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Editorial

RELEVANCE OF NON-TUBERCULOUS MYCOBACTERIA IN INDIA

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There is no doubt that tuberculosis caused by *Mycobacterium tuberculosis* has always been and still is a major public health problem in India. It has always been endemic and it is probably due to this endemicity that the other mycobacteria commonly reported from other countries were not able to come up. These other mycobacteria were previously known by various names as 'atypical', 'anonymous', 'mycobacteria other than tuberculosis (MOTT) or potentially pathogenic environmental mycobacteria (PPEM). But, today the terminology of non-tuberculous mycobacteria (NTM) given by the International Working Group on Mycobacterial Taxonomy is universally accepted. "Atypical mycobacteria", the term commonly used is actually a misnomer because they, as per the definition of the genus, are also typical mycobacteria. These organisms are acid fast bacilli, difficult to distinguish from *M. tuberculosis* on Ziehl Neelsen staining. On culture they can be differentiated based on their growth rate, colony morphology, niacin production and other biochemical tests. Lipid profile and molecular based techniques like PCR-RFLP, ribosomal RNA sequencing have further helped in speciation and today as many as 127 species[1] have been identified. These microorganisms are of low virulence and hence have mostly been considered as either colonizers or coincidental contaminants from the environment. However, this was true more than two decades ago when NTM were rarely associated with infection and disease but since 1980 the scenario has changed. With the AIDS pandemic and easy availability of immuno-compromised hosts, these organisms are now emerging as important pathogens. A new terminology i.e. 'other mycobacteriosis' is now used for the diseases caused by NTM and the disease is not only restricted to pulmonary and extra pulmonary sites but can also present as disseminated disease in severely immuno-compromised individual.

Non-tuberculous mycobacteria are ubiquitous in nature and are found as free living saprophytes in various environmental habitats especially in soil, dust, bio-films and water, including water from tanks, sewage, river and sea. The species, however, may differ from one geographical area to another. They are also important pathogens for a variety of mammals, birds, reptiles and fish. Infection with these organisms is probably acquired from the environment though the exact mode of transmission is still not very clear. Human to human and animal to human transmission has so far not been documented. Inhalation of contaminated aerosols is the presumed mode of inoculation for the lungs while ingestion of contaminated water and food results in gastrointestinal involvement. Cutaneous disease may occur by direct penetration of the skin or by inoculation on an abrasion or surgical wound as is seen in *M. abscessus, M. fortuitum, M. chelonae, M. marinum* and *M. ulcerans*. The bacteria may then colonise and/or directly invade the tissue. There is increase in mycobacterial replication which may initially result in intermittent bacteremia without dissemination and at this stage the patients may be asymptomatic as bacterial load is low. As the immuno-competence level falls with CD4 count becoming less than 100 per cumm, as is seen in AIDS, continuous bacteremia with dissemination may occur. Horsburgh in 1994 stated that such patients are like open culture plates and AIDS related immuno- suppression is the single most important risk factor associated with

disseminated NTM infection, especially for *Mycobacterium avium* Complex (MAC).[2] As many as 15-40 per cent of patients with MAC infection in United States have been reported to present with disseminated infection. This stage may be accompanied by clinical symptoms like cough, fever, weight loss, night sweats, fatigue, chronic diarrhorea, extra-hepatic obstruction and abdominal pain. Severe anemia is the hallmark of infection. Blood cultures are highly positive and frequent cultures can help detect the disease early. Organisms are found almost exclusively in the circulating monocytes where magnitude of mycobacteria may range from <1 to 10^2 colony forming units/ml, resulting in multiple organ disease with involvement of lymph nodes, spleen, bone marrow, lungs and gastrointestinal tract. On histopathology, the infected tissues are filled with large numbers of distended histiocytes packed with acid fast bacilli to the tune as high as 10^{10} colony forming units/gram of tissue. The unique feature in this is that in spite of this load the granulomatous reaction and necrosis are absent. There is no evidence that NTM can establish latent infection with subsequent reactivation as is seen in tuberculosis. Disseminated infection without AIDS is extremely rare, though these organisms can cause significant pulmonary and extra-pulmonary disease involving lymphnodes, bones, skin, wounds in immuno-competent host also. NTM have also been reported to cause nosocomial infections, particularly in hospitalized AIDS patients.

NTM have been observed to be an important cause of morbidity and mortality in Western countries but there is very little data from India. National AIDS Control Organization (NACO) in one of its publications in 2000[3] had mentioned that *Mycobacterium avium intracellulare (MAI)* (common isolates of the West) has not been reported from our country so far. We all know that in order to cause disease any parasite needs a suitable host and an appropriate external environment to complete its life cycle. By 2000, there were sufficient reports to indicate that both existed in India. Being opportunistic organisms NTM needed immuno-compromised hosts. The first case of HIV seropositivity was reported from Chennai in 1986 and by 2000, a total of 98,451 HIV seropositives and 13,304 AIDS affected individuals were reported in our country[3]. In addition there were patients immuno-compromised due to other causes. Thus there was no dearth of available hosts.

The evidence that they are present in our environment was clearly given by TRC Chennai. Paramasivan et al (1985)[4] in their pioneering study from BCG study area had reported *M. avium-intracellulare* (MAI) to be the most frequently isolated species (22.6% of all NTM) followed by *M terrae* (12.5%) and *M. scrofulaceum* (10.5%). Later in 1994 Kamala *et al*[5] demonstrated that MAI and *M. scrofulaceum* were present in water and dust and could be isolated from the sputum samples of individuals in that area. *M. fortuitum* was shown to be present in the soil.

