different populations,[5] in the form of cline and TB incidence in the world population also vary among different population groups[2]; therefore, the association of TB and ABO blood group polymorphism might be important issues to study.

With regard to evolutionary aspects of human blood group, it has been well documented that all the world population possesses specific blood group which is susceptible or resistant with specific disease.[6] To the best of our knowledge, the present work is the maiden attempt on the study of the association of ABO blood group with TB in Eastern India among the Bengalee Hindu caste population from West Bengal. In this circumstance, the objective of the present study is to understand the association of ABO blood group polymorphism and TB in Bengalee Hindu caste population.

2. Material and methods

The present study consists of 100 clinically diagnosed TB of Bengalee adult patients with age ranging from 18 to 80 years from K.C. Roy TB hospital Jadavpur and Bengal Tuberculosis Association, Kolkata. The blood sample has been collected in EDTA tubes and transported to Human Genetics Laboratory of Department of Anthropology, University of Calcutta in ice bucket. On the other hand, 100 apparently healthy adult individuals (having no history of TB in the family) with age range 18–80 from Bengalee population from the same area has also been collected by finger puncture in EDTA tubes and transported to Human Genetics Laboratory, Department of Anthropology in an ice bucket. Informed verbal consent has been obtained from each of the participants. ABO blood grouping was done by standard technique[7] and allele frequencies of ABO blood groups were computed by maximum likelihood estimation.[8] Descriptive and inferential statistics were done by SPSS (version 16) software. The cut-off value was set as $p = 0.05$.

3. Results

Distribution of ABO blood group and their allele frequencies (Table 1) demonstrated 21% A blood group, 34% B blood group, 25% AB blood group, and 20% with O blood group among the TB patients, while the controls revealed 20% of A blood group, 37% B blood group, 10% AB blood group, and 33% having O blood group. On the other hand, allele frequency estimations demonstrated highest allele frequency of B allele (0.39) followed by allele O (0.39) and A allele (0.35). On the contrary, control group presented highest allele frequencies of O (0.57), followed by B (0.27), and least in A (0.16). However, the allele frequencies of the controls were found to be in corroboration with earlier study from Bengalee Hindu Caste population.[9] The distribution of ABO blood groups of both the TB patients ($Chi^2 = 3.63$, 1df, $p > 0.05$) and the controls ($Chi^2 = 0.48$, 1df, $p > 0.05$) were found to be in Hardy Weinberg equilibrium.

However, it has been found (Table 2) that there exists a significant difference ($Chi^2 = 9.98$, 3df, $p < 0.05$) of ABO blood group distribution among the controls and TB due to significant excess ($p < 0.05$) of AB blood group and significant decrease ($p < 0.05$) of O blood group among the TB patients in comparison to the controls. Furthermore, the logistic regression analysis revealed that individuals with A blood group have 1.73 times (95% CI 0.76–3.96) greater chance of developing TB than individuals with O blood group. Individuals with B blood group have 1.52 times (95% CI 0.73–3.13) greater chance of developing TB than individuals with O blood group. Individuals with AB blood group have 4.13 times (95% CI 1.64–10.35) greater chance of developing TB than individuals with O blood group. Individuals with non O blood group have 1.97 times (95% CI 1.04–3.75) greater chance of developing TB than individuals with O blood group. It would be apparent from the present study that significant increase ($p < 0.05$) of AB blood group and significant decrease ($p < 0.05$) of O blood group have been found among TB patients in comparison to control. Therefore, the present study stimulates further population screening for the association of TB and ABO blood group polymorphism in different population.

Table 1 – Distribution of ABO Blood group phenotypes and allele frequencies in tuberculosis patients and controls.

	N	ABO phenotype				ABO allele frequency			Chi^2 (1df)
		A	B	AB	O	A	B	O	
TB patients	100	21 (21.00)	34 (34.00)	25 (25.00)	20 (20.00)	0.26	0.35	0.39	0.48
Controls	100	20 (20.00)	37 (37.00)	10 (10.00)	33 (33.00)	0.16	0.27	0.57	3.63

Figures in the parenthesis denote the percentage.

Table 2 – Distribution of ABO blood group among tuberculosis patients and controls.

	N	A	B	AB	O	Chi^2 (3df)
TB Patients	100	21 (21.00)	34 (34.00)	25 (25.00)	20 (20.00)	9.81*
Controls	100	20 (20.00)	37 (37.00)	10 (10.00)	33 (33.00)	

Figures in the parenthesis show the percentage values.
* $p < 0.05$.

4. Discussion

TB remains major infectious disease in developing countries. Several risk factors have been reported to be associated with susceptibility of TB.[6] Apart these factors, ABO blood group is one of the factors which are responsible for TB envisaged from present case-control study among Bengalee caste Hindu population. Furthermore, previous studies have been demonstrated on the ABO blood group association with infectious diseases. O blood group has selective advantage against severe malaria and cholera. Subsequently, A blood group has selective advantage against small pox.[3] The present study demonstrated that AB blood group has significant ($p < 0.05$) predominance in TB patients than control group. Moreover, the present study also revealed an increased risk associated with the decrease of O allele frequency. The present study corroborated with earlier study[10] and envisaged the utilization of ABO blood group for screening and understanding the susceptibility of TB and could be effective in public health issues.

Conflicts of interest

The authors have none to declare.

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REFERENCES

1. Chatterjee A, Mistry N. MIRU-VNTR profiles of three major *Mycobacterium tuberculosis* spoligotypes found in western India. *Tuberculosis*. 2012;93:250–256.
2. *WHO Global Tuberculosis Report 2015*. http://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020summary.pdf?ua=1 Accessed 11.03.2016.
3. Anstee JD. The relationship between blood group and disease. *Blood*. 2015;115:4635–4643.
4. Rao BN, Reddy VD, Sahu PS, Veerendra Kumar A, David MA, Yugandhar P. The ABO blood group distribution and pulmonary tuberculosis. *J Clin Diagn Res*. 2012;6:943–946.
5. Mourant AE, Kopec AC, Sobczak KD. *The Distribution of the Human Blood Groups and Other Polymorphisms*. London: Oxford University Press; 1976.
6. Skripal IG. ABO system of blood groups in people and their resistance to certain infectious diseases (prognosis). *Mikrobiol Z*. 1996;58:102–108.
7. Boorman KE, Dodd BE, Lincolin PJ. *Blood Group Serology*. New York: Churchill Livingstone; 1977.
8. Cavalli-Sforza LL, Bodmer WF. *The Genetics of Human Populations*. San Francisco: W.H. Freeman and Company; 1971.
9. Bandyopadhyay AR, Chatterjee D, Chatterjee M, Ghosh JR. Maternal Fetal Interaction in the ABO system: a comparative analysis of healthy mother and couples with spontaneous abortion in Bengalee population. *Am J Hum Biol*. 2011;23:76–79.
10. Jain RC, The ABO. blood groups and pulmonary tuberculosis. *Tubercle*. 1970;51:322–323.

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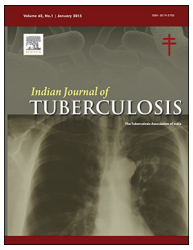

Original Article

A retrospective cohort study of 756 cases of abdominal tuberculosis: Two decades single centre experience

Poras Chaudhary [a,*], *Rajiv Kumar* [a], *Neelam Ahirwar* [b], *Ishaq Nabi* [b], *Santosh Gautam* [b], *Chandrakant Munjewar* [b], *Ajay Kumar* [c]

[a] *Associate Professor, Department of General Surgery, Lady Hardinge Medical College and Associated Dr RML Hospital, New Delhi, India*
[b] *Postgraduate Student, Department of General Surgery, Lady Hardinge Medical College and Associated Dr RML Hospital, New Delhi, India*
[c] *Director Professor and HOD, Department of General Surgery, Lady Hardinge Medical College and Associated Dr RML Hospital, New Delhi, India*

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ABSTRACT

Aim/objective: India accounts for the highest tuberculosis burden in the world, and abdominal tuberculosis has been an endemic surgical and gastroenterological problem. Aim of this study is to present our two decades experience on abdominal (gastrointestinal) tuberculosis.
Method: 756 patients, who received standard antituberculous treatment with or without surgical treatment with the diagnosis of abdominal tuberculosis from January 1996 and May 2014, were reviewed retrospectively. On the basis of clinical presentation, four groups of clinical presentation were identified and various diagnostic measures used in different groups were studied. Numeric values were determined as percent or mean ± standard deviation. Kruskal–Wallis test was used for quantitative results and chi-square test was used for qualitative results between groups. p value of less than 0.05 was considered to indicate the statistical significance.
Results: The duration of symptoms was variable in this study. Out of 756 patients, 64 patients gave definite past history of tuberculosis. Most of the patients in the acute pain abdomen group required surgery while most patients in chronic pain group responded well to medical management. There was significant difference in mortality among the four groups ($p = 0.025$).
Conclusion: Prognosis seems significantly related to the severity of disease, with graver prognosis and less symptomatic improvement in more seriously ill presentations.

1. Introduction

Tuberculosis is a disease of great public health importance in India. Not only does tuberculosis afflict 3.1 million people in India,[1] but it is also estimated that the lifetime risk for acquiring tuberculosis is 10%.[1] Mycobacterium tuberculosis is an acid fast bacillus that is aerobic, non-motile, non-sporing and non-capsulated. These bacteria are readily ingested by phagocytes but are resistant to intracellular killing. Source of infection for tuberculosis is a sputum positive (open) case of pulmonary tuberculosis. Tuberculosis affects all ages. Factors

* *Corresponding author*. Tel.: +91 11 9891447358; fax: +91 1123404410.
E-mail address: drporaschaudhary@yahoo.com (P. Chaudhary).
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that predispose a host are: genetic susceptibility, age, immune-competence, stress, nutrition and coexisting illness. Social factors such as poor quality of life, poor housing, overcrowding and undernutrition are important for tuberculosis infection and subsequent disease.[2] After the development of primary tuberculosis (characterized by Ghon's focus, Ghon's complex and Ranke's complex), the development of secondary tuberculosis, progressive pulmonary tuberculosis and extra-pulmonary tuberculosis are all dependent on the immune-competence of the host.

Abdominal tuberculosis is defined as tubercular infection of the abdomen involving parts of gastrointestinal tract, peritoneum, omentum, mesentery and its nodes and other solid intra-abdominal organs like spleen, liver and pancreas. It is one of the most common forms of extrapulmonary tuberculosis.[3] Despite the advent of effective antitubercular chemotherapeautic drugs, abdominal tuberculosis continues to persist as an endemic surgical and gastroenterological problem in tropics. With spread of AIDS, tuberculosis has become increasingly frequent in urbanized world also.[4,5]

In patients with abdominal tuberculosis, the highest incidence of disease is noted in the gastrointestinal tract and in the peritoneum followed by mesenteric lymph nodes. Within the GI tract, the ileocaecal area is the most common site of involvement.[6,7]

It is difficult to clinch the diagnosis in a patient with abdominal tuberculosis because of its protean manifestations mimicking several diseases and requires a high index of suspicion. The patient's subjective complaints on admission usually guide the diagnostic procedures. Inspite of development in diagnostic tools, it usually takes a long time to get accurate diagnosis in clinical practice.

This study aims at investigating the relation of various symptomatic presentations with clinical diagnosis and prognosis of abdominal tuberculosis and to find out the percentage of abdominal tuberculosis requiring conservative/surgical treatment.

2. Method

A record total number of 756 patients who received standard antiuberculous treatment with or without surgical treatment with the diagnosis of abdominal tuberculosis (excluding solid organs like liver, pancreas, spleen, kidney) in surgical unit-6 at Dr Ram Manohar Lohia hospital, New Delhi between January 1996 and May 2014 were reviewed retrospectively. The data were collected from in-patient and out-patient department record and directly observed treatment, short course (DOTS) centre at Dr Ram Manohar Lohia hospital. Patients who had abdominal tuberculosis as a part of miliary tuberculosis, presence of gastrointestinal malignancy and patients with HIV were excluded.

The early symptoms, associated constitutional symptoms, clinical examination findings, family history of tuberculosis and parameters including age, gender, duration since the onset of symptoms before seeking any form of treatment were evaluated. Based on clinical presentation, four groups of clinical presentation were identified and various diagnostic measures used in different groups were studied.

Group 1: chronic abdominal pain with or without associated constitutional symptoms.

Group 2: ascites with or without pain abdomen (acute or chronic), with or without constitutional symptoms of tuberculosis.

Group 3: abdominal mass with or without ascites, with or without pain abdomen, with or without constitutional symptoms.

Group 4: acute pain abdomen with or without any history of chronic pain abdomen.

Diagnostic procedures namely abdominal ultrasound (US), X-ray chest PA view, barium meal follow through, contrast enhanced computed tomography (CECT), colonoscopy, haemogram with ESR, Liver and renal function tests, sputum for acid fast bacilli, ascitic fluid adenosine deaminase, PCR, and laparoscopy which had been performed were evaluated. Surgical treatment, disease and treatment associated morbidity and mortality were also evaluated. The protocol was approved by the ethical review board of the institute.

2.1. *Statistical analysis*

Numeric values were determined as percent or mean ± standard deviation. Kruskal–Wallis test was used for quantitative results and chi-square test was used for qualitative results between groups. p value of less than 0.05 was considered to indicate the statistical significance.

3. Results

There were 362 patients in acute abdomen group (Table 1). There were 410 male and 346 female patients (Table 1). There was no significant difference in sex distribution across the four groups ($p = 0.692$). Table 2 shows mean age in each group. The predominant age group commonly affected was 11–20 years

Table 1 – Number of patients and sex distribution in each group.

Group	Number of patients		Sex			
	Frequency	Percent	Male		Female	
			Frequency	Percent	Frequency	Percent
Chronic pain	227	30	106	46.7	121	53.3
Ascites	91	12	46	50	45	50
Mass	76	10	32	40	44	60
Acute abdomen	362	48	226	62.5	136	37.5

Table 2 – Mean age and distribution of symptoms in each group.

Group	Age		p value	Duration of symptoms		p value
	Mean	Standard deviation		Mean	Standard deviation	
Chronic pain	27.87	11.843	0.152	11.5	11.050	0.317
Ascites	20.17	3.920		7.167	2.994	
Mass	36	9.513		17	16.522	
Acute abdomen	28.23	9.939		12.517	11.548	

Table 3 – Analysis of clinical features.

Clinical features	Frequency	Percent	p value
Symptoms			
Abdominal pain	756	100	0.00
Loss of appetite	586	78	0.652
Loss of weight	481	64	0.001
Fever	496	66	0.059
Distension	481	64	0.018
Menstrual complaints	151	43.5	0.306
Constipation	236	34	0.018
Diarrhoea	121	16	0.197
Nausea/vomiting	586	78	0.173
Signs			
Pallor	378	50	0.018
Peripheral lymphadenopathy	62	8	0.647
Abdominal distension	482	64	0.018
Doughy feel	106	14	0.015
Ascitis	121	16	0.00
Tenderness	437	58	0.055
Abdominal lump	77	10	0.00
Guarding/rigidity	242	32	0.018
No obvious clinical signs	53	7	

(32%). For females predominant age group was 11–20 years and for males 21–30 years. There was no significant difference in age distribution across the four groups ($p = 0.152$).

The duration of symptoms was variable in this study. The mean duration of symptoms in each group is shown in Table 2. There was no significant difference in duration of symptoms across the four groups ($p = 0.317$). The common symptoms and signs in 756 patients are given in Table 3.

Out of 756 patients, 64 patients gave definite past history of tuberculosis, 48 patients had pulmonary tuberculosis in past. Family history of tuberculosis was found in 38 patients. Haemoglobin levels were less than 10 gram% in 302 patients and were less than 8 gram% in 103 patients. The ESR was found to be raised in almost all the cases with values of more than 30 mm/h in 582 patients. The mean and standard deviation of haemoglobin and ESR level of four groups is given in Table 4. The white cell counts were raised significantly (>11,000/cu. mm) in 81 patients. Montoux test was done in 658 patients and was found to be positive in 546 patients. There was significant difference in montoux positivity across the four groups ($p = 0.019$). Highest positivity was found in acute abdomen group (100%) while least in chronic pain group (64.3%). The chest X-ray was normal in 511 patients. Table 5 shows various pulmonary lesions. Chest X-ray findings were compared between the four groups and it was found that there was no significant difference across the four groups ($p = 0.310$). Plain X-ray abdomen in erect posture (Table 5) was done in all the patients and it was found to be normal in 262 (32.1%) patients. Findings suggestive of tuberculosis were found in 87.5% of acute abdomen group while in 20% of mass abdomen group. Plain-ray abdomen findings were significant across the four groups ($p = 0.004$).

Ultrasonography whole abdomen was done in all the patients and findings are summarized in Table 5. Ascitic fluid of 209 patients was subjected to cytobiochemical examination and in all of these patients, the ascitic fluid was exudative in nature and after excluding all other causes, the ascitic fluid was considered to be tubercular in origin. There was significant difference in ascitic fluid cell count in between the four groups (0.00). Patients in the ascites group had highest mean cell count (321.50) while acute abdomen had the least (37.0). Table 4 summarizes the ascitic fluid protein and adenosine deaminase (ADA) levels. There was significant difference in ascitic fluid protein and ADA levels in between the four groups (0.00).

Barium meal follow through (BMFT) was done in 443 patients. In some patients, BMFT was not done as other investigations were already done to support the diagnosis and in others emergency laparotomy had to be done for complications such as perforation peritonitis or intestinal obstruction. Out of 443, BMFT was suggestive of tuberculosis in 107 patients.

Table 4 – Haemoglobin, ESR, ascitic fluid protein and ADA in four groups.

Group		Haemoglobin	ESR	Ascitic fluid protein	Ascitic fluid ADA
Chronic pain	Mean	12.2133	43.67	0.87	9.07
	Standard deviation	2.8710	20.038	1.506	18.862
Ascitis	Mean	9.8333	44.83	3.42	84.53
	Standard deviation	3.0302	14.372	0.286	13.207
Mass	Mean	9.7200	37.20	0.64	9.80
	Standard deviation	1.0473	12.834	1.431	21.913
Acute abdomen	Mean	9.5167	49.71	0.42	6.58
	Standard deviation	2.6705	22.204	1.143	17.968

Table 5 – Findings of imaging studies.