Much later in 2004 a similar study from JALMA has demonstrated among many mycobacteria, the presence of *M. avium, M. kansasii, M. terrae, M. fortuitum* and *M. chelonae* in water and *M. avium, M. terrae* and M. chelonae in soil.[6]

More recently, a study from Sewagram, Wardha (2007)[7], in order to establish correlation, collected soil and water samples from the environment of those patients from whom NTM were isolated in the clinical samples. They reported 20 isolates from soil and five from water. Four of the soil isolates were identified as MAC and one of them was from the environment of a patient suffering from the same infection. However, the molecular typing did not show the strain to be the same as that isolated from the patient.

The fact that NTM colonise the respiratory system even of immuno competent individuals was well established even before 2000. There were several reports [8-13] on their isolation from patients suspected of pulmonary tuberculosis but their role as pathogens was always doubtful. In one of the field studies[14] their prevalence among 6265 symptomatics of tuberculosis, was reported as 2.4/ 1000.

The data on pathogenicity of NTM in India is still scarce and till date only limited studies are available. In a study conducted in 2001 Narang et al using Paraffin Baiting Technique for the first time, showed the presence of NTM in stool of HIV seropositive patients – 4 isolates were MAC and 2 *M. fortuitum*.[15] No NTM was isolated from HIV seronegative subjects indicating clearly that NTM can easily colonise the gut of immuno-compromised people like those living with HIV AIDS but not of normal immuno-competent individuals. On extending the study further the same authors in 2005 again demonstrated for the first time NTM mycobacteraemia in HIV seropositive patients. This was the first report demonstrating disseminated NTM infection in India[16] where NTM were isolated from 6 HIV seropositive patients (8.4%) of which three were positive for MAC (4.23%) and another three for *M. simiae* (4.23%), a rare isolate to cause mycobacteraemia.

The CD counts in such patients as stated earlier were less than 100 cells/cumm and the same was demonstrated in a study[7] where 6 NTM were isolated again by blood culture from HIV sero-positive patients. Infact one of the MAC isolate from blood and stool of the same patient on molecular typing was proved to be the same strain.

NTM are emerging as important causative agents of pulmonary and extra pulmonary disease in HIV seropositive and AIDS patients and, therefore in these patients acid fast bacilli seen on sputum smear or in tissues may not necessarily be *M. tuberculosis.* Thus there is a need to perform cultures to isolate and speciate these mycobacteria and specific drugs should be administered, since treatment strategies differ with each species. Treatment should be initiated based on drug susceptibility testing. Mycobacteremia is common in disseminated disease and, therefore, blood culture can clinch the diagnosis at an early stage. It is also observed that timely initiation of antiretroviral therapy can bring down the rate of NTM infection in these patients. In the Johns Hopkins cohort with advanced HIV disease, the proportion developing disseminated MAC (DMAC) infection had fallen from16% before 1996 to 4% after 1996, with a rate of less than 1% per year in 2004.[17] In India Governments initiative to start ART in large scale is also likely to show similar results. We in our hospital are already seeing signs of this trend. The rate of NTM bacteremia in AIDS patients coming to the hospital in 2002 was 8.5% but in 2006-07 we recorded it to be only 5.3%. Though no scientific study has been conducted, we personally feel that this could be due to the ART started in a big way at Nagpur just 80 km from our hospital which could be responsible for this fall. There is indeed a need to create awareness among both the clinicians and the microbiologists so that we are able to not only generate data for our country but also take necessary steps to diagnose and treat 'other mycobactriosis' which is also present as dual infection in PLWHA in our country. By doing so we can definitely add quality as well as years to the life of these patients.

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Original Article

PSYCHO-SOCIAL DYSFUNCTION: PERCEIVED AND ENACTED STIGMA AMONG TUBERCULOSIS PATIENTS REGISTERED UNDER REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME

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Summary

***Objective*:** To examine the perceived and enacted stigma experienced by TB patients and the community.

***Methods*:** We interviewed 276 TB patients registered for treatment during January-March 2004 in government health facilities of two Tuberculosis Units of south India. Data on perceived and enacted stigma were collected after two months of starting treatment, using a semi-structured interview schedule. In addition, four Focus Group Discussions were conducted among Directly Observed Treatment (DOT) providers and community members. Narrative summaries were also taken down to collect additional qualitative information.

***Results*:** Of the 276 patients, 190 (69%) were males. There was no significant difference between the genders in relation to social stigma. Perceived stigma was higher than enacted stigma in both genders and significantly higher among males (Low self esteem $p<0.05$), change of behavior of community ($p<0.05$), ashamed to cough in front of others ($p<0.05$).

***Conclusion*:** Considering the social and emotional impact of the disease, it is essential to adopt support strategies to enhance acceptance and for a successful health programme. **[*Indian J Tuberc 2008; 55:179-187*]**

***Key words*:** Tuberculosis, Perceived stigma, Enacted stigma, Psycho- social dysfunction

INTRODUCTION

Illness and chronic disease create multiple burdens for patients, including the necessity to deal with pain, suffering, reduced quality of life, premature mortality, financial costs and familial emotional trauma. Ultimately, society must bear the negative impact of the social consequences created by the combined effects of the disease on patients and their families.[1]

Tuberculosis (TB) is a classic example of a disease with both medical and social dimensions, characterised by its close relation to poor socio-economic conditions. Previous studies indicate that the stigma associated with TB adds to the burden of disease for both men and women particularly if they are of marriageable age.[2] A survey carried out in India in 1997, before implementation of Directly Observed Treatment Short-course (DOTS) strategy, estimated that 100,000 women were rejected by their families each year because of their TB disease.[3]

DOTS, the accepted, standard comprehensive strategy for the diagnosis, treatment and monitoring of TB world-wide, known as the Revised National Tuberculosis Control Programme (RNTCP) in India, was pilot-tested in 1993, and after rapid expansion since 1998, the entire country was covered by March 2006.[4] India's RNCTP is the second largest programme in the world based on population coverage and the large number of patients initiated on treatment.[5] The millennium development goal for TB is to reduce its incidence and mortality to 50% by 2015. However, one of the recognised barriers to TB treatment is the stigma associated with the disease. In the year 2004, a study done at our centre reported that both men and women TB patients aged <45 years registered under RNTCP felt equally inhibited discussing their treatment with friends and family.[6] Another study on "Perceptions of tuberculosis patients about their physical, mental and social well-being" reported that stigma remained unchanged even after completion of treatment.[7] In order to gain further insight into

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the issue of stigma related to TB, the present study was undertaken to examine the perceived and enacted stigma (actual discrimination) experienced by TB patients and the community perceptions on stigma related to TB.

MATERIAL AND METHODS

Settings

India's Revised National Tuberculosis Control Programme (RNTCP), an adoption of the internationally recommended Directly Observed Treatment Short course (DOTS) strategy, focuses on providing free quality sputum smear microscopy for diagnosis as well as quality drugs for treatment free of cost. This strategy also provides decentralized treatment services close to patients' residence under direct observation with the help of government health workers and community volunteers. The primary objective of RNTCP was to achieve 85% cure rate and to detect 70% of new sputum smear positive cases (Central TB Division, 2006). Treatment is administered under direct observation (DOT) on a thrice-weekly schedule in two phases: an initial intensive phase (IP) for 2-3 months, followed by a continuation phase (CP) of 4-5 months. The DOTS takes into account the patient's convenience and the responsibility of ensuring completion of the treatment by DOT provider. TB control programme is a felt-need oriented programme as more than 80% of persons

Table 1: Demographic, socio-economic characteristics of TB patients enrolled in the study (n = 276)

	Female (86)		**Male** (190)		**Total (276)**		p-value
	number	percentage	number	percentage	number	percentage	
Age(years)							
≤35	65	76	76	40	141	51	≤0.01
>35	21	24	114	60	135	49	
Marital Status							
Married	56	65	141	74	197	71	NS
Unmarried	30	35	49	26	79	29	
Literacy							
Illiterate	26	30	36	19	62	22	≤0.05
Literate	60	70	154	81	214	78	
Occupation							
Unemployed	73	85	33	17	106	38	≤0.01
Employed	13	15	157	83	170	62	
Income							
Nil	73	85	28	15	101	37	≤0.01
≤1000	7	8	57	30	64	23	
>1000-3000	6	7	105	55	111	40	

with chest symptoms have been reported to seek relief of symptoms on their own. TB awareness was not up to expectations due to poor literacy rate or lack of availability of effective communication channels resulting in improper health seeking behaviour and the treatment compliance.

Study area

This study was carried out in two Tuberculosis Units (TUs), Kancheepuram (rural) and Chennai (urban), covering a population of 1.1 million in the state of Tamil Nadu.

Table 2: Stigma related problems after disclosing the disease

	Factor	Percentage	
		Yes	No
Family	Looked down	24	76
(n = 252)	Change of attitude	11	89
	Keeping separate	10	90
Community	Looked down	54	46
(n = 140)	Problems faced from them	9	91
	Change of behaviour	47	53
Work place	Staff behaviour changed	7	93
(n = 170)	Discontinued job	26	74
	Job changed	9	91

Table 3: Perceived stigma among TB patients enrolled in the study

	No	%
The disease not revealed to		
Family	24	9
Friends/relatives/neighbours	136	49
Work-place	44	63
Reluctant to attend social function	74	27
Felt friends/relatives/neighbors avoiding	18	9
Feeling ashamed to cough	107	43
Felt others looked down upon	85	32
Among Unmarried		
Problems expected	19	63