Imaging findings		Frequency	Percent
Chest X-ray	Prominent hilars	92	12
	Pleural effusion	32	4
	Old Koch lesion (calcification)	77	10
	Active lesion (cavity)	29	4
	Fibrosis	15	2
	Normal	511	68
X-ray abdomen	Gas under diaphragm	182	24
	Multiple air fluid levels	237	32
	Ground glass appearance	75	10
	Calcifications	0	0
	Normal	262	34
Ultrasonography	Dilated bowel loops	496	66
	Thickened and matted loops	194	26
	Free fluid	347	46
	Mesenteric lymph node enlargement	197	26
	Hypertrophic ileocaecal junction with mass	75	10

ELISA was performed on 607 patients. Positive values were seen in 403 patients (66.39%). There was significant difference in ELISA positivity in between the four groups ($p = 0.002$). Colonoscopy was done 313 patients. Biopsy was attempted in all the patients and findings were suggestive of abdominal tuberculosis in 223 (70.6%) patients. Computed Tomography of abdomen was done in 298 patients and it was suggestive of tuberculosis in 114 (37.58%) patients.

Diagnosis of abdominal tuberculosis was based upon one of the criteria as described in Table 6. Table 6 shows treatment modality in each group and clearly shows that most of the patients in the acute pain abdomen group required surgery while most patients in chronic pain group responded well to medical management. There was significant difference across the groups of the number of patients getting treatment either in the form of medical or surgical intervention ($p = 0.010$).

Table 7 shows per-operative findings. Mesenteric lymphadenopathy and perforations were the most common findings. The disease was most commonly seen in small bowel followed by involvement of mesenteric lymph nodes (Table 7). Various procedures done are shown in Table 7. There were 5 cases in which nothing could be done because of dense adhesions and cocoon formation. Out of these 8 cases with cocoon, loop ileostomy was made in 3 cases and rest of the 5 cases were closed without exploring any further. All of these cases were put on standard antituberculous therapy. Out of these 8 cases, 4 were re-explored as they presented with recurrent episodes of intestinal obstruction. On exploration after 8 weeks of antituberculous therapy (ATT), it was found cocoon and adhesions were decreased and exploration with definite surgery was possible in these cases.

Patients once diagnosed were given standard ATT and followed for improvement or development of complications thereafter (Table 6). There was significant difference in mortality among the four groups ($p = 0.025$).

Table 6 – Diagnostic, treatment modality and complications and prognosis in four groups.

Management parameters		Frequency and percent	Chronic pain	Ascitis	Mass	Acute abdomen	Total
Diagnostic modality	AFB smear culture/PCR/ELISA	Frequency	91	75	31	120	317
		Percent	40	83.3	40	33.3	42
	Histopathology	Frequency	76	0	46	195	317
		Percent	33.3	0	60	54.2	42
	Therapeutic trial	Frequency	61	16	0	45	122
		Percent	26.7	16.7	0	12.5	16
Treatment modality	Medical	Frequency	211	61	62	153	487
		Percent	93.3	66.7	80	41.7	64
	Surgical	Frequency	16	30	14	209	269
		Percent	6.7	33.3	20	58.3	36
Complications and prognosis	Symptomatic improvement		100%	66.7%	100%	95.8%	
	Anastomotic leak		0	0	0	4	
	Faecal fistula		0	0	0	5	
	Burst abdomen		0	0	0	14	
	Drug side effects		5	4	0	12	
	Mortality		0	4	0	5	
	Relapse		4	4	0	0	

Table 7 – Operative findings and procedures.

Operative parameters	Findings	Frequency	Percent
Peroperative findings	Mesenteric lymphadenitis	112	42
	Perforation	78	29
	Adhesions	115	43
	Strictures/obstruction	52	19
	Tubercles	134	50
	Bands	15	5.5
	Pyoperitoneum	39	14.5
	Cocoon	08	03
Distribution of disease	Stomach	00	O0
	Duodenum	04	0.05
	Jejunum	30	3.9
	Ileum	260	34
	Caecum/appendix	16	2.1
	Colon	06	0.07
	Anorectal	04	0.05
	Mesenteric lymph nodes	247	33
	Peritoneum	276	36
	Solid organs (hepatobiliary/pancreatic/splenic)	11 (4/5/5)	1.5
Procedure	Primary repair of perforation	107	40
	Ileostomy	44	16
	Resection anastomosis	48	17
	Stricturoplasty	106	40
	Open peritoneal lavage	39	15
	Adhesiolysis	38	15
	No procedure on exploration	05	02

4. Discussion

Gastrointestinal tuberculosis is unique in a way that it presents in various ways, there are number of tests to support diagnosis but no single test is confirmatory except for direct histopathological proof, therefore, it becomes difficult to diagnose it with certainty. Medical treatment of gastrointestinal tuberculosis is same as that for other types of extrapulmonary tuberculosis (EPT) but it differs from other forms of EPT in that with initiation of antituberculous treatment, the chances of going into obstruction and thus need for surgical intervention increases in hyperplastic type of ileocaecal tuberculosis.

Diagnosis of tuberculosis in initial stages, when the patient presents with vague abdominal pain or any other vague symptoms without constitutional symptoms of tuberculosis or symptoms of intestinal obstruction, imaging study like US also fails to show anything, it becomes extremely difficult to diagnose gastrointestinal tuberculosis. Initial study of choice for any abdominal pathology is US and in initial stages of gastrointestinal tuberculosis, US may not show anything or fails to pick up small lesions such as tubercles or mesenteric lymphadenitis and following this normal US report, in majority of the cases, it is assumed that pain is probably due to amoebic colitis or some other parasitic infestation, which are again very common in India. This starts the chain of misdiagnosis and the patients are often put on symptomatic treatment which helps in progression of disease process. So, need of the hour is to recognize and arrest the disease at this early stage to stop its further progression and to prevent morbidity and mortality.

The reported incidence of coexistence of abdominal with pulmonary tuberculosis varies from 5 to 36%.[8] To diagnose the disease at an early stage, in addition to detailed clinical history, including past history of pulmonary tuberculosis or any other form of EPTB, stress should also be given to other minor but contributory factors such as socioeconomic status, BCG vaccination status, immunity status, and awareness about the disease, as they all might point towards tuberculosis. The most common symptom, in those who presented early before development of constitutional symptoms, was periumbillical pain, followed by fever which responded to wide spectrum antibiotics, increased frequency of bowel movements, changed consistency/frequency of stool, nausea, and weakness.

Out of 756 patients, most common symptomatic presentation was non-specific chronic abdominal pain present in all the patients. The clinical presentation depends on the site of involvement. Although a wide index of suspicion is required to diagnose abdominal TB in time, however, constellation of presentation such as abdominal pain (100%), nausea/vomiting (78%), distension of abdomen (64%) were most sensitive indicators of abdominal tuberculosis. Abdominal lump (10%) and diarrhoea (16%) were rare presentations. Most common signs observed in this study were abdominal distension (64%), tenderness (58%), and pallor (50%), while peripheral lymphadenopathy was found in only 8% of cases. None of the sign was suggestive of abdominal tuberculosis. Classical doughy abdomen was found in 14% of patients. A combination of good history and findings may suggest tuberculosis.

The sonographic findings are non-specific but may be of great help in supporting diagnosis when correlated appropriately in a given clinical situation. The characteristic features of early abdominal tuberculosis on sonography are mesenteric thickness of 15 mm or more and an increase in mesenteric echogenicity with mesenteric lymphadenopathy.[9] Fine septae may be seen in ascitic fluid. Till recently, barium studies have

been the most helpful part for diagnosing intestinal tuberculosis but now it has been replaced by CT scan of the abdomen as it can also diagnose extraintestinal foci of tuberculosis but for demonstrating mucosal lesions barium studies still remain superior.[10] In this study, Barium study was done in 443 patients and it was suggestive of tuberculosis in 336 patients. Colonoscopy is the easiest and direct method of establishing diagnosis of colonic tuberculosis and when combined with biopsies, it has a definite advantage over imaging studies.[11]

Adenosine deaminase (ADA) and interferon-r (IFN-r) in ascitic fluid are sensitive and specific markers for abdominal tuberculosis.[12] IFN-r is twice as expensive as ADA test, so, ADA is particularly useful in developing countries.

Conservative management is successful in a large number of patients with abdominal tuberculosis as concluded in various studies[13,14] and suggested by this study also. Conservative treatment includes initiation of standard antituberculous therapy along with symptomatic treatment.[14] Surgery is usually done for complications such as perforation, obstruction and fistula formation. Surgery is also done when there is no improvement in symptoms on conservative treatment. Obstruction is the most common complication of gastrointestinal tuberculosis which may be due to extensive adhesion formation or stricture formation. Fistulas and perforations are encountered less frequently. The reported incidence of enteric perforation ranges from 1 to 15%.[15] In the present study, 78 patients were found to have perforation. Cocoon formation is the most dreaded and difficult scenario. Nothing much can be done on exploration as adhesiolysis in such a situation may result in fistula formation which further complicates the disease. This was seen in 8 patients and all the cases were closed. Initiation of antituberculous drugs resulted in improvement in these patients.

Conventionally, abdominal tuberculosis patients have been treated with antituberculous drug regimens for 8–12 months duration.[13] Recently, a 6 month, short course chemotherapy regimen has been found to be as effective as the standard 12-month regimen.[14]

Prognosis seems significantly related to the severity of disease, with graver prognosis and less symptomatic improvement in more seriously ill presentations (acute abdomen group in this study). There is higher mortality in such patients. Post-operative course and complications were also severe in acute abdomen group and drug toxicities were also found to be more common in this group of patients. In our study, we had a large number of patients with acute presentations than chronic, this may be due to the fact that being a tertiary care referral centre, patients with more serious condition get referred, confounding the results of our study.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Dandapat MC, Mishra BM, Dash SP, Kar PK. Peripheral lymph node tuberculosis: a review of 80 cases. *Br J Surg*. 1990;77 (August (8)):911–912.
2. Park K. *Epidemiology of Communicable Diseases. Park's Textbook of Preventive and Social Medicine*. 21st ed. Bhanot Jabalpur; 2011:132–138.
3. Tribedi SD, Gupta DM. Intestinal tuberculosis in Bengal. *Indian Med Assoc*. 1941;11:41–44.
4. Aliyu MH, Salihu HM. Tuberculosis and HIV disease: two decades of a dual epidemic. *Wein Klin Wochenschr*. 2003;115:685–697.
5. Guth AA, Kim U. The reappearance of abdominal tuberculosis. *Surg Gynecol Obstet*. 1991;172:432–436.
6. Singh V, Jain AR, Agarwal AK, et al. Clinicopathological profile of abdominal tuberculosis. *Br J Clin Pract*. 1995;49:22–24.
7. Patel N, Amrapurkar D, Agal S, et al. Gastrointestinal luminal tuberculosis: establishing the diagnosis. *J Gastroenterol Hepatol*. 2004;19:1240–1246.
8. Hulnick DH, Megibow AJ, Naidich DP, et al. Abdominal tuberculosis: CT evaluation. *Radiology*. 1985;157:199–204.
9. Jain R, Sawhney S, Bhargava DK, et al. Diagnosis of abdominal tuberculosis: sonographic findings in patients with early disease. *Am J Roentgen*. 1996;165:1391–1395.
10. Vanhoenacker FM, De Backer AI, Op de BB, et al. Imaging of gastrointestinal and abdominal tuberculosis. *Eur Radiol*. 2004;14:103–115.
11. Pettengell KE, Pirie D, Simjee AE. Colonoscopic features of early intestinal tuberculosis: report of 11 cases. *S Afr Med J*. 1991;79:279–280.
12. Sathar MA, Simjee AE, Coovadia YM, et al. Ascitic fluid gamma interferon concentrations and adenosine deaminase activity in tuberculosis peritonitis. *Gut*. 1995;36:419–421.
13. Chuttani HK, Sarin SK. Intestinal tuberculosis. *Indian J Tuber*. 1985;32:117–119.
14. Balasubramanian R, Narayan M, Balambai R, et al. Randomized controlled trial of short course chemotherapy in abdominal tuberculosis: a five year report. *Int J Tuberc Lung Dis*. 1997;1:44–51.
15. Sharma MP. Abdominal tuberculosis. *Ind J Surg*. 2005;82:2106–2112.

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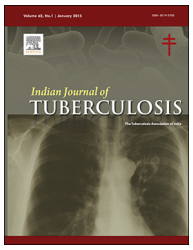

Original Article

TB management by private practitioners – Is it bad everywhere?

P.S. Rakesh [a,*], Shibu Balakrishnan [b], S. Jayasankar [c], R.V. Asokan [d]

[a] Amrita Institute of Medical Sciences and Research Center, Amrita Viswavidhyapeetham, Kerala, India
[b] WHO RNTCP Technical Assistance Project, WHO Country Office, India
[c] Project Director, Kerala State AIDS Control Society, India
[d] Dean Hospital, Punalur, Kerala, India

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ABSTRACT

Introduction: Poor prescribing practice is alleged to be one of the major factors fuelling the drug-resistant tuberculosis (DR TB) emergence. A study in Mumbai revealed the extent of inappropriate tuberculosis (TB) management practices of private practitioners and discussed that with the context of high DR TB. Kerala is rated among the well performing States in India as far as TB control is concerned with evidences for a lower level of TB transmission and DR TB. The current study was done in Kerala State to assess the prescribing practices of private sector doctors in the treatment of TB.

Methods: Survey questionnaire to write a standard prescription for treating TB was administered to private practitioners dealing with TB, who attended continuing medical education programme on TB at two major cities in Kerala.

Results: Responses from a total of 124 questionnaires were studied. None of them prescribed anti-TB regimen for less than 6 months. Only 7 (5.6%) prescribed a regimen without complete four drugs (H, R, Z, E) in the intensive phase. Out of the 81 doctors who prescribed private anti-TB regimen, 67 (82.7%) had of the opinion that not less than 80% of their patients complete the treatment for the prescribed duration.

Conclusion: The current study reports a reasonable TB management practice among the private sector doctors from a State with a low prevalence of DR TB and compliments the argument that effective treatment of TB following the principles of standards for TB care can prevent the emergence of DR TB.

1. Introduction

Emergence of drug-resistant tuberculosis (DR TB), particularly drug-resistant multidrug-resistant TB (MDR TB) and extensively drug-resistant TB (XDR-TB) is a matter of great concern. Sub-national drug-resistance surveys have indicated that the prevalence of MDR TB in India is 2–3% among new cases and 12–17% among re-treatment cases.[1] Indiscriminate use of anti-TB drugs, especially outside the Revised National TB Control Programme (RNTCP), has alleged to be contributing significantly to the emergence of drug-resistant TB in India.[2] Poor

* Corresponding author.
E-mail address: rakeshrenjini@gmail.com (P.S. Rakesh).
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prescribing practice is thought to be one of the major factors fuelling the MDR TB emergence.

The vision of India's National TB Control Programme is that the people suffering from TB receive the highest standards of care and support from healthcare providers of their choice. Private sector accounts for more than half of the TB care delivered in India with major challenges as far as quality of diagnosis and treatment is concerned.

A study in Mumbai two decades ago revealed the extent of inappropriate TB management practices of private practitioners (PPs).[3] The study was repeated recently in the same area and concluded that little seems to have changed over these years among doctors working in private sector regarding awareness and practice of prescribing anti-TB regimes.[4] Revealing that 106 practitioners had prescribed 63 different drug regimens for treatment of TB, the study highlighted the magnitude of the poor prescribing practices of PPs. The authors discussed this issue with the alarming trend of increasing incidence of MDR TB in Mumbai. We were wondering whether the awareness and practice of PPs are the same everywhere in India. Hence we conducted a similar study in two major cities of Kerala, where there is high concentration of PPs.

Kerala is rated among the well performing States in India as far as TB control is concerned with evidences for a lower level of TB transmission and DR TB.[5,6] Annual total TB case notification for 2014 was 69 per 100,000 populations. Private sector is well established in health care of the State accounting for more than 70% of all facilities and 60% of all beds. Some of the early initiatives for Public Private Partnership (PPP) for TB control were from the State of Kerala.[7,8] More than 100 designated microscopy centres in private hospitals and laboratories collaborate with the Government to provide RNTCP services. Of the cases registered under RNTCP, approximately 20% of sputum smear positive, 30% of smear negative and extra-pulmonary cases are contributed by private sector. Still a sizable number of TB patients are managed with private regimes. It is important to know whether the care offered to these patients meet standards, to reengineer the current PPP strategy if required.

2. Methods

Two continuing medical education sessions on latest diagnostic modalities and management of tuberculosis were organised for private sector doctors by Initiative for Promoting Affordable Quality TB tests (IPAQT) and their private sector laboratory partners at Thiruvananthapuram and Cochin, two largest cities in Kerala.[9] Doctors practicing modern medicine in the area who provide care for TB were identified and invited for continuing medical education (CME) by the private sector laboratory partners. CMEs were led by renowned faculties. Date and venue were selected appropriately for doctors to participate. Participation was voluntary; no incentives were offered for participation.

Prior to the beginning of the CME session, a short unlinked anonymous questionnaire was handed out to each of the attending doctors. The purpose of the study was described, confidentiality was ensured and they were given the freedom to not to fill the questionnaire if they feel to do so. The questionnaire included general information related to their private practice, TB related practice and a main question ''*to write a prescription for a previously untreated adult case of sputum-positive pulmonary tuberculosis weighing 50 kg*''. The doctors were expected to write a prescription and specify drugs, dosage and duration of treatment in three columns provided. Average time spent by doctors for filling the questionnaire was 5–10 min. The prescriptions written by the doctors were then analysed and compared for appropriateness with those recommended nationally.