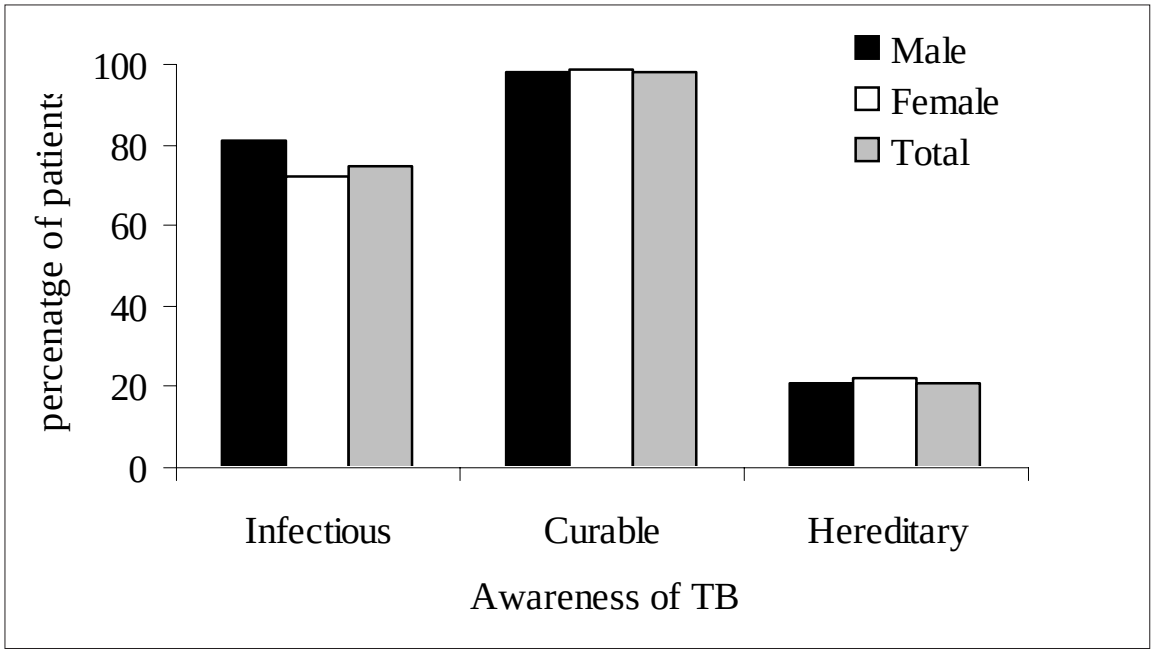

Figure 1: Awareness of disease among Tuberculosis patients

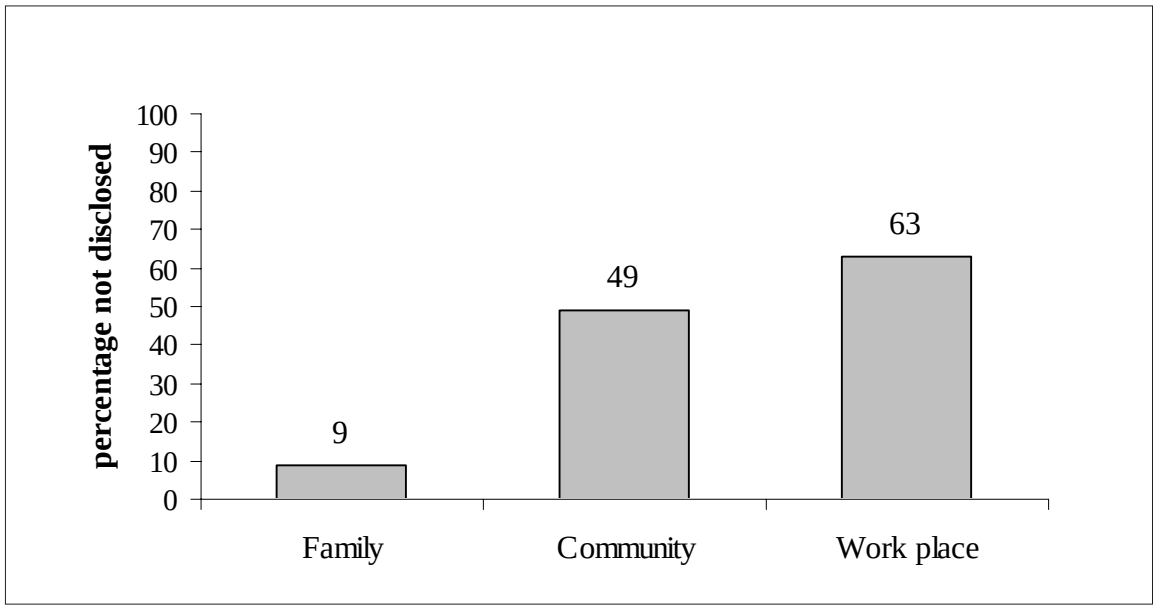

Figure 2: Proportion of TB patients who have not disclosed their illness to family, community and fellow workers

Study population

Three-hundred and fifty TB patients attending government health facilities during the first quarter (January-March) of 2004 formed the study population. Seventy-four patients could not be contacted due to the following reasons: transferred to other TUs (10), unwillingness for interviews (4) and the remaining 60 patients had defaulted from the treatment during IP. In all, 276 (79%) patients were interviewed at the clinics of the two TUs.

Tool for data collection

A semi-structured, pre-coded, pre-tested patient interview schedule was prepared on the basis of Explanatory Model Interview catalogue (EMIC).[8] The EMIC is not a fixed scale, but rather a frame work for flexible interviews and an instrument for studying illness related experience, its' meaning and related behaviour. This was used to obtain information from TB patients' problems faced in their houses, attitude of neighbors, friends and co-workers. Interview schedule included data on socio-economic and demographic characteristics, awareness of TB and the nature of their disclosure of their disease to family members, relatives, neighbours, friends and employers. The information was also elicited regarding behavioural changes such as maintaining appropriate personal distance and avoiding close contact activities with family members, neighbours, friends and employers. Data was collected by Medical Social Workers (MSWs) after obtaining informed written consent. All the interviews were conducted two months after initiation of Anti-TB Treatment (ATT).