3. Results

Of the total of 367 doctors invited, 234 attended the CMEs. One hundred and ninety-eight questionnaires were filled and returned. Among 198, 74 reported that they have not diagnosed or treated a case of TB in the last 1 year and their responses were excluded from the analysis. Responses from a total of 124 questionnaires were studied. The details of number of years in practice, usual number of TB patients diagnosed in a year and their speciality were shown in Table 1.

Of the 124 doctors, 58 (46.7%) doctors reported that they used to prescribe only daily anti-TB regimen. Overall 124 doctors prescribed nine regimens for treating tuberculosis. Of them 34 (27.4%) reported that they have put all the TB patients diagnosed by them on a RNTCP regimen and another 9 (7.2%) reported that they used to refer the patients diagnosed with TB to some specialists. Various regimens prescribed by the doctors were summarised in Table 2.

None of them prescribed anti-TB regimen for less than 6 months while 27 (33.3%) prescribed the drugs for 7–9 months and 10 (12.3%) prescribed the drugs for more than 9 months. Of them seven (5.6%) prescribed a regimen without complete four drugs (H, R, Z, E) in the intensive phase. Out of the 81 private anti-TB prescriptions, 3 (2.4%) had a quinolone. Streptomycin was prescribed by two (1.6%) doctors. Among them, 19 (15.3%) prescribed four drugs (HRZE) for the entire treatment duration.

Out of the 81 doctors, who prescribed private anti-TB regimen, 67 (82.7%) had of the opinion that more than 80% of their patients complete the treatment for the prescribed duration. The responses of doctors regarding duration and follow-up were tabulated in Table 3.

4. Discussion

Treating TB effectively and rationally is not only essential for good patient care but is also a key element in the public health response to TB control. The Standards for TB Care in India (STCI) has been developed by a collaborative effort of Government of India Central TB Division (CTD) and WHO country office for India as a way to engage with the Indian private sector for effective TB prevention and control.[10] We have set STCI as the gold standard to compare the anti-TB prescription practices of private sector doctors of Kerala.

In our study, about 45% of the doctors wrote prescriptions of drugs for longer than 6 months suggesting over rather than under treatment of their TB patients. Only around 5% prescribed a regimen without H, R, Z and E in the intensive

Table 1 – Characteristics of the doctors participated in the study (N = 124).

Characteristics	Categories	Frequency (%)
Number of years in practice	<5 years	22 (17.7%)
	6–15 years	51 (41.1%)
	16–25 ears	30 (24.1%)
	>25 years	21 (16.9%)
Number of new TB patients diagnosed in a year	<2	32 (25.8%)
	3–10	48 (38.7%)
	11–20	27 (21.7%)
	>20	11 (8.8%)
	No response	06 (4.8%)
Specialty	General practice	20 (26.1%)
	Internal medicine	46 (37.1%)
	Respiratory medicine	13 (10.4%)
	Paediatrics	16 (12.9%)
	Others	29 (23.3%)

phase. Overall picture suggested that the possibility of under treatment of TB patients in private practice was low. If the patients adhered to the prescribed treatment, a large majority were less likely to develop multidrug-resistance. More than 80% of the clinicians were of the opinion that not less than 80% of their patients complete treatment, though this needs to be studied further.

The proportion of DR TB among those subjected to culture and Drug Susceptibility Testing at Intermediate Reference Laboratory, Thiruvananthapuram (aggregate of patients who are positive on follow-up microscopy of sputum smear, retreatment cases, HIV positive TB cases and contacts of MDR TB) was less than 4% in the recent years. A recent study report from a tertiary care referral private hospital in Ernakulam performing CB NAAT (Cartridge Based Nucleic Acid Amplification Test) reported only 4 Rifampicin resistant cases out of 76 TB cases identified from 459 specimens, which also included sputum specimens from treatment failure and retreatment cases.[11] All these findings iterate that the prevalence of DR TB might be low in Kerala as compared to other parts of the country.

Table 2 – Summary of the anti-TB prescriptions by private sector doctors (N = 124).

Responses by doctors	Number (%)
Refer the patient to RNTCP	34 (27.4%)
Refer the patient to a physician/respiratory Medicine	09 (7.2%)
HRZE for intensive phase and HR for continuation phase	11 (8.8%)
HRZE for intensive phase and HRE for continuation phase	28 (22.5%)
HRE for intensive phase and HR for continuation phase	04 (3.2%)
HRZES for intensive phase and HRE for continuation phase	02 (1.6%)
HRZE + quinolone for entire duration	02 (1.6%)
HRZ + quinolone for entire duration	01 (0.8%)
HRZE for entire treatment duration	19 (15.3%)
HRE for entire duration of treatment	02 (1.6%)
No response	12 (9.6%)

Udwadia et al. discussed the poor prescribing practice of private sector doctors as a major factor fuelling the MDR TB epidemic in some parts of the country.[4] The current study compliments the discussions of Udwadia et al. by highlighting the brighter side of the coin, that is, a reasonable TB management practices among the private sector doctors in an area with a low prevalence of DR TB.

Kerala State has achieved near universal literacy for both males and females and many of the maternal and child health indicators are comparable to countries with more advanced economies. This has been generally attributed to inter-sectoral factors such as the spread of education, political awareness, development of road networks and transportation, social movements and greater health consciousness of the people. However, the role of the health care sector itself cannot be ignored. Many Public Private Partnership strategies for TB control started in the State during early years of RNTCP implementation itself. Government of Kerala has endorsed International Standards of TB Care in 2007. Indian Medical Association played an important role in sensitising private sector doctors through a series of CMEs and training programmes using RNTCP Technical and Operational guidelines from 2005 onwards through IMA-GFATM-RNTCP-PPM initiatives. While deigning the PPM strategies also, State TB Control team has given due importance to promotion of standards rather than attracting private doctors to RNTCP.

A recent experience from Practical Approach to Lung Health pilot project implementation in Kerala has shown that a clear treatment protocol, good quality training and continuous supervision and monitoring resulted in rationalising the prescribing practices and improvement in the quality of care for chronic respiratory disease patients.[12] In the context of TB, STCI gives an opportunity to rationalise the prescribing practices for TB in the country, if disseminated well among doctors with a mechanism to monitor and supervise.

The present study collected information from doctors who were invited for a CME session. This might have introduced a volunteer bias with a likelihood of only those doctors who wanted to update their knowledge or those who had the time available attended the CME. The delegates represented a good mix of doctors ranging from general practitioner to chest specialists and we feel it as a good representative cross-section

Table 3 – Responses of doctors regarding duration of private anti-TB regimen and follow-up (N = 81).

Question	Categories	Number (%)
For how long (duration) you usually insist for private anti-TB treatment for a new TB case (N = 81)	Less than 6 months	0 (0%)
	6 months	36 (44.4%)
	7–9 months	27 (33.3%)
	More than 9 months	10 (12.3%)
	No response	08 (9.8%)
Out of 10 new cases you initiated on private anti-TB treatment, how many of them would have completed the treatment for the duration fixed by you (N = 81)	Less than 60%	06 (7.4%)
	60–80%	08 (9.8%)
	More than 80%	67 (82.7%)

of the doctors dealing with TB in two major cities of Kerala. The recent study in Mumbai was also done prior to a CME session. Conducting one-to-one interviews with practicing doctors would have been ideal but it is more time and resource intensive. Many other system doctors were included in the study at Mumbai, but in Kerala, the other system doctors were not legally permitted to prescribe anti-TB drugs. It is also possible that what the doctors reported could reflect only their knowledge and not necessarily their practices. Despite these limitations, the study has many public health implications.

To summarise, the study reports a reasonable TB management practice among the private sector doctors from a State with a low prevalence of DR TB and compliments the argument that effective treatment of TB following the principles of Standards for TB care can prevent the emergence of DR TB.

Conflicts of interest

R.V. Asokan is the National Working Group Member and previous National Co-ordinator of IMA-GFATM-RNTCP-PPM Project. P.S. Rakesh had served as Technical Consultant, IMAGFATM-RNTCP-PPM project, Kerala State. Dr. S. Jayasankar is the Former State TB Officer, Kerala State.

REFERENCES

1. Government of India. *TB India 2012. Annual Status Report*. New Delhi: Central TB Division; 2012.
2. Institute of Medicine (US). *Facing the Reality of Drug-Resistant Tuberculosis in India: Challenges and Potential Solutions: Summary of a Joint Workshop by the Institute of Medicine, the Indian National Science Academy, and the Indian Council of Medical Research*. Washington, DC: National Academies Press; 2012. Available from: http://www.ncbi.nlm.nih.gov/books/NBK92617/.
3. Uplekar MW, Shepard DS. Treatment of tuberculosis by private general practitioners in India. *Tubercle*. 1991;72:284–290.
4. Udwadia ZF, Pinto LM, Uplekar MW. Tuberculosis management by private practitioners in Mumbai, India: has anything changed in two decades? *PLoS ONE*. 2010;5(8):e12023.
5. Kumar S, Radhakrishna. Chadha VK, et al. Prevalence of tuberculous infection among school children in Kerala. *Indian J Tuberc*. 2009;56:10–16.
6. Joseph MR, Shoby CT, Amma GR, Chauhan LS, Paramasivan CN. Surveillance of anti-tuberculosis drug resistance in Ernakulam District, Kerala State, South India. *Int J Tuberc Lung Dis*. 2007;11(4):443–449.
7. Kumar MK, Dewan PK, Nair PK, et al. Improved tuberculosis case detection through public–private partnership and laboratory-based surveillance, Kannur District, Kerala, India, 2001–2002. *Int J Tuberc Lung Dis*. 2005;9:870–876.
8. WHO. *Public–Private Mix for DOTS, Global Progress. Report of the Second Meeting of the PPM Subgroup for DOTS Expansion, New Delhi*. 2004.
9. The Initiative for Promoting Affordable and Quality TB Tests (IPAQT). Available from: http://www.ipaqt.org/index.php [accessed 01.03.16].
10. World Health Organization. *Standards of TB Care in India*. WHO SEA Regional Office and Central TB Division, MOHFW, Govt. of India; 2014. Available from: http://www.searo.who.int/india/mediacentre/events/2014/stci_book.pdf.
11. Sadia K. Experiences with GeneXpert/Rif assay at a tertiary care centre. In: *Paper Presented at TB New Approaches and Developments*. 2015.
12. Ellangovan K, Balakrishnan S, Rakesh PS, et al. *Prescribing Practices Become Rationalized – Results From Practical Approach to Lung Health Pilot Project in Primary Health Care Setting in Kerala*. Thiruvananthapuram: Govt. of Kerala; 2016 [unpublished report].

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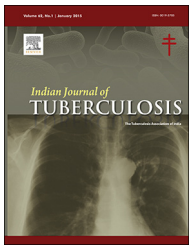

Original Article

Study of factors influencing response and outcome of Cat-IV regimen in MDRTB patients

Arun Kumar Yadav [a], *Ashok Kumar Mehrotra* [a,*], *S.P. Agnihotri* [b], *Shivani Swami* [c]

[a] *Associate Professor, Department of Respiratory Medicine, NIMS Medical College, Jaipur, Rajasthan, India*
[b] *Professor, Institute of Respiratory Medicine, SMS Medical College, Jaipur, Rajasthan*
[c] *Assistant Professor, Department of Respiratory Medicine, NIMS Medical College, Jaipur, Rajasthan*

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ABSTRACT

Background: CAT IV regimen or the standardized drug regimen (SDR) under the Revised National Control Program (RNTCP) uses six second-line anti-tubercular drugs in the initial intensive phase (IP). These drugs have many side effects and toxicity; they are less efficacious and have poor acceptability. The present study was conducted to evaluate the efficacy and outcome of Cat-IV regimen and the factors which influence the treatment outcome in MDR TB patients.

Methods: It was a prospective observational study, which was done in the CAT II treatment failure, LPA proven MDR TB patients, above the age of 18 years, who were referred to DOTS Plus center for treatment. The study was approved by the hospital ethics committee and patient consent was obtained before inclusion.

Results: We observed culture conversion in 63.04% and ADR in 96.5%, default in 15.65%, and death in11.3% cases. The factors which influenced outcome included low body weight, long duration of illness cavitatory disease and indulgence in both tobacco & alcohol. The radiological favorable response strongly and significantly correlated with the bacteriological and clinical response during the IP.

Conclusion: We suggest that the efficacy can be further augmented by reducing default and controlling deaths which accounts for substantial numbers and occur mostly during IP.

1. Introduction

The global prevalence of MDR TB in 2102 was estimated as 650,000 cases with an annual incidence of 3.6% in newly diagnosed and in 20.2% cases in retreatment cases. Out of these cases 9.6% were the extreme drug resistant (XDR) cases.[1,2] Srinath Reddy[1] and Bahera et al.[3] reported incidence of MDR TB in 2.1–2.3% in newly diagnosed and 17–17.4% in retreatment cases in India. RNTCP under the programmatic management of drug resistant tuberculosis (PMDT) or DOTS Plus strategy adopted CAT IV regimen, as standardized drug regimen (SDR) for the treatment of MDR TB since 2007. These CAT IV drugs have poor acceptability because of more side effects and toxicity, irregular availability, high cost and limited efficacy (61%).[4] The present study was conducted to study the

* *Corresponding author at*: 111/199, Vijay Path, Mansarovar, Jaipur 302020, Rajasthan. Tel.: +91 9983224412/9636036298.
E-mail address: mehash49@yahoo.co.in (A.K. Mehrotra).

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efficacy of the regimen and the factors which influence the overall outcome.

2. Material and methods

Definition of MDR-TB Case: ''A patient of pulmonary tuberculosis who has a proven resistance either to ''Rifampicin''(R) and ''Isoniazid'' (H) both or R alone or with one or more anti-tubercular drug from an RNTCP accredited drug sensitivity testing (DST) laboratory.

The study was a prospective observational study, conducted on CAT II failure patients registered at a DOTS Plus site in Jaipur district of Rajasthan in 2012. One hundred and twenty (120) sputum culture positive MDR-TB cases, above the age of 18 years, who gave written consent, were included in the study.

The exclusion criteria included patients residing outside Jaipur district, history of second line anti-tubercular drug treatment for over 1 month, presence of major psychiatric illness, human immunodeficiency virus (HIV) infection, pregnancy, transferred out or transferred in cases, and patient unwilling to give consent for inclusion into the study.

115 patients fulfilled the inclusion criteria. The reasons for the exclusion of 5 patients were, transferred out (2), major psychiatric illness (1) and h/o second line anti-tubercular treatment over one month duration (2).

RNTCP DOTS-Plus Guidelines–2010 methodology[5] was strictly adhered to, in the study. All patients were admitted for pretreatment evaluation before initiation of CAT IV treatment. A good clinical history and baseline data of the patient were recorded. Detailed clinical examination of the respiratory system and screening examination of all other systems were done on each patient. Baseline laboratory tests were done, which included complete blood count (CBC), blood sugar random, liver function tests (LFT), renal Function tests (RFT), thyroid stimulating hormone (TSH), serum electrolytes, serum uric acid, routine urine examination, urine for a pregnancy test for all female patients, HIV serology, X-ray chest PA view and special investigations, whatsoever required for the patient. CAT IV SDR treatment included Kanamycin; six days a week plus daily supervised with cycloserin, ethionamide, ethambutol, pyrazinamide and levofloxacin in initial intensive phase (IP) as per weight band dose schedule mentioned in Table 1. The patients were observed for drug tolerance and adverse drug reactionS (ADRS) during the hospital stay, which were managed with symptomatic treatment and/or temporary discontinuation of possible offending drug. Patients, who tolerated the drugs, were discharged and transferred to their respective DOT center

Table 1 – Weight band guided doses schedule of CAT IV drugs under RNTCP and their common side effects.

S.No	Drug	Weight bands govern doses			Common side effects
		16–25 kg	26–45 kg	46–70 kg	
1	Aminoglycosides; Kanamycin	500 mg	500 mg	750 mg	Ototoxicity, Nephrotoxicity, Vertigo, Electrolyte imbalance
2	Levofloxacin	250 mg	750 mg	1000 mg	GIT symptoms: diarrhea, vomiting, and abdominal pain Central nervous system (CNS): dizziness and convulsions, Photo toxicity and Skin rash, photosensitivity, Nephrotoxicity, Cardio-toxicity, Arthralgia Tendinopathy and tendinitis
3	Ethionamide	375 mg	500 mg	750 mg	Gastro-intestinal: epigastric discomfort, anorexia, nausea, metallic taste, vomiting, excessive salivation, and sulfurous belching, Hepatitis Psychiatric: hallucination and depression, Hypothyroidism and goiter with prolonged administration, Gynaecomastia, menstrual disturbances, impotence, Acne, headache, and peripheral neuropathy
4	Ethambutol	400 mg	800 mg	1200 mg	Visual disturbance: acuity of vision, scotomas, constriction of field of vision
5	Pyrazinamide	500 mg	1250 mg	1500 mg	Arthralgia, Hyperuricaemia, Hepatitis, Pruritis with or without rash
6	Cycloserine	250 mg	500 mg	750 mg	CNS: dizziness, slurred speech, convulsions, headache tremor, and insomnia Psychiatric: confusion, depression, altered behavior, and suicidal tendency Hypersensitivity reaction
7	Pyridoxine	50 mg	100 mg	100 mg	
Reserve drugs;					
To be substituted for change of any of the above drug					
1	Na-PAS (80%weight/volume)	5 g	10 g	12 g	Gastro-intestinal: anorexia, nausea, vomiting, and abdominal discomfort, Hepatic dysfunction, Skin rash, GIT symptoms may be due to the bulk of drugs and/or due to ethionamide, PAS, pyrazinamide and ethambutol Hypokalemia, Hypothyroidism and goiter with prolonged administration
2	Moxifloxacin (Mfx)	200 mg	400 mg	400 mg	
3	Capreomycin (Cm)	500 mg	750 mg	1000 mg	

Table 2 – Categorisation of bacteriological response.