Box 1. Narrative summaries from patients

- *I did not reveal my disease to my family members since I will be separated from others*
- *I am scared to tell my disease to my husband and mother-in- law because of fear of rejection*
- *Myself keeping away from others to avoid spread of infection*
- *I want my children to be married without any problems. My disease may create problems.*
- *I feel ashamed of coughing in front of others since they may look down upon me.*
- *My employer does not know about my disease. If he knows, I will be sacked, also my colleagues will avoid me*
- *After knowing my disease, my husband left me with three children and started living with another woman*
- *After my diagnosis as TB , my mother-in-law sent me to my parents house*
- *Even after cure, I was not allowed to do household work*

In addition, Focus Group Discussions (FGDS) were conducted among DOT providers and community members. The FGDs examined community contexts, perceptions and explanation of TB with particular consideration of stigma related problems anticipated and actually faced at home, community, and at work-place. The group discussions were conducted in the local language by a moderator and were recorded by an observer. Six FGDs were conducted among men and women in both rural and urban areas. Each group comprised eight to ten members with men and women aged 15-60 years. The discussions were based on a semi-structured topic guide covering the research questioner on TB stigma. Discussions were recorded verbatim and transcribed.

Definitions used

Stigma A powerful and discrediting social label that radically changes the way individuals view themselves and are viewed by others (National Institute of Health, 2000)

Enacted stigma Refers to actual discrimination or un-acceptability.[9]

Felt or perceived stigma Refers to the fear of discrimination or acceptability.[9]

Data management

The statistician scrutinized the data for completeness and consistency. Data was entered and analysed using SPSS and Epi-Info (version 6.04d Centers for Disease Control, Atlanta, GA, 2001). Univariate analysis was used to compare perceived and enacted stigma among males and females and the Chi-square test was used to test the difference in the proportions of responses. The level of statistical significance was defined as $p<0.05$.

RESULTS

Demographic and socio-economic profile of study population

Of 276 TB patients interviewed, 190 (69%) were males. The demographic and socio-economic characteristics of these patients were as follows: 51% were ≤35 years of age, 78% literates, 62% employed, 71% married and 40% were getting monthly income of > Rs.1000 (1$=Rs 45). The following characteristics were significantly different between male and female genders: aged ≤35 (40% vs 76%; $p<0.01$), literates (81% vs 70%; $p<0.05$), employed (83% vs 15%; $p<0.01$) and personal monthly income > Rs.1000 (55% vs 7%; $p< 0.001$) Table-1.

Of these, majority of TB patients (62%) had a history of TB in their family but only about a quarter of them were aware of other TB patients in their village (21%).

Awareness of tuberculosis among patients

Seventy-five per cent of both male and female patients knew that TB is infectious in nature (male 81%; female 72%), curable (male 98%; female 99%) and equal proportion of both sexes reported that TB is hereditary (male 21%; female 22%) Figure-1.

Perceived stigma

Since the data on perceived and enacted stigma in males and females were similar, it was combined and presented in Table-2 and Table-3.

Table-2 describes perceived stigma in terms of person, family, community and work place in both genders. One third of the patients were reluctant to attend social functions and they felt that others looked down on them. Forty-three per cent of the patients felt ashamed to cough in front of others, it was significantly higher among males (76% vs 24%; $p<0.05$). About 9% felt that friends/relatives/ neighbors avoided them.

The disease status was not revealed by patients to family members by 9%, to the community by 49% and to their work spot colleagues by 63%. Among unmarried patients, anticipated problems in terms of getting married due to their disease was reported in 63% (Table-2).

Enacted stigma

Table-3 describes enacted stigma in the context of family, community, and work place in both genders. Of the patients who disclosed their disease to the family, 24% felt they were looked down upon, 21% were not allowed to do house hold activities, 10% were kept isolated, 8% found change in the behaviour of family members and 23% did not receive additional care.

Among married patients, 18% were reluctant to discuss their disease with their spouses, 28% faced problems in sexual life and 8% were (male 7%, female 12%) rejected and separated from the spouse. It was also observed that among these patients, 57 (69%) male and 26 (31%) female received family support from their parents-in-law.

Among the patients who had disclosed their disease to the community, 54% felt they were valued 'less', 47% experienced change in behaviour towards them and 9% faced rejection due to their disease. Of the total 170 employed patients, 37% disclosed their disease at work place and among them about one fifth experienced change in the behaviour of their colleague and more than two thirds had to discontinue their job.

From FGDs among the community members and DOT providers, it was observed that blood in sputum and persistent cough were considered as symptoms for TB. They said that there was stigma attached to the disease. Many of them said that most of the patients disliked to be called as TB patients. It was noted that unmarried patients especially females experienced difficulties in getting married. They also informed that some of the patients do not want to reveal their disease to their employers/ co-workers since they felt that they will be sent out of jobs/rejected by the community. In all, the FGDs, perceived stigma was expressed more by the members than enacted stigma.

Narrative summaries were also taken down to collect additional qualitative information (Box 1).

DISCUSSION

The main finding of this study was that perceived stigma was more than enacted stigma in the context of personal, family, community and work place interactions among both male and female TB patients enrolled under RNTCP.

In the present study, one third of the TB patients were reluctant to attend social functions due to their illness. Similar findings were observed in an earlier study from our centre, where before, during and at the end of treatment, 38%, 30% and 24% of TB patients were reluctant to attend social gatherings. This study highlighted the fact that perceived stigma remained unchanged even after completing treatment.[7] More than one third of the present study population felt that others looked down upon them and they were ashamed to cough in front of others. This is corroborated with study done at Centre of Health Research and Development (CHRD), Maharastra[10] where 43% of male and 60% females think less of self, reflecting a low self esteem. Studies from other parts of India reported that stigma and ostracism have been associated with chronic illnesses like leprosy, mental illness and TB.[10] A study on HIV positive individuals from Chennai brings out the finding that actual (enacted) stigma experienced among those infected with HIV is much less (26%) as compared to the fear of being stigmatised or perceived stigma (97%).[11] The programme managers should recognize this social issue and adopt appropriate strategies to reduce the stigma attached to TB.