Response type	Description of response
Favorable response	Culture conversion occurred at 3 months and remained negative in next two consecutive months with sputum samples taken 30 days apart of the last sample.
Poor response	Culture conversion could not be achieved in 6 months of IP or reverted to positivity during IP.
Death	Death occurring during the course of treatment.
Default	Interruption of treatment for 2 consecutive months for any reason after successful treatment of at least one month.

Table 3 – Classification of radiological lesions. Type of disease: (1) cavitary/non cavitary, (2) unilateral/bilateral.

Extent of disease	Description of lesions
Minimal	Non cavitary, involving one or both lungs but total lesion volume not exceeding one lung zone, regardless of distribution.
Moderate	More advanced than minimal lesions but total lesion volume not exceeding one lung volume, the total diameter of the cavity or cavities, if present, not exceeding more than 4 cm.
Far advanced	Lesions more advanced than moderate, total parenchymal involvement more than one lung volume and total cavity/ cavities diameter more than 4 cm.

Table 4 – Classification of radiological response.

Radiological improvement	When the lesions disappeared in present chest X-ray which was present in the previous X-ray and the signs of healing were evident.
Radiological deterioration	When new shadows/cavities appeared in previous non cavitary area or appearance of new cavities at different site with non-resolution of previous lesions.

for further course of treatment as per program guidelines. The CP consisted of 4 drugs, that is, cycloserine, ethionamide, levofloxacin and ethambutol to be given under direct supervision for 18 months.[5] The DOT provider of the area was trained in identification of the common side effects listed in Table 1.

Follow-up assessment was done on clinical, bacteriological, and radiological response and ADRs, defaults, and deaths were recorded for analysis.

Patients were examined every month for the first 3 months for documenting change in symptoms, appetite, weight gain, and ADR. S. creatinine estimation was done monthly during Kanamycin treatment and thereafter at every 3 months. Other tests were done as and when required during the follow-up.

The sputum was collected and sent to IRL Jaipur every month after the completion of 3rd, 4th, 5th, 6th month for direct smear and culture examination. Patients who became culture negative and remained negative for two consecutive months were switched to CP at 7th months. For those who failed to convert or reverted to positivity, their IP was extended for 1 month, every time, maximum up to 3 months, total 9 months IP. Irrespective of the culture conversion status, the patients were switched over to CP of 18 months. Follow-up sputum examinations by direct smear and culture were done at 9, 12, 15, 18, 21 and 24 months during regular IP and maximum up to 27th month in extended IP. A case is considered smear or culture converted when two consecutive sputum samples were found negative for AFB at 30 days apart from the start of MDR TB treatment.[5] Response to treatment was categorized as favorable, poor, default and death as detailed in Table 2.

Regular motivation and remotivation at every visit during treatment was adhered to by the health staff.

Chest radiographs were taken at the beginning of treatment and thereafter at 6 months interval or earlier if required and read by two independent viewers. The radiological lesions were categorized as unilateral or bilateral, cavitary or non cavitary with the additional mention of hyperinflation/ bronchiectasis/progressive massive fibrosis/involvement of lymph node and/or pleura. As per guidelines of the National TB Association of USA 1961, the lesions were classified as minimal, moderate and far advanced as described in Table 3 and response was recorded as improvement, deterioration or static lesions as per Table 4.

Data analysis was done using Microsoft excel software and SPSS software. Chi square test was used for statistical significance.

3. Observations

A total 115 patients qualified for final analysis of results in the study. The base line details of demographic profiles, anti-tubercular treatment history, and bacteriological and radiological extent of disease at the time of inclusion in the study have been shown in Table 5.

4. Discussion

The overall response to treatment has been tabulated in column 1 and compared with earlier studies in column 2, 3, 4 of Table 6.

The response to treatment in our study was at par with Singla et al.,[4] Joseph et al.[6] and Jain et al.[7] Male outnumbered female and more MDR cases were in the age group 20–55 years.

Table 5 – Demographic profile and clinical status of the patients at the time of inclusion in the study.

Characteristics	Median [range] or *n* (%)
Age in years	35.5 ± 13.5 [<20 to >60]
Sex M/F [M:F]	73/42 [1.73:1]
Residence [U:R]	115 [59:56]
Literacy [(I + P): Rest (M + HS + G + PG)]	115 [65:50]
Illiterate (I) = 30, Primary (P) = 35, Middle (M) = 29,	
High school (HS) = 13, Graduate (G) = 6, Post-Graduate (PG) = 2	
Socio-economic status [Upper middle: Lower]	0 8:107
Lower[Lower Upper (85)/Lower Middle (9)/Lower Lower (13)]	
Weight of the patient	≤26 kg = 1 (0.87%)
	26 to ≤45 kg = 86 (74.78%),
	≥45 kg m = 28 (24.35%)
BMI	15.22 ± 86.96
Underweight (BMI < 18.5)	100 (86.96%)
Normal (18.5–24)	15 (13.04%)
Addiction [No: Yes]	63:52
Smoker (37), Tobacco chewer (24), Alcoholic (31), Dual (23)	
Treatment history	
1. Total duration of illness in months	Mean duration 23 ± 18.17
	<6 m (12), 6–12 m (20),
	12–24 m (36), >24 m (47)
2. Previous treatment status	
(i) H/o previous anti tubercular treatment spells	1 (41), 2 (43), 3 (23), 4 (5), 5 (3)
(ii) DOTS/Non DOTS	67/48
(iii) Defaults during previous treatments	Yes (39)/No (76)
3. MDR status (LPA proven)	
(i) Rifampicin (R) + Isoniazid (H)	86 (74.78%)
(ii) Rifampicin alone	29 (25.22%)
4. Delay in treatment	
(i) <30 days	77 (66.96%)
(ii) >30 days	38 (33.04%)
5. Bacteriological status	
5.1 Sputum negative, culture positive:	36 (31.30%)
5.2 Both Sputum and culture positive:	79 (68.70%)
6. Radiological status	
6.1 Cavitary/non cavitatory	57 (49.57%)/58 (50.43%)
6.2 Extent of disease	Minimal: 10 (8.7%)
	Moderately advanced: 32 (27.83)
	Far advanced: 73 (63.48%)

These observations are compatible to our social and family setup where the male has more opportunities to encounter infection than female due to more outdoor movement and at this age, both sexes face the stress of poverty, family making, social and family responsibilities, and job relates migrations etc. Compared to male, female fared better in our study but the observation was statistically insignificant ($p = 0153$). We observed more disease in low socioeconomic groups (93.04%) and poor literacy group (56.52%) patients. Rodriguez et al.[8] and Pant et al.[9] also observed that 87% of their patients belonged to low socioeconomic group and 77% were illiterate. Association of poverty and Tuberculosis has been known for ages. Poverty has a direct bearing on nutrition and hygiene and in turn, on disease development and prognosis. In our study also 87% patients had a low BMI 15.22 ± 2.47, and over 75% patients were underweight. The culture conversion occurred

Table 6 – Overall outcome of study and comparison with earlier studies.

Response	Present study	Singla R[4]	Joseph p[6]	Jain K[7 b]	Bhatt G[13]
Favorable	63.48%	61%	66%	45%	–
Poor[a]	9.57%	21%	13%[a]	32%[a]	–
Default	15.65%	18%	13%	13%	7.41%
Death	11.30%	19%	8%	19%	–
Co morbidities	74.78%	–	–	–	7.4%
Addiction to tobacco/alcohol or both	20%	–	–	–	57%
Culture conversion @ 3 months	59.13%	82%	84%	82%	62.8%
Culture conversion @ 6 months	68.43%	98%	92%	94%	67.2%

[a] Poor response group% includes failed culture conversion till 9 months, default and deaths.
[b] Jain et al. outcome at 24 months of therapy.

within 3 months in normal weight patients and took longer in underweight patients weighing <45 kg m. This was statistically significant ($p = 0.047$). Gupta et al.[10] observed that malnutrition delayed recovery and carried high mortality. The significant observation of our study was the better response to treatment in the lowest of the low socioeconomic group patients ($p = 0.024$). We hypothesize that this group might have had preserved sensitivity to drugs, due to relatively less availability of medical treatment in the past. We found 20% of our patients had dual indulgence in alcohol and smoking. Jain et al.,[7] Barroso et al.[11] and Bhatt et al.[12] also observed similar dual indulgence in 57%, 21%, and 39% cases respectively, in their studies. The commodities were observed in relatively more (74.78%) in our patents, as compared to Bhatt et al.[12] (7.4%). Anemia accounted for 56.22% and Obstructive airway disease (OAD) in 24.35%, other Co morbidities were very few in numbers. The anemia was expected from malnutrition in our patient which could be the cause or the effect of tuberculosis. Barroso et al.[11] observed COAD in less numbers 9% and DM in 8.39% of their study group MDR TB patients. The increased occurrence of COAD in our study may be due to difference in quantity, type and smoking habits in our study population. Bothamley et al.,[13] were of the opinion that smoking increases non-specific immunity as compared to specific immunity to tuberculosis and thus produces more disease as compared to delayed hypersensitivity. Extension of IP was significantly more required in poor response group (81.81%) as compared to 13.69% patients in favorable response group ($p = 0.002$). This is explainable by the occurrence of far advanced (63.48%) and cavitatory disease (58.5%) in this group, which are the known factors for delayed culture conversion needing the extension of IP.

5. Bacteriological response

In our study, 59.13% (68/115) patients converted culture negative in 3 months and 63.48% of patients at the end of 6 months under field conditions. The mean duration of culture conversion was 3.33 ± 0.091 months in both genders. Other studies have reported culture conversion in the range of 53–92%.[6,14] Low conversion in our study could be due to more of, far advanced and cavitatory disease in our patients. Patients with shorter duration of illness (<6 months) and minimal lung lesions significantly showed better response and took less time for culture conversion, but this could not attain statistical insignificant ($p = 0.22$). None other demographic factors significantly affected favorably for culture conversion in our study.

Factors which delayed conversion included low body weight (<45 kg m) ($p = 0.05$) and far advanced disease ($p < 0.05$). Joseph et al.[6] have reported similar observations. In the favorable response group cavitatory disease was associated with delayed culture conversion but this did not achieve statistical significance ($p > 0.382$). dela Cruz et al.[15] and Rao et al.[16] had similar observations in their MDR TB patients.

In the poor treatment response group, the patient either failed culture conversion at all or later reverted to culture positivity. This can be attributed to more of the cavitatory disease ($p < 0.05$) and longer duration of illness in these patients. None other factors significantly contributed to poor response.

6. Radiological response

In our study the 27.83% patients had moderately advanced and 63.48% far advanced disease. The cavitation was observed in 58.5% patients. Dhingra et al.[17] found moderately advanced disease in 44.44%. Waseem et al.[18] found more moderately advanced disease and the cavitatory disease (49.57%) in their patients. Cavitation has been observed in MDR TB in 50–81% cases in various studies.[12,18,19] We observed favorable response, i.e. radiological resolution of lesions in 40% and in 19.13% patients lesions remained static. Subhash et al.,[14] Dhingra et al.,[17] and Waseem et al.[18] have reported favorable response in 32.5%, 78% and 67% patients respectively. The radiological favorable response correlated significantly with bacteriological response in 63.01%patients ($p < 0.05$) in our study. The radiological favorable response also strongly correlated significantly with the clinical improvement in symptoms ($p < 0.001$). We, therefore, propose that radiological clearance can be used as a good surrogate marker of favorable response. This need to be affirmed in future studies.

7. Adverse drug reactions (ADR)

ADRs were noted in 96.5% (111/115), single ADR in 18.25% and multiple in 78.25%. Earlier studies have reported ADR in the range from 19 to 72%.[17,18] Bloss et al.[19] and Shin et al.[20]observed ADR in 79% and 73% cases and required withholding of offending drug in 64% and 29% patients respectively. Torun et al.,[21] Nathonson et al.,[22] Yew et al.,[23] had to change the regimen in their patients in 56%, 30% and 19% patients respectively. 12 (10.81%) of our patients also required a change of regimen but none required permanent discontinuation of the regimen. The more ADR in our study may be due to better surveillance, over enthusiastic reporting or due to geographical, inherent and genetic factors.

We observed nausea and vomiting in (77.39%) and minor elevations in liver enzyme levels in 12 (10.43%) and 2 needed temporary suspension of probable offending drugs; ethionamide, pyrazinamide, and para-aminosalicylic acid (PAS). Hepatotoxicity due to ethionamide and proethionamide has been reported from 2–5% cases in various studies.[22,24,25] Rossouw and Saunders[26] reported toxicity to PAS in 0.3% patients. Ototoxicity occurred in 30.43% of our patients; pure vestibular in 28, pure cochlear in 5, and mixed in 2 patients. Dizziness and vertigo in 27.8% (32), tinnitus in 1.74% and hearing loss occurred in 4.3% (5), permanent for high frequency in 4 and for both higher and the low frequency in 1 patient. The various types of ototoxicity from different parts of the world have been reported in 2.6–46%.[6,21,22,24,27–30] We observed less serious neuropsychiatric events; headache (42.60%), sleep disturbance (20%), numbness(0.87%) acute psychosis(5.21%), and seizures(0.87%) which were manageable by symptomatic treatment and reassurance. We did not encounter any patient with suicidal tendency. Other studies have reported various psychiatric disorders from 3.1 to 21% cases.[19–22,27,31] Renal dysfunction occurred in 2 patients (1.74%). One recovered after the withdrawal of ''Kanamycin'' and had favorable response to treatment and the other one died. The other studies observed

renal dysfunction in 1.2–9.8%.[19,20,22,27] Thyroid dysfunction (TSH > 10 IU/ml) was not observed in our study, but other studies have reported in 3.5–17.2% patients.[20,22]

8. Defaults

We observed 18 (15.65%) defaults in our study, which were mainly in IP. Joseph et al.[6], Singla et al.[4] and Jain et al.[7] reported similar default rate in 13–18% of their patients.

9. Death

Deaths occurred in 11.30% patients in our study, which is comparable with other studies (8–19%).[4,6,7,12] Significantly more deaths occurred in urban patients ($p < 0.01$) patient. We attribute this to higher environmental pollution and higher stress levels in urban population. The majority of death occurred within the IP (mean 3.39 ± 1.2 months), in delayed treatment (>30 days) and in cavitatory disease ($p < 0.025$) but initial drug resistance did not significantly affect the overall response rate. Yew et al.[23] and Shin et al.[32] have reported similar observations in their study. We hypothesize this to be due to the physiological effects of loss of lung parenchyma.

10. Limitations of study

The limitations include limited to a single district and duration, small size of study group, reporting bias being a domiciliary study, limited to IP only.

11. Conclusion

From our study, we conclude that longer duration of illness, radiological advance and cavitatory disease, delay in starting treatment, ADRs, treatment default are the factors which determine the overall outcome of treatment. The success rate of CAT IV treatment can be augmented by reducing deaths (11.3%) and default (15.65%). We have observed that the deaths were more in patient where the treatment was delayed and in cavitatory disease. These are prevented by early diagnosis and timely treatment and treatment of intercurrent infections. The causes of default vary from patient to patient and can also be reduced if they are taken care of on customized basis.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. World Health Organization. *Global Tuberculosis Control: Report*. 2011. Available from: http://www.whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf [accessed 21.04.12].
2. World Health Organization. *Global tuberculosis report*. 2012. Available from: http://www.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf [accessed 04.10.13].
3. Behera D. Issues in the management of drug resistant tuberculosis in India. *Lung India*. 2013;30:269–272.
4. Singla R, Sarin R, Khalid UK, et al. Seven-year DOTS-Plus pilot experience in India: results, constraints and issues. *Int J Tuberc Lung Dis*. 2009;13:976–981.
5. *Revised tuberculosis Control Program guidelines*. Nirman Bhavan, New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health & Family Welfare; 2010 . 9.15.18.22-24.29.40-47.
6. Joseph P, Desai VBR, Mohan NS, et al. Outcome of standardized treatment for patients with MDR-TB from Tamil Nadu, India. *Indian J Med Res*. 2011;133:529–534.
7. Jain K, Desai M, Solanki R, et al. Treatment outcome of standardized regimen in patients with multidrug resistant tuberculosis. *J Pharmacol Pharmacother*. 2014;5:145–149.
8. Rodriguez M, Monedero I, Caminero JA, et al. Successful management of multi drug resistant tuberculosis under programme conditions in the Dominican Republic. *Int J Tuberc Lung Dis*. 2013;17:520–525.
9. Pant R, Pandey KR, Joshi M, et al. Risk factor assessment of Multi Drug Resistance Tuberculosis. *J Nepal Health Res Council*. 2009;15:89–92.
10. Gupta KB, Gupta R, Atreja A, et al. Tuberculosis and nutrition. *Lung India*. 2009;26:9–16.
11. Barroso EC, Salani Mota RM, Oliveira, et al. Risk factor for acquired multi drug resistant tuberculosis. *J Pneumol*. 2003;29:89–97.
12. Bhatt G, Vyas S, Trivedi K. An epidemiological study of multi drug resistance tuberculosis cases registered under revised national tuberculosis control programme of Ahmadabad city. *Indian J Tuberc*. 2012;59:18–27.
13. Bothamley GH. Smoking and tuberculosis: a chance or causal association? *Thorax*. 2005;60:527–528.
14. Subhash HS, Ashwin I, Jesudasan MV, et al. Clinical characteristics and treatment response among patient with Multi drug Resistant Tuberculosis: a retrospective study. *Indian J Chest Dis Allied Sci*. 2003;45:97–103.
15. dela Cruz MBS, Quelapio MID, Tupasi TE. Determining the time to Culture Conversion on patients enrolled in Makati Medical Centre Directly Observed Treatment-Short Course Clinic. *Phillipp J Intern Med*. 2003;41:281–284.
16. Rao SN, Mookerjee AL, Obasanjo OO, Chaisson RE. Errors in the treatment of tuberculosis in Baltimore. *Chest*. 2000;117:734–737.
17. Dhingra VK, Rajpal S, Mittal A, et al. Outcome of Multi-drug Resistant tuberculosis cases treated by Individualized Regimens at a Tertiary level clinic. *Ind J Tuberc*. 2008;55:15–21.
18. Waseemn Saeed. Arshad Naeem. Jamal Ahmad. Retrospective audit of patients treated for MDR–TB in retreatment category. *J Ayub Med Coll Abbottabad*. 2009;21(2). http://www.Ayubmed.Edu.Pk/JAMC/PAST/21-2/Waseem.pdf.
19. Bloss E, Kuksa L, Holtz TH, et al. Adverse events related to multidrug-resistant tuberculosis treatment, Latvia, 2000–2004. *Int J Tuberc Lung Dis*. 2010;14:275–281.
20. Shin SS, Pasechnikov AD, Gelmanova IY, et al. Adverse reactions among patients being treated for MDR-TB in Tomask. *Russia Int J Tuberc Lung Dis*. 2007;11:1314–1320.
21. Torun T, Gungor G, Ozmen I, et al. Side effects associated with the treatment of multidrug resistant tuberculosis treatment. *Int J Tuberc Lung Dis*. 2005;9:1373–1377.
22. Nathenson E, Gupta R, Hanumani P, et al. Adverse events in the treatment of multidrug resistant tuberculosis: results from the DOTS-Plus initiative. *Int J Tuberc Lung dis*. 2004;8:1382–1384.