In our study, 10-25% of the patients experienced negative reactions from the family members. However, in observations reported by a study conducted prior to implementation of RNTCP, 60% of the patients reported negative reactions.[12] Similarly a study from New Delhi reported severe psycho-social dysfunction in personal, familial, vocational, social and cognitive areas among patients with TB.[13] Patients, who revealed their disease to the community, faced negative reactions such as being looked down upon by the community and change of behaviour and rejection by community members. Under DOTS strategy there is scope to

motivate the patient's family to provide family support and involvement of community DOT providers. These factors might have contributed for the reduction in negative reactions.

Not in conformity with the popular belief that perceived stigma is associated with poor awareness of TB among patients and community, the present study showed awareness on TB diagnosis and treatment to be good among TB patients (75% knew that TB is of infectious nature and 98% were aware that TB is curable). With the idea that better understanding of the disease may result in more social support and reduction of perceived stigma, Leprosy control and HIV/AIDS programmes have been successful in reducing stigma using the direct and indirect approach through qualitative research and awareness programmes.[14,15] Also WHO has initiated a global pragramme for lymphatic filariasis to improve knowledge and attitudes of Egyptian school children, which included messages on Mass Drug Administration (MDA) and stigma reduction through a comic book. A well-accepted comic book for children is a proven way to reduce stigma and increased knowledge about disease prevention and treatment.[16] So, the authors feel that in the area of tuberculosis, more studies are needed to explore the relationship between awareness and stigma reduction.

In the present study, employed patients faced problems such as loss/discontinuation of the job. The participants of the FGDs among the community members and DOT providers corroborated these findings. Hence there is a need to sensitize the community and the employers on TB and control programme.

We found that both male and female patients faced rejection by spouse due to their illness. Similar findings were reported by the earlier studies from our centre, 15% of married women were rejected by their families on account of tuberculosis,[3] 2% of male and 4% female facing rejection due to their illness.[6] Married women from western India had expressed fear of rejection from husbands and harassment by in-laws.[17-19] This is in agreement with the estimates made in India that every year 1,00,000 women are rejected by their family members on account of their illness .[4]

Problems related to marriage prospects were expressed by 63% of unmarried patients from this study. Uplekar et al., from Maharastra report that parents of young women do not want to reveal their daughter's illness or do not want to send them for Directly Observed Treatment (DOT) due to difficulties that may arise in marrying them off.[2]

CONCLUSION

This present report highlights psycho-social dysfunctions faced by TB patients registered under RNTCP in south India. Understanding of these issues will help the providers in planning more comprehensive efforts to educate the community on TB and thereby reduce the social sufferings faced by the people with tuberculosis. Currently the entire country is covered by RNTCP and every year more than one million patients are being initiated on treatment. The findings of this study bring out the need to provide adequate psycho-social support to patients enrolled in the programme, which will help in enhancing their compliance.

Limitations of the study

This study has been done on tuberculosis patients attending TB clinics of Tamil Nadu for DOT treatment and therefore may not be representative of TB in its wider context. A major limitation of this study is that we used a cross-sectional design, which is based on a one time interview. Another limitation was that we could interview only 79% of the patients enrolled in the identified cohort.

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Original Article

STUDY OF RELAPSE AND FAILURE CASES OF CAT I RETREATED WITH CAT II UNDER RNTCP – AN ELEVEN YEAR FOLLOW UP*

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Summary

Objective: To analyse the treatment outcome of Cat I smear positive relapse and failure cases and their fate when treated with Cat II regimen under RNTCP.

Methods: All Cat I smear positive relapse and failure TB patients treated with Category II regimen from 1994 to 2005 in a chest clinic of Delhi were analysed in this retrospective study. The re-treatment outcome data for relapse and failure cases of Cat I when treated with Cat II regimen was reviewed.

Results: The study population included 5576 registered as Cat I sputum positive cases in Gulabi Bagh chest clinic from 1994 to 2005. A total of 190 (3.4%) failed on Cat I regimen. Further out of 4905 (87.9%) successfully treated Cat I patients, 442 (9%) presented as relapses. The treatment success rate for relapse and failure cases of Cat I when subsequently treated with Cat II regimen were 76.4% and 48.8% respectively, with a significantly higher failure rate (27.6%) among Cat I failures subsequently treated with Cat II regimen.

Conclusion: The failure cases of Cat I subsequently treated with Cat II were observed to have a significantly lower success rates ($p<0.05$) as compared to relapse cases. The need for reappraisal of Cat II re-treatment regimen for failure cases among Cat I is suggested. ***(Indian J Tuberc 2008; 55: 188-191)***

Key words : Tuberculosis, Relapse, Failure, Treatment outcome

INTRODUCTION

Under the Revised National Tuberculosis Control Programme, the patients are classified and treated according to categories[1]. Category I which includes, new cases of smear positive pulmonary TB, seriously ill newly diagnosed sputum negative and seriously ill extra-pulmonary cases, is given $2H_3R_3Z_3E_3/4H_3R_3$ and Category II which includes patients who are either smear positive relapse, failure, treatment after default or sub category-others or have already taken treatment for more than one month prior to reporting is treated with $2S_3H_3R_3Z_3E_3/1H_3R_3Z_3E_3/5H_3R_3E_3$ regimen. According to scientific knowledge and principles of treatment of tuberculosis, a single drug should not be added to a failing regimen[2]. However, cases of Cat I who fail to respond to the treatment or the cases who relapse after successful treatment and report back to the facility, are treated with Cat II regimen under RNTCP.