23. Yew Wai Wing. Chen Kuen Chi. Chau Hung Chi, et al. Out of patients with Multidrug Resistant Pulmonary Tuberculosis treated with Oflxacin/Levofloxacin-containing regimens. *Chest*. 2000;117:744–751.
24. Baghaei P, Tabarsi P, Dorriz D, et al. Adverse effects of multi drug treatment tuberculosis with a standardized regimen. A report from Iran. *Am J Ther*. 2011;18:e29–e34.
25. A comparison of the toxicity of proethionamide and ethionamide: a report from the research committee of British Tuberculosis Association. *Tubercle*. 1968;48:125–135.
26. Rossouw JE, Saunders SJ. Hepatic complications of antituberculous therapy. *Q J Med*. 1975;XLIV:1–16.
27. Masjedi MR, Tabarsi P, Chitsaz E, et al. Outcome of MDR-TB patient with standardized regimens, Iran 2002–2006. *Int J Tuberc Lung Dis*. 2008;12:750–755.
28. Duggal P, Sarkar M. Augiologic monitoring of multidrug resistant tuberculosis patients on aminoglycoside treatment with long term follow-up. *BMC Ear Nose Throat Disord*. 2007;7:5.
29. Sturdy A, Goodman A, José RJ. Multidrug-resistant tuberculosis (MDR-TB) treatment in the UK: a study of injectable use and toxicity in practice. *J Antimicrob Chemother*. 2011;66:1815–1820.
30. Shin SS, Hyson AM, Castaneda C, et al. Peripheral neuropathy associated with treatment for multidrug tuberculosis. *Int J Tuberc Lung Dis*. 2003;7:347–353.
31. Vega P, Sweetland A, Acha J, et al. Psychiatric issues in the management of patients with multi drug resistant tuberculosis. *Int J Tuberc Lung Dis*. 2004;8:749–759.
32. Shin SS, Pasechnikov AD, Gelmanova IY, et al. Treatment outcomes in an integrated civilian and prison MDR-TB treatment program in Russia. *Int J Tuberc Lung Dis*. 2006;10:402–408. Erratum in: Int J Tuberc Lung Dis. 2006 Oct; 10(10):1183.

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Case Report

Tubercular sialadenitis of parotid gland – An extremely rare case series

Anand Agrawal [a,*], *Chandermani* [b], *Monika Gathwal* [c], *Amrita Duhan* [c]

[a] *Associate Professor & Head, Department of Respiratory Medicine, BPSGMC(W), Khanpur Kalan, Sonepat, Haryana, India*

[b] *Department of Respiratory Medicine, BPSGMC(W), Khanpur Kalan, Sonepat, Haryana, India*

[c] *Department of Pathology, BPSGMC(W), Khanpur Kalan, Sonepat, Haryana, India*

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ABSTRACT

Tuberculosis is a potentially fatal infectious disease caused by Mycobacterium Tuberculosis. It most commonly involves the lungs (Pulmonary Tuberculosis), although it can involve any organ system in the body. However even in a country like India which has high burden of this disease, the tubercular invasion of parotid gland is extremely rare. Here we describe two such cases. Both patients were immune competent and presented with fever and swelling in the parotid region. They were diagnosed as tuberculosis of parotid gland by ultrasound guided fine needle aspiration and confirmed bacteriologically.

1. Introduction

Parotid gland tuberculosis is a rare entity among extra pulmonary tubercular cases. The first case of parotid tuberculosis was reported in von Stubenrauch in 1894.[1] Thereafter, only around 100 cases have been reported globally in last 100 years.[2] However, bacteriologically proved cases have rarely been reported. Isolated parotid gland tuberculosis is often misdiagnosed as parotid gland tumour. Here we are reporting two such cases where the diagnosis was proven bacteriologically this case to highlight the unusual solitary nature of the lesion in the absence of any other tubercular focus in the body, diagnosed as tubercular by detecting mycobacterium tuberculosis in FNAC.

2. Clinical record

2.1. *Patient-1*

An 18 year old female presented with chief complaint of a painless swelling over the right parotid region of 2 months duration. The swelling was located just below the right pinna, and it was insidious in onset, gradually progressive and not accompanied by any other symptoms. She also gave history of fever everyday during evening since last two months. There was no previous history of tuberculosis in the patient and her family, but she was taking antibiotic by local doctor for last one month. Past history was also significant for periodontal disease and tooth abscess one year ago following which her

* *Corresponding author*. Tel.: +91 9315441089.
E-mail address: ashidocbps@yahoo.com (A. Agrawal).

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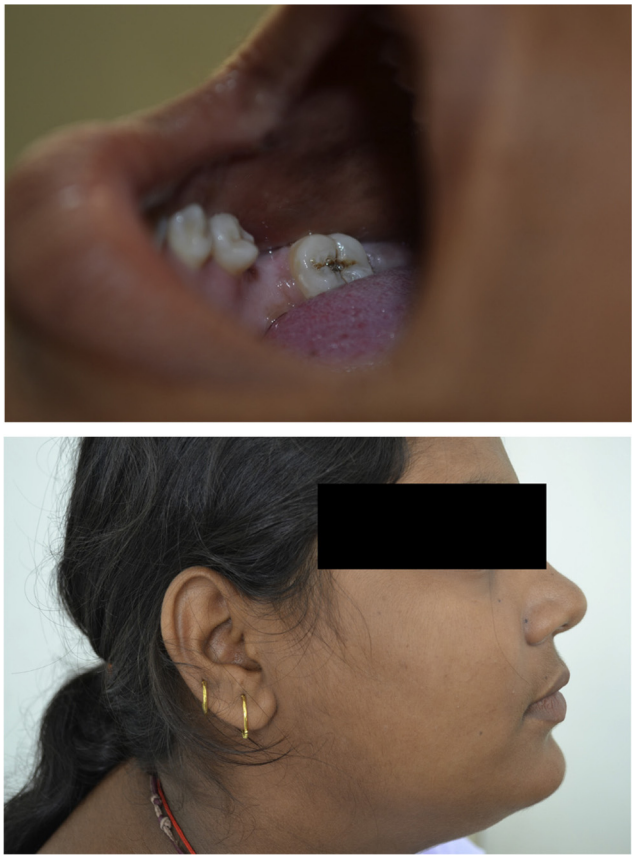

Fig. 1 – (a) Photograph showing dental extraction of a Premolar in Right lower jaw of Patient-1. (b) Gross photograph showing parotid swelling in Patient-1.

first premolar of the right lower jaw was extracted (Fig. 1a). On examination, the swelling was firm & non-tender, around 2 cm × 1.5 cm in diameter in size and ill defined borders (Fig. 1b). The skin overlying the swelling was normal. Routine investigation shows, Haemoglobin 12g%, TLC (Total leukocyte count) 9000/dl Polymorph 76%, Lymphocyte 20%, Eosinophil 3% Monocyte1%. Monteux was positive (22 mm after 72 hour), LFT (Liver function test), KFT (Kidney function test) within normal limit, sputum for AFB was negative, X ray chest PA view within normal limit, Urine examination for routine and microscopic was normal.

USG of parotid region showed multiple necrotic area in parenchymal region with debris. USG guided FNAC was done and pus was aspirated from necrotic area. Staining using modified ZN (Ziehl–Neelsen) stain showed mycobacterium tuberculosis. No malignant cells were seen in cytopathology and only necrotic debris was present in background.

After diagnosing the case antitubercular treatment was commenced and she was symptomatically improved after the therapy.

2.2. *Patient-2*

A 36 year old male was diagnosed as a case of sputum positive pulmonary tuberculosis one year ago and started on appropriate regimen consisting of 4 anti-tubercular drugs (H, R, Z, E)

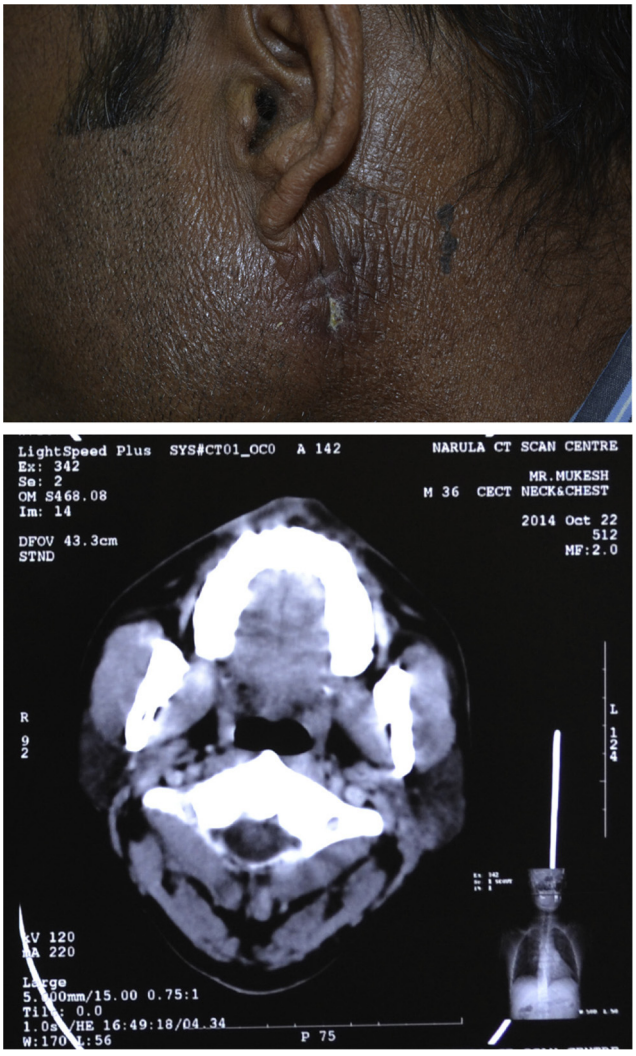

Fig. 2 – (a) Gross photograph showing parotid swelling in Patient-2. (b) CT scan of Patient-2 showing left Parotid swelling.

for the same. After 2 months of therapy, he was symptomatically improved and thereafter defaulted on treatment. He now presented with chief complaints of fever & generalised weakness since last 6 months and swelling in the left parotid region since last 3 months (Fig. 2a,b). He also complained of shortness of breath and easy fatiguability. The parotid swelling was firm and 2 cm × 2 cm in size. All parameters of his haemogram were normal, except for a slightly reduced haemoglobin (Hb = 8.5gm%, TLC = 9800, N = 61%, L = 30%, M = 8%, E = 1%). LFT and RFT were in normal limits. Sputum stained positively for AFB by ZN stain. Skiagram of Chest in PA view was suggestive of miliary Tuberculosis. An excision biopsy from the parotid region was taken and showed parts of parotid gland with large area of necrosis and ill defined epithelioid cell granulomas. ZN Staining with 20% Sulfuric Acid was positive.

After making the diagnosis, he was started on Antitubercular therapy and also counselled not to default on treatment again and educated about the dangers of defaulting on ATT.

3. Discussion

Extra pulmonary tuberculosis (EPTB) represents approximately 25% of overall tubercular morbidity, although the most common is lymph node tuberculosis while other forms are pleural, skeletal, CNS, Pericardial, abdominal, genito-urinary, miliary, cutaneous, otorhinolaryngeal, breast and disseminated tuberculosis are less common.[3] Parotid tuberculosis, an extremely rare form of EPTB, usually presents as a unilateral swelling or abscess involving the parenchyma of the gland either through haematogenous spread or from infection of lymph nodes within or around it.[4] Diagnosis is difficult because there are no specific clinical, radiological or biological signs of the disease. Only bacteriological and histopathological findings can confirm the diagnosis.

Tuberculous sialadenitis may develop secondary to infection in the oral cavity. Direct extension to salivary gland parenchyma by the bacillus may occur by way of the glands ductular system, although salivary glands are relatively immune to tuberculosis because of thiocynates ions and proteolytic enzymes like lysozymes, which impart antibacterial property and Continuous flow of saliva which prevents lodging and growth of mycobacterium is also an important inhibitory factor,[2] spread of infection by lymphatic vessels, particularly from infected tonsils and external auditory canal, plays an important role.[1]

Ultrasound represents the initial imaging modality of choice for the assessment of palpable abnormalities of the parotid gland, demonstrate whether a palpable lesion arises within the parotid gland, or is periparotid in location, and identify those entities that may not need surgical intervention. Sonographic examination of the parotid swelling contributes substantially in the diagnosis of parotid TB infection[5] while direct visualization of mycobacterium tuberculosis in ZN (Ziehl–Neelsen) staining after making smear of USG guided FNAC specimen, is diagnostic, as in present case.

Four drug regimens (rifampicin, isoniazid, ethambutol and pyrazinamide) in the intensive phase followed by two drugs (rifampicin and isoniazid) in continuation phase is a recommended treatment regimen. Out of the two cases discussed above, case-1 is an extremely rare presentation of extra pulmonary paucibacillary tuberculosis, primarily because of its isolated nature and absence of any history of tuberculosis in the patient or her family while Case-2 provides a clear example that defaulting on Anti-tubercular treatment may lead to either drug resistant tuberculosis or disseminated to rare site.

Although prevalence of tuberculosis is increasing day by day in endemic countries, the involvement of extra pulmonary sites like major salivary glands is still very rare which creates a diagnostic dilemma. Hence it needs good clinical acumen, clinical suspicion and patience to diagnose the case before the treatment is commenced.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Maheshwari V, Jain A, Varshney M, Alam K, Gaur K, Sharma SC. Warthin's tumour with coexistent tuberculosis. *BMJ Case Rep*. 2011;2:1–3.
2. Patankar SS, Chandorkar SS, Garg A. Parotid gland tuberculosis: a case report. *Indian J Surg*. 2012;74:179–180.
3. Handa U, Mundi I, Mohan S. Nodal tuberculosis revisited: a review. *J Infect Dev Ctries*. 2012;6:6–12.
4. Garg R, Verma SK, Mehra S, Srivastawa AN. Parotid tuberculosis. *Lung India*. 2010;27:253–255.
5. Wu S, Liu G, Chen R, Guan Y. Role of ultrasound in the assessment of benignity and malignancy of parotid masses. *Dentomaxillofac Radiol*. 2012;41:131–135.

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Case Report

Chest wall tuberculous ulcer: A rare complication of pulmonary tuberculosis

Sajjad Hussain *

Consultant Surgeon, District Hospital, Kargil, Ladakh, Jammu and Kashmir 194103, India

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ABSTRACT

Tuberculous ulcer of the anterior chest wall as a result of direct extension from underlying pleural and pulmonary tuberculosis is a very rare entity. Its clinical presentation may resemble a tumor or abscess. Isolated chest wall tuberculous ulcer without bone involvement is even rarer. An illustrated case report is presented.

1. Introduction

Tuberculous ulcers of the chest wall as a complication of pulmonary tuberculosis are very rare and infrequently encountered even in the countries endemic to tuberculosis. Tuberculosis of musculoskeletal system accounts for 1–2% of all types of tuberculosis. Tuberculosis of chest wall makes up 1–5% of all cases of musculoskeletal tuberculosis.[1] As the condition is rare and its clinical presentation may resemble pyogenic abscess or tumor, diagnosis of non-healing chest wall tuberculous ulcer remains a challenge and requires a high index of suspicion.[2]

2. Case report

A 50 year old woman presented with a 6 month history of non-healing right anterior chest wall ulcer. This lesion had developed as a subcutaneous nodule, gradually increased in size and evolved into ulcer. Before visiting our surgical department, the patient had been diagnosed as having a ruptured pyogenic abscess at primary health centre, but as the treatment with antibiotics and regular aseptic dressing was unsuccessful, she was referred to surgical clinic. The physical examination revealed a 3 × 5cm ulcer with undermined edges and an indurated base. The base also showed sloughing. The skin surrounding the ulcer was hyperaemic and hyperpigmented (Fig. 1). A provisional diagnosis of tuberculous ulcer was made. She also had a history of low-grade fever and productive cough over two months. She had no past history of tuberculosis or any anti-tubercular drugs intake. Also there was no history of hemoptysis, chest pain, dyspnoea or swelling on any other side of body. On respiratory system examinations, crepts were present on right side of chest. Rest of systemic examination was absolutely normal.

In laboratory investigation, ESR, complete blood count, liver function test, renal function test were within normal limit.

* Tel.: +91 (0) 1985233427, +91 9419110021 (mobile).
E-mail address: drsajjadms@gmail.com

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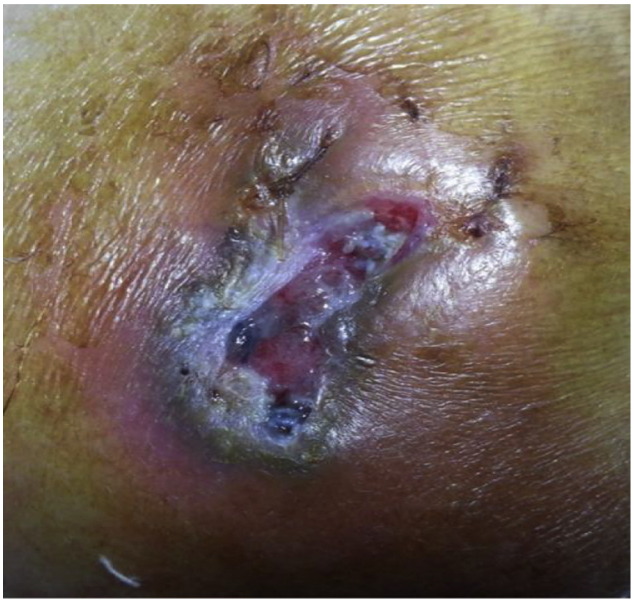

Fig. 1 – Anterior chest wall ulcer.

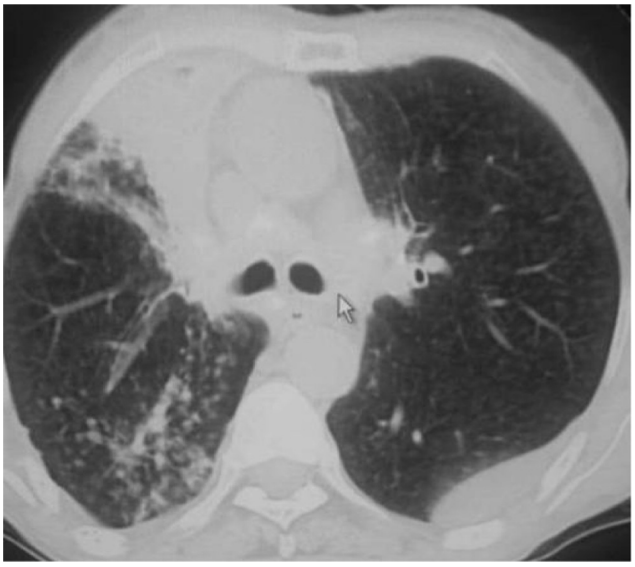

Fig. 3 – CT scan chest showing pleouro-pulmonic disease with direct extension to right anterior chest wall.

Monteux test was positive (15 mm) but sputum smear was negative for acid fast bacilli. Facility for culture of sputum was not available. Further workup included skin biopsy, polymerase chain reaction for mycobacterium tuberculosis, chest x-ray and CT scan chest. Histological examination showed epithelioid cell granulomas with inflammatory cell infiltrates in the dermis. No evidence of malignancy was seen (Fig. 2). A radiograph of the chest revealed opacity of right upper pulmonary lobe. CECT of thorax was performed (Fig. 3) which revealed consolidation patch in the right medio-basal region of upper lobe of lung, firmly attached to the anterior thickened pleura and right anterior chest wall. No any fistula or thoracic bony involvement was seen. Minimal loculated fluid collection in left posterior dependent area of pleural space was noticed. Lymph nodes were enlarged with diffuse calcific changes.

Patient was diagnosed as a case of pulmonary tuberculosis with tuberculous ulcer of right anterior chest wall as a result of direct extension from underlying pleural and pulmonary parenchymal disease. Anti-tubercular treatment (combination of isoniazid, rifampicin, ethembutol and pyrazinamide) was started immediately after the diagnosis. With the anti-tubercular therapy (extended course), the ulcer healed completely.

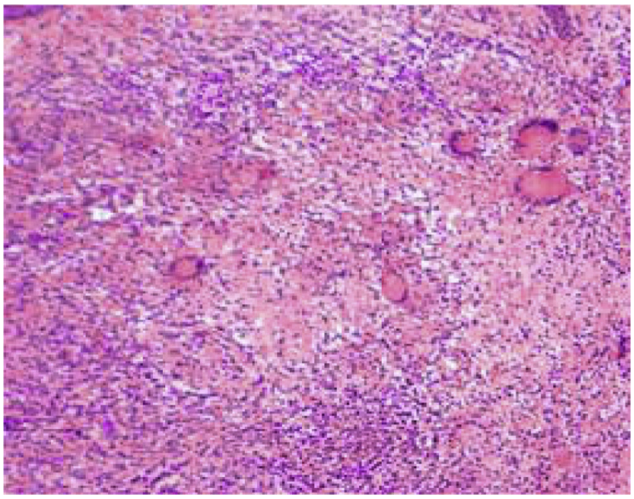

Fig. 2 – Histology showing granuloma.

3. Discussion

Anterior chest wall tuberculous ulcer as a complication of pulmonary tuberculosis is very rare and may result from bursting of a tubercular abscess through skin. The disease is usually slow-growing and has an insidious course. It has an unusual presentation like a chronically discharging sinus or a non-healing ulcer.[3]

Tuberculosis of musculo-skeletal system accounts for upto 1–2% of all types of tuberculosis. Tuberculosis of chest wall makes up 1–5% of all cases of musculoskeletal tuberculosis.[2]

Three mechanisms have been suggested to explain the pathogenesis of tuberculosis of chest wall: direct extension from underlying pleural or pulmonary parenchymal tuberculosis, hematogenous spread, and direct extension from a lymphadenitis in the chest wall.[4] Our case showed tubercular consolidation of right upper lobe, firmly attached to the thick anterior pleura and right anterior chest wall, suggesting direct pulmo-pleuritic extension. Direct extension of underlying pulmonary tuberculosis is the least common cause of chest wall tuberculosis compared with the hematogenous and lymphatic spread.[5]

The diagnosis of the tuberculosis of the chest wall depends either on bacteriogenic or histopathological confirmation, or both.[6,7] In our case, the combination of symptoms, positive tuberculin skin test, positive edge biopsy report and radiographic findings strongly suggest the diagnosis of tuberculosis.

The optimal treatment strategy is controversial. There is general agreement that anti-tubercular therapy with extended course is the treatment of choice.[2] If the clinical suspicion is high, drugs should be started immediately after the appropriate microbiological and histological samples have been taken, although some authors have recommended wide surgical removal of all diseased tissues combined with anti-tubercular drugs,[8] the response to anti-tubercular therapy alone as a primary therapy is usually good, as in this case.

4. Conclusion

Chest wall tuberculous ulcer secondary to direct extension from underlying pulmo-pleuritic tuberculosis is very rare and this type of complication has been rarely reported in world literature so far. Anti-tubercular therapy alone is the cornerstone of the treatment. Wide debridement and resection may be required in few cases.

Conflicts of interest

The author has none to declare.

REFERENCES

1. Theodossis SP, Vassilis NP, Antonis M, et al. Anterior chest wall tuberculous abscess: a case report. *J Med Case Reports*. 2007;1:152–159.
2. Abass AM, Osama S, Khaled MA, Kamal MA, Idrees SB. Multiple abscess of the chest wall: rare complication of pulmonary tuberculosis. *Internet J Infect*. 2014;13:68–70.
3. Gun-Wook K, Hyun-Je P, Hoon-Soo K, et al. Delayed diagnosis of scrofuloderma misdiagnosed as a bacterial abscess. *An Demerol*. 2012;24:70–73.
4. Josemir BS, Ana RF, Claudia EF, Marcia HO, Perla GS, Vanessa LSM, et al. Cutaneous tuberculosis: epidemiologic, etiopathogenic and clinical aspects- part I. *An Bras Dermatol*. 2014;89:219–229.
5. Khalil A, Le-Breton C, Tassar M, et al. Utility of CT scan for the diagnosis of Chest wall tuberculosis. *Eur Radiol*. 1999;9:1638–1642.
6. Kim YT, Han KN, Karg CH, Sung SW, Kim JH. Complete resection is mandatory for tubercular cold abscess of the chest wall. *Ann Thorac Surg*. 2008;85:273–277.
7. Paparramidis TS, Papadopoulos VN, Michalopoulous A, et al. Anterior wall tuberculous abscess: a case report. *J Med Case Rep*. 2007;26:152–154.
8. Manuchehr A, Zahra P, Gilda A, Sarrah M. Surgical treatment of chest wall tuberculosis. *Tanaffos*. 2010;9:28–32.

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Case Report

Sinonasal tuberculosis: Report of three atypical cases

Junaid N. Malik, Sabeena Jan, Seema Monga *, Sudhir Bahadur*

HIMSR & HAHC Hospital, Otorhinolaryngology & Head & Neck Surgery, Jamia Hamdard, Hamdard Nagar, Delhi 110062, Delhi, India

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ABSTRACT

Primary sinonasal/nasal tuberculosis is rare amongst the commonly seen cases of extrapulmonary tuberculosis.

We report three cases, two of primary sinonasal tuberculosis and one case of nasal tuberculosis in otherwise healthy patients. The diagnosis was based on radiological and histopathological findings. Treatment with antitubercular drug therapy was successful in all three of them.

Sinonasal region tuberculosis, despite its rarity, should be added to differential diagnosis of nasal and paranasal sinus disorders particularly with intractable symptoms. Radiological imaging and nasal endoscopy with biopsy should be supplemented for confirmation.

1. Introduction

Tuberculosis, considering the entry of infection, most frequently affects the lungs. However, during the past two decades, extrapulmonary tuberculosis has emerged as a major public health problem, and it mainly manifests in the head and neck region. Cervical tuberculous lymphadenopathy is its most common form.[1] Nasal and sinonasal tuberculosis, either primary or secondary to pulmonary infection, is rare and very few cases have been reported in literature. Sinonasal tuberculosis is generally secondary to either a pulmonary tuberculosis or a retrograde involvement of the nose by lupus vulgaris of the facial skin. Only rarely it presents as a primary disease, which may be caused by infected aerosol inhalation or traumatic inoculation by fingers.[2] We report atypical clinical presentations, management and outcome in three immunocompetent patients with histopathologically confirmed nasal and sinonasal tuberculosis but no pulmonary involvement.

2. Clinical cases

2.1. *Case I*

A 5-year-old boy presented to ENT OPD with symptom of painless right-side proptosis of 2 months duration. He had no nasal symptoms. The child had fever and decreased appetite. Local examination revealed right proptosis, with normal eye movements and normal visual acuity (Fig. 1a).

The anterior rhinoscopy was normal. However, the right ear examination revealed presence of granulation tissue. The Hb was 9 g%, ESR was 24 mm and sputum was negative for AFB staining. Similarly HIV and HBsAg tests were negative.

* *Corresponding author*. Tel.: +91 9811124342.
E-mail address: dr.seema.monga@gmail.com (S. Monga).

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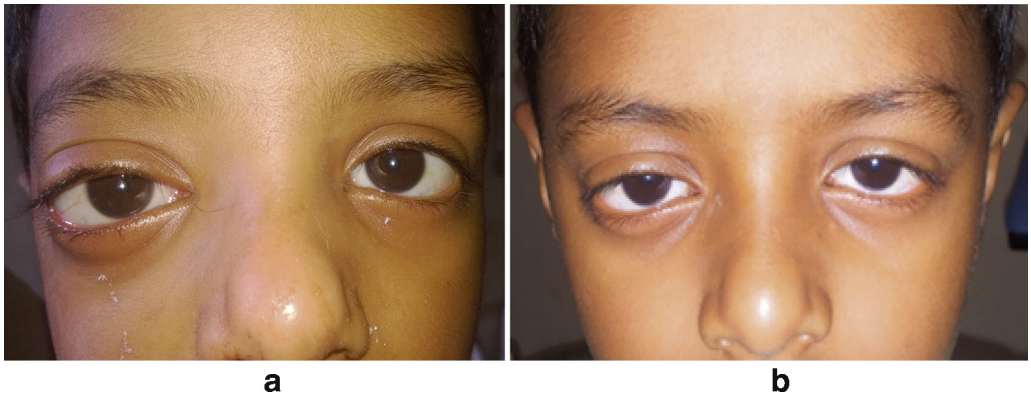

Fig. 1 – Proptosis at presentation (a) and after 6 months follow-up (b).

Remaining investigations including RBS and kidney function tests (KFT) were normal.

The CT scan of nose and paranasal sinuses (PNS) suggested right-sided complete opacification of ethmoid sinuses, with erosion of lamina papyracea. There was also presence of small subperiosteal abscess along superomedial aspect of the right orbit (Fig. 2). His chest X-ray was normal. Diagnostic nasal endoscopy was carried out under GA and biopsy was taken from a friable mass involving the ethmoid sinuses. Histopathology revealed presence of sinonasal tuberculosis.

He was started on antitubercular treatment. Two months later, his proptosis had completely disappeared, and six 6 later, he was disease free (Fig. 1b).

2.2. *Case II*

A 30-year-old man presented with history of intractable pain, epistaxis and nasal obstruction for a short duration of 15 days. Local examination revealed broadening of dorsum of nose with mild tenderness. Anterior rhinoscopy showed mucopurulent discharge with congested and edematous mucosa. His ESR was 32 mm and Mantoux was positive. The remaining investigations, including haemogram, KFT, sputum examination and tests for HIV, HBsAg and ultrasonography abdomen, were normal.

The CT scan of PNS was suggestive of ethmoid sinusitis with edematous septum (Fig. 3). Chest X-ray was normal. Nasal endoscopy revealed septal mucosa was boggy, friable and extremely tender. Both the middle turbinates and ethmoid sinuses were oedematous. Biopsy was taken from friable lesion involving the septal and edematous ethmoid sinus mucosa. HPE was suggestive of sinonasal tuberculosis.

The patient was started on antitubercular treatment. He showed excellent response to treatment with quick resolution of symptoms and was disease free after 6 months of therapy.

2.3. *Third III*

A 34-year female housewife presented with complaints of progressively increasing left-side nasal obstruction, and epistaxis off and on for the previous 6 months. There were no other constitutional symptoms. Anterior rhinoscopy showed left-side reddish-pink granulations arising from the nasal mucosa that bled on touch (Fig. 4a). Neck examination revealed bilateral submandibular lymphadenopathy, which was not significant. The remaining clinical examination was essentially normal. Routine investigations, including X-ray of the chest, were normal. The ESR was raised (28 mm). Mantoux was positive (20 × 20 mm).

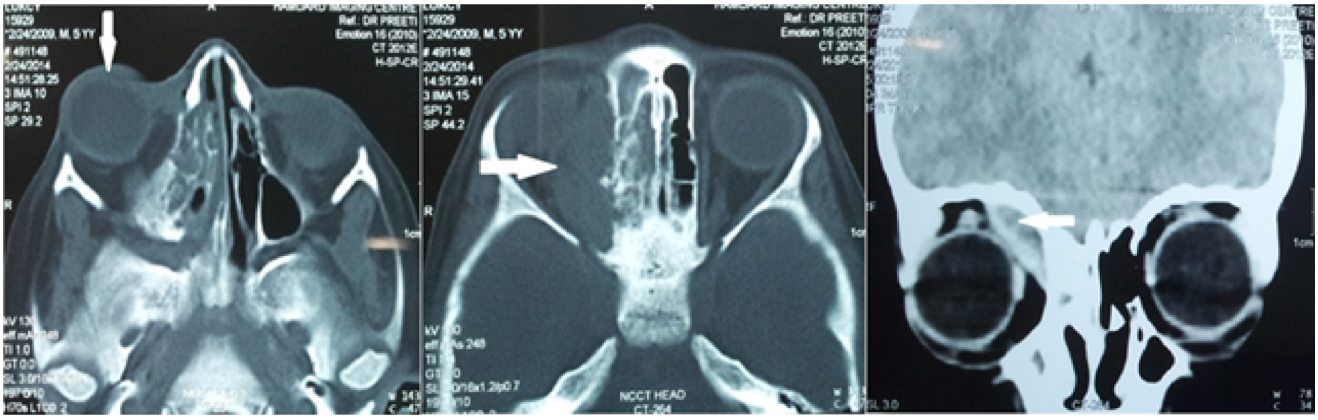

Fig. 2 – CT cuts showing right proptosis and periorbital abscess.

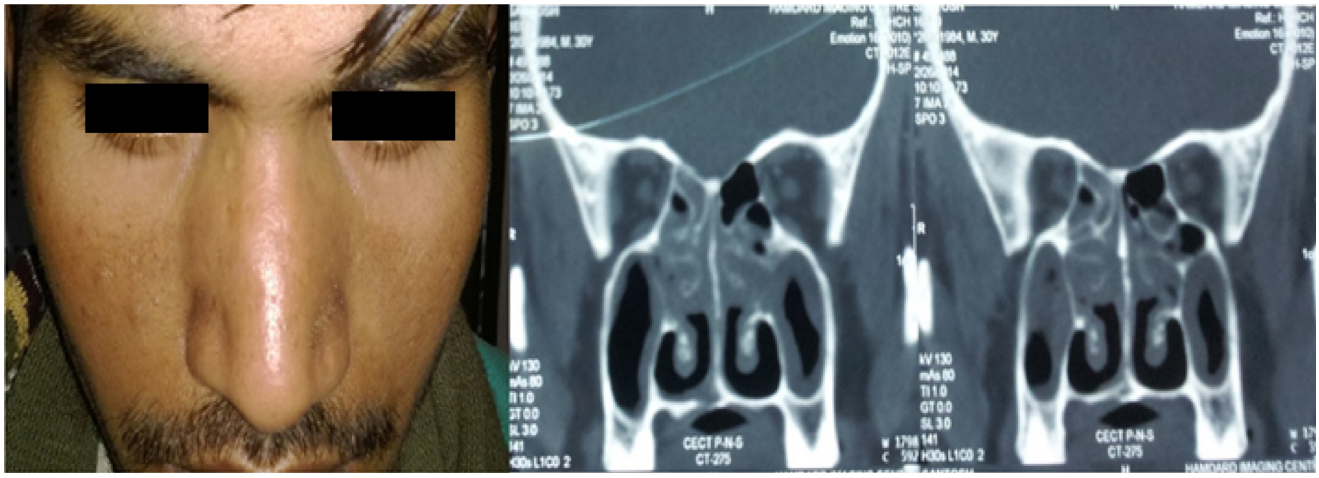

Fig. 3 – Photo showing widening of nasal bridge and bilateral ethmoidal involvement.