It is believed that relapses in case of tuberculosis usually have same strain of organisms and therefore are unlikely to be resistant[3,4]. Santha et al[5] showed that 17% of the cases of Cat I failure had drug resistance to Rifampicin and Isoniazid and therefore justified the use of Cat II regimen in Cat I failure cases. Evidence-based research would be more appropriate to solve this dilemma. With that point in view, we analyzed the treatment outcome results of the failure cases and self-reporting relapse cases of Cat I who were treated with Cat II regimen since 1994 to 2005.

MATERIAL AND METHODS

It is a retrospective study from Gulabi Bagh Chest Clinic where the RNTCP was launched in 1993 as pilot project with a population of 10 lakhs and had in all 10 DOT-cum-microscopy centres in the domiciliary area in addition to seven DOT Centres. As per norms of RNTCP, one Health Visitor and one Lab Technician are posted at each microscopy-cum-DOT Centre, whereas only a Health Visitor is available at the DOT Centre. Data is maintained in TB register under the supervision of District Tuberculosis Officer as per RNTCP

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policy. Data pertaining to treatment outcome of Cat I smear positive cases was assessed and analyzed. Although it is not mandatory to follow up the cases and there is no budget provision for this activity under RNTCP relapse and failures of Cat I patients were recorded by the health visitors under the guidance of MOTC. Information about their time of presentation after completion of Cat I treatment alongwith their Cat I registration numbers was recorded and maintained. All these cases were carefully followed-up after registering them under Cat II treatment between 1994 to 2005 to assess their subsequent treatment outcome.

RESULTS

A total of 5576 Cat I sputum positive cases were registered and treated under RNTCP in the Gulabi Bagh Chest Clinic from 1994 to 2005. Treatment outcome of these patients for each year has been shown in Table 1.

Table 1: Treatment outcome of patients registered under RNTCP from 1994 to 2005

Year	Total Registered	Cured/Comp.	Died	Failure	Defaulters	T.O.	Relapsed Till 31.12.2006
1994	478	448 (93.8%)	9 (1.8%)	4 (0.8%)	17 (3.6%)	0	70* (15.6%)
1995	513	440 (85.7%)	9 (1.8%)	8 (1.5%)	54 (10.5%)	2 (0.5)	54 (12.3%)
1996	428	366 (85.5%)	11 (2.5%)	10 (2.4%)	40 (9.4%)	1 (0.2)	49 (13.4%)
1997	455	386 (84.8%)	9 (1.9%)	14 (3.1%)	44 (9.8%)	2 (0.4)	43 (11.1%)
1998	341	293 (85.9%)	8 (2.3%)	19 (5.6%)	21 (6.2%)	0	28 (9.6%)
1999	444	385 (86.7%)	13 (2.9%)	17 (3.8%)	29 (6.6%)	0	24 (6.2%)
2000	483	431 (89%)	9 (2.2%)	19 (3.9%)	24 (4.9%)	0	29 (6.7%)
2001	414	368 (89%)	2 (0.5%)	19 (4.5%)	23 (5.5%)	2 (0.5)	30 (8.1%)
2002	462	409 (88.5%)	7 (1.5%)	22 (4.8%)	24 (5.2%)	0	35 (8.6%)
2003	491	442 (90%)	8 (1.6%)	16 (3.3%)	25 (5.1%)	0	24 (5.4%)
2004	463	408 (88%)	6 (1.5%)	17 (3.6%)	32 (6.9%)	0	29 (7.1%)
2005	604	529 (87.6%)	10 (1.6%)	25 (4.1%)	37 (6.2%)	3 (0.5)	27* (5.1%)
Total	**5576 (100.0%)**	**4905 (100.0%) (87.9%)**	**101 (1.8%)**	**190 (3.4%)**	**370 (6.6%)**	**10 (0.3)**	**442 (9.0%)**

* Significant decline $z=4.21$, $p<0.05$

Relapse cases of Cat I Smear positive cases

A total of 442 (9%) out of 4905 patients relapsed after successful outcome (Table 1). These patients, who presented on their own to the chest clinic as relapses of the Cat I treatment, were carefully, followed-up after registering them for Cat II treatment under RNTCP.

Although there is no provision for follow-up of successfully treated cases under RNTCP, in the present study an effort was made to collect the information on self-reporting relapses of Cat I who were treated with Cat II regimen. This was possible due to the efficient record-keeping and vigilance of area health visitors and STS and as per instructions of the DTO. The time of relapse of successfully treated cases was also observed. A total of 68.5% (303) of relapses reported to chest clinic within first year ($\div^2$=23.5 for 11d.f., $p<0.05$). Moreover 50% of the total relapses were within first six months of completion of treatment. Out of these 442 relapse cases, 405 (91.6%) could be followed-up and 390 were again treated with cat II RNTCP regimen. Of these, 298 (76.4%) had a successful outcome.

Failure Cases of Cat I smear positive cases

In all, 190 (3.4%) cases out of 5576 failed in Cat I regimen. Out of these, 127 (66.8%) were re-registered for Cat II treatment. Of these, 48.8% had a successful outcome.

A comparison of results of treatment of relapse and failure cases of Cat I positive cases subsequently treated in Cat II under RNTCP revealed that while the success rate was 76.4% for relapse group, it was only 48.8% for failure groups (Table 2).