The CECT PNS showed a mildly enhancing soft-tissue lesion in the left nasal cavity and vestibule (Fig. 5). Diagnostic nasal endoscopy was carried out and biopsy was taken, which on HPE revealed tuberculosis.

The patient was started on ATT, to which she responded well with resolution of the nasal lesion (Fig. 4b). At 6 months of follow-up, she was doing well.

3. Discussion

Antitubercular chemotherapy and public health measures have led to a considerable decline in the incidence of tuberculosis by the middle of the 20th century. However, since 1986, a steady and progressive rise in the number of cases has been reported world over.[3] AIDS is one of the factors responsible for resurgence of tuberculosis. Poverty leading to overcrowding, substandard living conditions and inadequate access to health care are other implicated factors.[2]

Herzog in the 18th century described 20 cases of primary nasal tuberculosis among overall 80 published cases of nasal tuberculosis.[4] However, in an extensive review of medical literature published in 1977, Butt found only 35 cases of nasal tuberculosis.[5] Moon et al. examined the relative frequency of 220 head and neck lesions with tuberculosis and reported that only two cases involved sinonasal cavities.[6]

Primary sinonasal tuberculosis is rare and represents a diagnostic challenge to specialists because the clinical presentation of infective diseases, granulomatous disorders and neoplastic conditions are similar and non-specific.[2,7]

The symptoms of sinonasal tuberculosis may imitate features of rhinosinusitis. The most common symptom of nasal tuberculosis is nasal obstruction, which occurs due to the formation of foul smelling crusts. Mucoid/mucopurulent rhinorrhea, postnasal discharge, scaling, epistaxis and fetor may also occur. Nasal lesions may be asymptomatic. Constitutional symptoms like weight loss and night sweats may not be consistently present. Nasal lesions demonstrate pale red or pink granulations or ulceration of the cartilaginous portion on the septum or the inferior turbinate. Occasionally, septal perforation, cleft of the nasal ala or facial abscesses may occur if treatment is delayed. A chest X-ray is useful to rule out pulmonary tuberculosis.[8]

The low incidence of nasal tuberculosis may be explained by the protection afforded by ciliary movement, the bactericidal action of nasal secretions and the filtering action of the

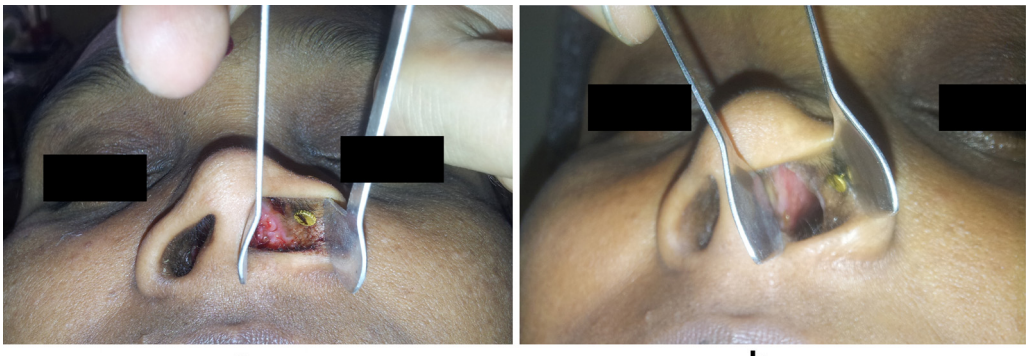

Fig. 4 – Anterior rhinoscopy showing left-side reddish-pink granulations arising from the nasal mucosa (a) and resolution after ATT (b).

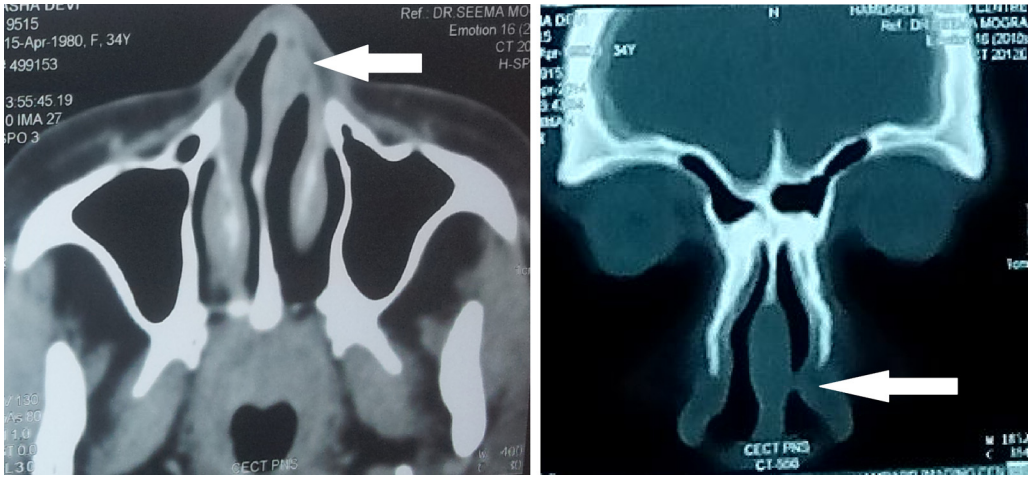

Fig. 5 – CT sections showing the site of lesion with normal sinuses.

nasal vibrissae. It has also been postulated that the nasal mucosa is inherently resistant to mycobacterial growth. Previous injury to nasal mucosa may also facilitate inoculation of *Mycobacterium tuberculosis*.[2] The sinuses are involved either by direct extension or via the blood stream.

Initial CT or MR imaging may reveal nasal soft-tissue nodules and mucosal thickening involving the PNS. Later, bone destruction and soft-tissue masses similar to neoplastic process might be present. Calcification within the lesion may be occasionally seen.[9]

The differential diagnosis should include granulomatous diseases of nose such as leprosy, mycoses, sarcoidosis, squamous cell carcinoma and lymphoma.[7] The diagnosis is confirmed by the presence of caseating granulomas, Langhans type giant cells and identifying or isolating tuberculous bacilli from the tissue removed during biopsy or surgery. Nasal secretions and swab specimens have a very low yield and should not be used to rule out this condition.[10] Recent techniques of DNA amplification by PCR have greatly improved the sensitivity of morphological detection. Also culture can now be accelerated by the use of recent technology such as BACTEC, so as to be available in less than a week.[11]

For tuberculosis involving both the nasal cavity and the PNS, antituberculous chemotherapy is the mainstay, and sinus surgery may be done additionally. The basic principles of treatment of pulmonary tuberculosis are also suitable for extrapulmonary tuberculosis. Therefore, for patients with extrapulmonary tuberculosis, a 6- to 9-month regimen (2 months of isoniazid, rifampicin, pyrazinamide and ethambutol followed by 4–7 months of isoniazid and rifampicin) is recommended as initial therapy.[12] Multidrug resistant tuberculosis (MDRTB) is however an increasing global problem and should the response to treatment be unsatisfactory, response to second line treatment is necessary. Second line therapy is based on culture sensitivity and is best advised by an internist.

Adequate local treatment including frequent nasal douching and office follow-up for removal of crusts will also be important.[8]

4. Conclusion

Sinonasal tuberculosis, despite its rarity, should be added to the differential diagnosis of nasal and paranasal sinus disorders. Any patient with persistent nasal symptoms should be investigated with CT scan and nasal endoscopy. A biopsy should be carried out for further confirmation. Antitubercular medication with/without surgical debridement is the mainstay of the treatment.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Al-Serhani AM. Mycobacterial infection of the head and neck: presentation and diagnosis. *Laryngoscope*. 2001;111:2012–2016.
2. Goguen LA, Karmody CS. Nasal tuberculosis. *Otolaryngol Head Neck Surg*. 1995;113:131–135.
3. Johnson IJ, Soames JV, Marshall HF. Nasal tuberculosis – an increasing problem? *J Laryngol Otol*. 1995;109:326–327.
4. Waldman SR, Levine HL, Sebek BA, Parker W, Tucker HM. Nasal tuberculosis: a forgotten entity. *Laryngoscope*. 1981;91:11–16.
5. Butt AA. Nasal tuberculosis in the 20th century. *Am J Med Sci*. 1997;313:332–335.
6. Moon WK, Han MH, Chang KH, et al. CT and MR imaging of head and neck tuberculosis. *Radiographics*. 1997;17(March–April (2)):391–402.
7. Hughes RG, Drake-Lee A. Nasal manifestations of granulomatous disease. *Hosp Med*. 2001;62:417–421.
8. Choi YC, Park YS, Jeon EJ, Song SH. The disappeared disease: tuberculosis of the nasal septum. *Rhinology*. 2000;38:90–92.
9. Hall RE, Delbalso AM, Carter LC. Radiography of the sinonasal tract. In: Delbalso AM, ed. In: *Maxiilofacial Imaging*. Philadelphia: WB Saunders; 1990:139–207.

10. Waldman SR, Levine HL, Sebek BA, Parker W, Tucker HM. Nasal tuberculosis: a forgotten entity. *Laryngoscope*. 1981;91 (January (1)):11–16.
11. Williams RG, Jones TD. Mycobacterium marches back. *J Laryngol Otol*. 1995;109:5–13.
12. Blumberg HM, Burman WJ, Chaisson RE, et al. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America: treatment of tuberculosis. *Am J Respir Crit Care Med*. 2003;167:603–662.

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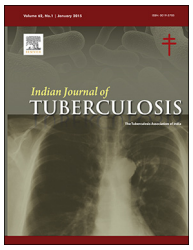

Case Report

Mycobacterium abscessus complex bacteremia due to prostatitis after prostate biopsy

Chung-Hua Chen [a,*], *Jesun Lin* [b], *Jen-Shiou Lin* [c], *Yu-Min Chen* [d]

[a] *Division of Infectious Disease, Department of Internal Medicine, Changhua, Taiwan, ROC*
[b] *Department of Urology, Changhua, Taiwan, ROC*
[c] *Department of Laboratory Medicine Changhua Christian Hospital, Changhua, Taiwan, ROC*
[d] *Department of Pharmacy Changhua Christian Hospital, Changhua, Taiwan, ROC*

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ABSTRACT

We present the case of a 49-year-old man, who developed *Mycobacterium abscessus* complex (*M. abscessus* complex) bacteremia and prostatitis after prostate biopsy. The patient was successfully treated with amikacin with imipenem-cilastatin with clarithromycin. Infections caused by *M. abscessus* complex have been increasingly described as a complication associated with many invasive procedures. Invasive procedures might have contributed to the occurrence of the *M. abscessus* complex. Although *M. abscessus* complex infection is difficult to diagnose and treat, we should pay more attention to this kind of infection, and the correct treatment strategy will be achieved by physicians.

1. Introduction

The rapid growing non-tuberculous mycobacterium (NTM) has increasingly been reported during recent decades, with the trend of the attribution to surgical procedures and immunocompromised patients.[1] Common clinical pathogens of rapid growing mycobacterium (RGM) group include the *Mycobacterium abscessus* complex (*M. abscessus* complex), *M. chelonae*, *M. fortuitum* and *M. smegmatis*. Throughout the world, these organisms have been implicated in an increasing number of infections in both immunocompetent and immunocompromised hosts. However, genitourinary infections caused by NTM are quite rare and only a few cases have been reported.[2] Thus, data on the natural history and optimal therapy for this disease entity are very limited. We reported one case of *M. abscessus* complex bacteremia and genitourinary infections following prostate biopsy.

2. Case report

A 49-year-old man has benign prostate hyperplasia (BPH) and was regularly followed up for prostate specific antigen (PSA) level at a local clinic. For elevated PSA level noted, he underwent prostate biopsy. He had had fever, chills, and burning when urinating since 5 days after the procedure. Hence, he was admitted under the diagnosis of acute prostatitis resulted after prostate biopsy. His symptoms relieved after amikacin (AMK) therapy for 1 week, then he

* *Corresponding author at*: 135 Nanhsiau Street, Changhua 500, Taiwan. Tel.: +886 4 7238595 5976; fax: +886 4 7227289.
E-mail address: changhua@cch.org.tw (C.-H. Chen).

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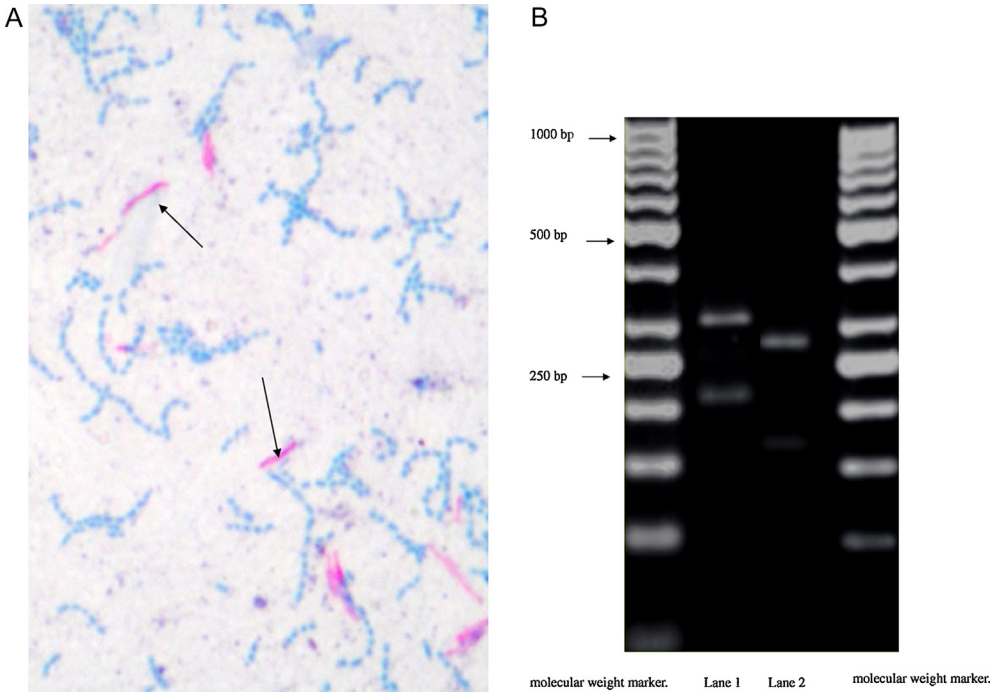

Fig. 1 – The mycobacterial findings showed the result of Ziehl Neelsen staining showed acid-fast positive bacteria (A) and patterns of restriction fragment length polymorphism analysis obtained from digestion of the amplified hsp65 gene of the isolate from this patient with *HphI* (Lane 1) and *HpaII* (Lane 2) respectively (B).
***Note*: molecular weight marker is the 50 bp molecular weight marker.**

was discharged. However, right scrotum painful mass and urinary discomfort developed since 6 days after discharge, and he went to our institute, and he was admitted under the impression of epididymo-orchitis and prostatitis. On admission day, the temperature was 37 °C, the blood pressure 116/76 mm Hg, and the pulse 100 beats/min. The appearance of the scrotum was swelling and erythematous, and the left scrotum was more severe than the right side. There was local tenderness under digital rectal examination. The laboratory data showed leukocytosis, but other values were within normal range. After admission, he was prescribed cefmetazole 1 g every 8 h and AMK 500 mg every 12 h for empirical therapy. The mycobacterial culture of blood was positive for growth at admission day 4, and the Gram stain of blood sample showed mycobacterium like microorganism. The findings of Ziehl Neelsen staining showed acid-fast positive bacteria (Fig. 1). The Mycobacterium was sub-cultured into Lowenstein Jensen media and BACTEC™ MGIT-960 (Mycobacterium Growth Indicator Tube 960 system) for mycobacterial culture. Mycobacterium abscessus complex was reported according to the fingerprint pattern of the restriction fragment length polymorphism analysis (Fig. 1). The regimen of antibiotics was exchanged into imipenem-cilastatin (IMP) 500 mg every 8 h and AMK 500 mg every 12 h. He received debridement for testicular abscess. The pathological finding of left scrotum tissue showed compatible with mycobacterial infection (Fig. 2). After treated with IMP and AMK for 14 days, he underwent antibiotic therapy with oral clarithromycin (CAM) 500 mg, 1# BID. His disease was total cured after treated for 6 months.

3. Discussion

This is a first case of *M. abscessus* complex bacteremia in an immunocompetent patient following prostate biopsy. Infection with *M. abscessus* complex is usually caused by injections of substances contaminated with the bacterium or through invasive medical procedures employing contaminated equipment or material.[1–3] This current case demonstrated that not only the immunocompromised patients but also the immunocompetent patients could receive the infection of *M. abscessus* complex during various types of medical procedures.

The treatment of this type of infection showed a poorly established evidence. In general, treatment of infections due to *M. abscessus* complex consists of surgical debridement and administering the appropriate combination of antibiotics for a prolonged period of time. The regimens for the NTM species infection was suggested to be based on in vitro susceptibility. *M. abscessus* complex and *M. chelonae* are usually susceptible to CAM and AMK; they are also susceptible to cefoxitin and IMP. A combination therapy was recommended due to the reports of resistance to various drugs. A combination of medical and surgical therapy is likely to produce optimal results in severe cases. The data revealed that a surgical intervention may play an important role in treating this type of infection. In this case, we choice combination regimen (AMK with IMP with CAM), and successfully treated this patient.

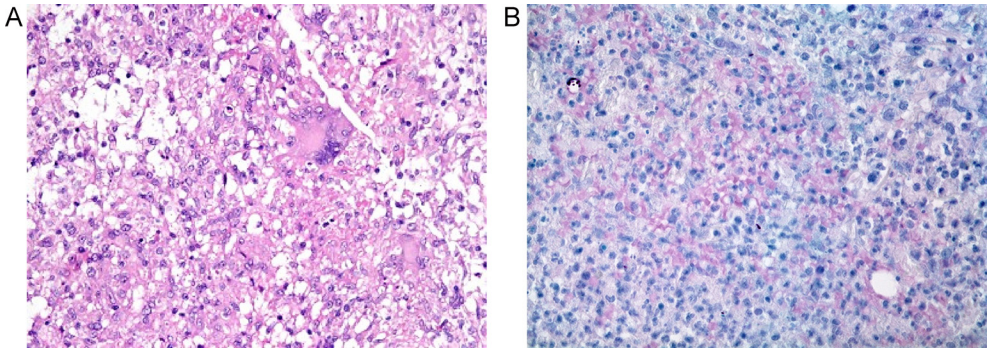

Fig. 2 – Skin biopsy specimens showed caseation necrosis in left scrotum tissue (hematoxylin–eosin stain and acid-fast stain, original magnification ×40).
(A) Histological examination showed a subcutaneous abscess with suppurative granulomatous inflammation (hematoxylin–eosin stain, original magnification ×40).
(B) An acid-fast stain revealed multiple acid-fast organisms, many arranged in chains, some located within vacuoles (Acid-fast stain, original magnification ×40).

There are many researchers paid attention to post-procedure cutaneous *M. abscessus* complex infection.[4] We reviewed literature for *M. abscessus* complex infection, and listed a summary at supplemental file. In our case, this patient underwent an invasive procedure (prostate biopsy), then acute prostatitis developed about 2 weeks later. *M. abscessus* complex infection was confirmed by the specimen culture of blood, skin lesion, and infectious testicular lesion.

In this study, we detailed our experiences and emphasized the clues to the diagnosis in the following way: a rapid identification and recognition of the character of the infection, and ordering mycobacterium culture, especially when the common bacterial culture showed no growth. We should pay more attention to this kind of infection, and the correct treatment strategy will be achieved by physicians.

Conflicts of interest

The authors have none to declare.

Acknowledgement

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REFERENCES

1. Uslan DZ, Kowalski TJ, Wengenack NL, Virk A, Wilson JW. Skin and soft tissue infections due to rapidly growing mycobacteria: comparison of clinical features, treatment, and susceptibility. *Arch Dermatol.* 2006;142:1287–1292.
2. Keller M, Mak A, Thibert L, Rene P, Klein MB. Mycobacterium haemophilum epididymal abscess in a renal transplant patient. *J Clin Microbiol.* 2008;46:2459–2460.
3. Stout JE, Gadkowski LB, Rath S, Alspaugh JA, Miller MB, Cox GM. Pedicure-associated rapidly growing mycobacterial infection: an endemic disease. *Clin Infect Dis.* 2011;53:787–792.
4. Song JY, Sohn JW, Jeong HW, Cheong HJ, Kim WJ, Kim MJ. An outbreak of post-acupuncture cutaneous infection due to Mycobacterium abscessus. *BMC Infect Dis.* 2006;6:6.

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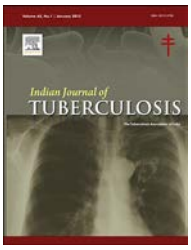

Abstracts

Modulation of dendritic cell and monocyte subsets in tuberculosis-diabetes co-morbidity upon standard tuberculosis treatment

Pavan Kumar N, Moideen K, Sivakumar S, Menon PA, Viswanathan V, Kornfeld H, Babu S. *Tuberculosis* September 2016;**100**. http://dx.doi.org/10.1016/j.tube.2016.10.004

Type 2 diabetes mellitus (DM) is a major risk factor for the development of active pulmonary tuberculosis (PTB), with development of DM pandemic in countries where tuberculosis (TB) is also endemic. However, the effect of anti-TB treatment on the changes in dentritic cell (DC) and monocyte subset phenotype in TB-DM co-morbidity is not well understood. In this study, we characterized the frequency of DC and monocyte subsets in individuals with PTB with (PTB-DM) or without coincident diabetes mellitus (PTB-NDM) before, during and after completion of anti-TB treatment. PTB-DM is characterized by diminished frequencies of plasmacytoid and myeloid DCs and classical and intermediate monocytes at baseline and 2 months of anti-TB treatment but not following 6 months of treatment completion in comparison to PTB-NDM. DC and monocyte subsets exhibit significant but borderline correlation with fasting blood glucose and glycated hemoglobin levels. Finally, while minor changes in the DC and monocyte compartment were observed at 2 months of treatment, significantly increased frequencies of plasmacytoid and myeloid DCs and classical and intermediate monocytes were observed at the successful completion of anti-TB treatment. Our data show that coincident diabetes alters the frequencies of innate subset distribution of DC and monocytes in TB-DM co-morbidity and suggests that most of these changes are reversible following anti-TB therapy.

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Occupational exposure and tuberculosis among medical residents in a high-burden setting: An open-cohort study

Rao SA, Kadhiravan T, Swaminathan RP, Mahadevan S. *Int J Tuberc Lung Dis* 2016;**20(9)**:1162–1167. http://dx.doi.org/10.5588/ijtld.15.0638

Setting: Postgraduate (PG) residency programme of a tertiary care teaching hospital in southern India.
Objective: To estimate the incidence of tuberculosis (TB) among PG residents, determine the frequency of exposure to infectious TB patients and assess whether particular specialties were associated with higher risk of exposure and incident TB.
Design: We assembled an open cohort of PG residents who were on the academic rolls for more than 3 months at any time between December 2011 and January 2013. We collected data both retrospectively and prospectively using two surveys—an entry survey at study initiation or entry into the cohort, and an exit survey at residency completion or study closure.
Results: Among 398 PG residents enrolled in the study, we identified five cases of incident TB during a cumulative follow-up period of 10 962 person-months. The incidence rate was 547 per 100 000 person-years, which was 3.1 times the incidence in the general population. Nearly two thirds ($n = 257$, 65%) of the residents were exposed to at least one infectious patient. Across the three specialty-based risk strata, there was an ordered increase in the median number of exposures ($P < 0.001$) and evaluation for presumptive TB ($P = 0.024$), as well as a trend towards higher incident TB.
Conclusion: TB incidence is significantly higher among PG residents than in the general population.

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Dotting the Three I's for collaborative TB-HIV activities: Evaluation of a pilot programme in Kathmandu, Nepal

Sah SK, Sahu SK, Lamichhane B, Bhatta GK, Bhandari KB, Owiti P, Majumdar SS. *Public Health Action* 2016;**6(3)**:169–175. http://dx.doi.org/10.5588/pha.16.0012

Setting: The three government tertiary care hospitals providing care for people living with the human immunodeficiency virus (PLHIV) in Kathmandu, Nepal.
Objectives: To assess (1) the screening cascades for intensified case finding for tuberculosis (TB), (2) isoniazid preventive therapy (IPT), including demographic and clinical factors associated with treatment interruption, and (3) TB infection control (IC) in the health facilities.
Design: A cross-sectional study of new PLHIV enrolled from January 2012 to December 2014.
Results: Among 572 registered PLHIV, 91% were on antiretroviral therapy. Of those registered, 561 (98%) were screened for TB and 73 (13%) were diagnosed with TB (17 [25%] sputum smear-positive, 17 [25%] smear-negative and 35 [51%] extrapulmonary). Among the 488 (87%) PLHIV without active TB, 157 (32%) were initiated on IPT, of whom 136 (87%) completed treatment and 17 (11%) interrupted treatment. Those who experienced adverse events were 12 times more likely to interrupt IPT. TB IC showed gaps in personal control measures and supporting structures and policies.

Conclusion: The implementation of the Three I's for collaborative TB-HIV activities in pilot sites in Nepal was successful and should be scaled up.

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Improved tuberculosis outcomes with daily vs. intermittent rifabutin in HIV-TB co-infected patients in India

Jenks JD, Kumarasamy N, Ezhilarasi C, Poongulali S, Ambrose P, Yepthomi T, Devaraj C, Benson CA. *Int J Tuberc Lung Dis* 2016;**20(9)**:1181–1184. http://dx.doi.org/10.5588/ijtld.15.0997
Setting: Y R Gaitonde Centre for AIDS Research and Education, Chennai, India.
Objective: To compare anti-tuberculosis treatment outcomes in individuals with human immunodeficiency virus (HIV) and tuberculosis (TB) co-infection on atazanavir/ritonavir (ATV/r) antiretroviral therapy (ART) plus daily rifabutin (RBT) 150 mg with those on ATV/r plus thrice-weekly RBT 150 mg.
Design: A retrospective study was conducted of two HIV-TB co-infected cohorts between 2003 and 2014. Basic demographic and TB outcome data were obtained from an electronic database and patient records. The χ^2 and Fisher's exact test were used to compare daily and intermittent RBT treatment groups.
Results: Of 292 individuals on an ATV/r-based ART regimen plus RBT, 118 (40.4%) received thrice-weekly RBT and 174 (59.6%) daily RBT. Patients in the two RBT treatment groups were similar in sex, age, previous history of TB, site of TB and acid-fast bacilli smear status. More individuals in the daily vs. the intermittent RBT group achieved clinical cure (73.0% vs. 44.1%, $P < 0.001$), with no significant differences in relapse/recurrence or all-cause mortality between groups.
Conclusion: There were higher rates of clinical TB cure in individuals on a boosted protease inhibitor-based ART regimen with daily RBT compared to intermittently dosed RBT. Optimal RBT dosing in this setting requires further investigation.

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Drug-induced hypothyroidism during anti-tuberculosis treatment of multidrug-resistant tuberculosis: Notes from the field

Munivenkatappa S, Anil S, Naik B, Volkmann T, Sagili KD, Akshatha JS, Buggi S, Sharada MA, Kulkarni S, Chadha VK, Moonan PK. *J Tuberc Res* August 23, 2016. http://dx.doi.org/10.4236/jtr.2016.43013
We followed 188 euthyroidic persons undergoing treatment for multidrug resistant tuberculosis (MDR-TB) in the state of Karnataka, India to determine the incidence of hypothyroidism during anti-tuberculosis treatment. Overall, among MDR-TB patients with valid thyroid stimulating hormone (TSH) values, about 23% developed hypothyroidism (TSH value ≥10 mIU/ml) during anti-tuberculosis treatment; the majority (74%) occurring after 3 months of treatment. Among 133 patients who received a regimen that contained ethionamide, 42 (32%) developed hypothyroidism. Among 17 patients that received a regimen that contained para-aminosalicylate sodium, 6 (35%) developed hypothyroidism. Among 9 HIV positive patients on antiretroviral treatment, 4 (44%) developed hypothyroidism. These results differ from previously reported 4% incidence of hypothyroidism amongst patients who passively reported thyroidal symptoms during treatment, suggesting routine serologic monitoring of TSH throughout the course of treatment for MDR-TB is warranted.

http://dx.doi.org/10.1016/j.ijtb.2016.11.023

SLCO1B1 gene polymorphisms do not influence plasma rifampicin concentrations in a South Indian population

Ramesh K, Hemanth Kumar AK, Kannan T, Vijayalakshmi R, Sudha V, Manohar Nesakumar S, Bharathiraja T, Lavanya J, Swaminathan S, Ramachandran G. *Int J Tuberc Lung Dis* 2016;**20(9)**:1231–1235. http://dx.doi.org/10.5588/ijtld.15.1007
Objective: To determine the effect of *SLCO1B1* gene polymorphisms (*rs*11045819, *rs*4149032 and *rs*4149033) on rifampicin (RMP) concentrations in adult tuberculosis (TB) patients from south India.
Methods: We genotyped adult TB patients for three *SLCO1B1* gene polymorphisms—*rs*11045819, *rs*4149032 and *rs*4149033—and compared 2-h post-dosing RMP concentrations of the different genotypes for each of the polymorphisms. Plasma RMP was determined using high-performance liquid chromatography. Genotyping was performed using direct sequencing.
Results: Among the 256 study patients, minor allele frequencies were respectively 0.01 (A), 0.46 (C) and 0.07 (A) for *rs*11045819, *rs*4149032 and *rs*4149033 polymorphisms; genotype distributions followed Hardy–Weinberg equilibrium. RMP concentrations did not significantly differ between the different genotypes of the three polymorphisms.
Conclusion: This is the first study to show that *rs*11045819, *rs*4149032 and *rs*4149033 polymorphisms in the*SLCO1B1* gene did not influence RMP concentrations in Indian patients.

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Global burden of drug-resistant tuberculosis in children: A mathematical modelling study

Dodd PJ, Sismanidis C, Seddon JA. *Lancet Infect Dis* 2016;**16(10)**:1193. http://dx.doi.org/10.1016/S1473-3099(16)30132-3
Background: After infection with *Mycobacterium tuberculosis*, children are at an increased risk of progression to tuberculosis disease; a condition that can be challenging to diagnose. New estimation approaches for children have highlighted the gap between incidence and notifications of *M tuberculosis*, and suggest there are more cases of isoniazid-resistant and multidrug-resistant (MDR) disease than are identified. No work has yet quantified the burden of drug-resistant infection, or accounted for other types of drug resistance or sampling uncertainty.
Methods: We combined a mathematical model of tuberculosis in children with an analysis of drug-resistance patterns to produce country-level, regional, and global estimates of drug-resistant infection and disease. We determined drug resistance using data from the Global Project on Antituberculosis Drug Resistance Surveillance at WHO, from surveys and surveillance reported between 1988 and 2014. We combined 1000 sampled proportions for each country from a Bayesian approach with 10 000 sampled country estimates of tuberculosis disease incidence and *M. tuberculosis* infection prevalence. We estimated the proportions of tuberculosis cases at a country level with isoniazid monoresistance, rifampicin monoresistance, multidrug resistance (MDR), fluoroquinolone-resistant multidrug resistance, second-line injectable-resistant multidrug resistance, and extensive multidrug resistance with resistance to both a fluoroquinolone and a second-line injectable (XDR).
Findings: We estimated that 850 000 children developed tuberculosis in 2014; 58 000 with isoniazid-monoresistant tuberculosis, 25 000 with MDR tuberculosis, and 1200 with XDR tuberculosis. We estimate 67 million children are infected with

M. tuberculosis; 5 million with isoniazid monoresistance, 2 million with MDR, and 100 000 with XDR. Africa and southeast Asia have the highest numbers of children with tuberculosis, but the WHO Eastern Mediterranean region, European region, and Western Pacific region also contribute substantially to the burden of drug-resistant tuberculosis because of their much higher proportions of resistance.
Interpretation: Far more drug-resistant tuberculosis occurs in children than is diagnosed, and there is a large pool of drug-resistant infection. This finding has implications for approaches to empirical treatment and preventive therapy in some regions of the world.

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Pharmacokinetics of thrice-weekly rifampicin, isoniazid and pyrazinamide in adult tuberculosis patients in India

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Objective: To study the pharmacokinetics of rifampicin (RMP), isoniazid (INH) and pyrazinamide (PZA) in adult tuberculosis (TB) patients and examine factors that influence drug pharmacokinetics.
Methods: Adult TB patients ($n = 101$) receiving thrice-weekly anti-tuberculosis treatment in the Revised National TB Control Programme (RNTCP) were studied. The study was conducted at steady state after directly observed drug administration. RMP, INH and PZA concentrations were estimated using high-performance liquid chromatography and *NAT2* genotyping by real-time polymerase chain reaction.
Results: RMP peak concentration (C_{max}) was sub-therapeutic (<8 μg/ml) in 88% of the patients. The C_{max} of RMP, INH and PZA at 2 h was observed in respectively 83.2%, 97.0% and 92.1% of the patients. The C_{max} and area under the curve from 0 to 8 h ($AUC_{0–8}$) of PZA was lower in TB patients with diabetes mellitus than in non-diabetics. Significant associations were observed between the C_{max} and the $AUC_{0–8}$ of RMP, INH and PZA with drug doses; RMP with category of treatment; INH with smoking, body mass index and *N*-acetyl transferase 2 genotype; and PZA with sex and smoking.
Conclusions: Several risk factors for drug concentration variations were identified. Two-hour post-dosing drug concentrations mimicked C_{max}. A high proportion of TB patients had RMP C_{max} below the expected range, which is a matter of concern.

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Tradeoffs in introduction policies for the anti-tuberculosis drug bedaquiline: A model-based analysis

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Background: New drugs for the treatment of tuberculosis (TB) are becoming available for the first time in over 40 y. Optimal strategies for introducing these drugs have not yet been established. The objective of this study was to compare different strategies for introducing the new TB drug bedaquiline based on patients' resistance patterns.
Methods and findings: We created a Markov decision model to follow a hypothetical cohort of multidrug-resistant (MDR) TB patients under different bedaquiline use strategies. The explored strategies included making bedaquiline available to all patients with MDR TB, restricting bedaquiline usage to patients with MDR plus additional resistance and withholding bedaquiline introduction completely. We compared these strategies according to life expectancy, risks of acquired resistance, and the expected number and health outcomes of secondary cases.
For our simulated cohort, the mean (2.5th, 97.5th percentile) life expectancy from time of initiation of MDR TB treatment at age 30 was 36.0 y (33.5, 38.7) assuming all patients with MDR TB received bedaquiline, 35.1 y (34.4, 35.8) assuming patients with pre-extensively drug-resistant (PreXDR) and extensively drug-resistant (XDR) TB received bedaquiline, and 34.9 y (34.6, 35.2) assuming only patients with XDR TB received bedaquiline. Although providing bedaquiline to all MDR patients resulted in the highest life expectancy for our initial cohort averaged across all parameter sets, for parameter sets in which bedaquiline conferred high risks of added mortality and only small reductions in median time to culture conversion, the optimal strategy would be to withhold use even from patients with the most extensive resistance. Across all parameter sets, the most liberal bedaquiline use strategies consistently increased the risk of bedaquiline resistance but decreased the risk of resistance to other MDR drugs. In almost all cases, more liberal bedaquiline use strategies reduced the expected number of secondary cases and resulting life years lost. The generalizability of our results is limited by the lack of available data about drug effects among individuals with HIV co-infection, drug interactions, and other sources of heterogeneity, as well as changing recommendations for MDR TB treatment.
Conclusions: If mortality benefits can be empirically verified, our results provide support for expanding bedaquiline access to all patients with MDR TB. Such expansion could improve patients' health, protect background MDR TB drugs, and decrease transmission, but would likely result in greater resistance to bedaquiline.

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