DISCUSSION

In the present study, majority of the cases relapsed within one year after completion of Cat I regimen it is presumed that the same may be true for Cat II treatment regimen also. The median follow-up was 6.4 years after Cat II treatment in the present study therefore was sufficiently long. Follow-up results of the cases of Cat I 'failure' and 'relapse' cases treated under Cat II, therefore are likely to represent the actual state of affairs under Revised National Tuberculosis Control Programme.

In the present study, follow-up of failure and relapse cases of Cat I treatment subsequently treated under Cat II has shown that while relapse sub-group had a successful outcome of 76.4%, the Cat I failure cases treated with Cat II regimen showed a very low success 48.8% ($p<0.05$). In contrast, the success results for 2006 cohorts as reported by RNTCP performance report[6] were 72.5% and 55.7% for relapse and failure groups respectively. In a smaller study by Dhingra et al[7] also, a lower success rate for failure group (63.1%) as compared to relapse group (73.7%) was reported. However, the follow-up period was shorter (median duration of 26.5m and 18.5m respectively) and sample size was also small. Similar comparable results have been reported by Khatri *et al*[8] and Chadha *et al*[9].

Table 2: Treatment outcome of failure and relapse cases of Cat I positive relapse and failure cases put on Cat II regimen

Type of cases	Total no. of cases	Completed/ Cured	Died	Failure	Default
Cat I **failure** cases put on Cat II	127 (100.0)	62 (48.8)	8 (6.3)	35 (27.6)	22 (17.3)
Cat I **relapse** cases put on Cat II	390 (100.0)	298 (76.4)	20 (5.1)	24 (6.2)	48 (12.3)

The proportion of patients failing under RNTCP is a matter of concern since the cases who fail not only transmit the infection to others but may also infect others with organisms which may be resistant to the first line drugs. The treatment of such cases with Cat II retreatment regimen may not meet expected results. The proportion of Cat I failure cases showing MDR strains has varied in different studies. While a study from Malawi found 0% MDR strain[10], another study from Lima[11] reported 73% MDR strains for Cat I failure cases. Santha et al[5] reported that only 17% of Cat I failure were having MDR strains thereby justifying that Cat I failure cases may be treated by Cat II regimen even if that means adding just one drug to the failing regimen.

The present study found that 27.6% of patients failed with Cat II regimen in failure group as compared to only 6.2% in relapse group ($p<0.05$). The proportion of patients failing Cat II regimen has been reported higher by other studies with failure group showing higher failure rates in many studies[11,12]. Similar results have been reported under Revised National Tuberculosis Control Programme from all over the country with a failure rate of 15.1% for failure group as compared to relapse group 5.2%[6]. Dhingra et al[7] also observed a failure rate of 21.1% in the failure group as opposed to 5.3% in the relapse group.

Cat I failure and relapse cases when registered for Cat II treatment get only one new drug i.e. streptomycin; treatment duration however is prolonged to eight months but the dictum "Never add a single drug to failing regimen"[2] is not followed. Under RNTCP in India, 17,769 failure cases were treated with Cat II regimen in 2006[14]. **Since the failure cases have significantly higher failure rate with Cat II regimen, treatment schedule for such cases requires rethinking and reconsideration to have higher successful results.**

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Original Article

SCREENING OF BULK DRUG SAMPLES AND ANTI-TUBERCULOSIS PRODUCTS FOR THE PRESENCE OF THERAPEUTICALLY LESS ACTIVE DIASTERIOMERIC *(R,S)* FORM OF ETHAMBUTOL DIHYDROCHLORIDE

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Summary

Background: The present study was carried out to screen various ethambutol dihydrochloride (EB2HCl) bulk drug samples and anti-tuberculosis (anti-TB) products for the presence of less active *(R,S)*-EB2HCl.

Methodology: Samples of pure EB2HCl were received gratis from various companies and the formulations were procured from local market, and also from a Directly Observed Treatment Short-course (DOTS) centre. Some products available in the institute from Global Drug Facility were also included in the study. In total, 5 API samples and 35 formulations containing EB2HCl were investigated. These were subjected to evaluation for the presence of *(R,S)*-EB2HCl using a previously published differential scanning calorimetric method. The thermograms were recorded between 25 ºC and 250 ºC at a rate of 10 ºC/min.

Results: 1 API sample and 12 formulations were found to contain *(R,S)*-EB2HCl up to an extent of 30-100%. One of the DOTS centres supply was also found to contain ~97% of the less active isomer.

Conclusion: The presence of therapeutically inactive form of the EB2HCl from 30-100% in approximately 30% of the products in the local market is an alarming finding, which means low quality anti-TB products are in circulation. The same may be contributory to the developing resistance of the drugs against the mycobacterium.

[*Indian J Tuberc 2008; 55:192-198*]

Key Words: Ethambutol, Isomeric impurity, Sub-standard drugs, Anti-TB formulations

INTRODUCTION

Tuberculosis (TB) is one of the most common causes of morbidity and mortality in the world today. Despite all the efforts, the disease is not coming to grip, and has been rightly declared as a global emergency[1]. In this scenario, it becomes necessary that each and every factor that is contributory to the increasing scourge of the disease is identified and taken care of.

In our laboratory, an area of intense focus is the quality and stability of anti-TB drugs, which are available either as single drug products or fixed-dose combinations (FDCs). Our earlier findings have been reported in a series of publications[2-9]. We previously found that the presence of ethambutol hydrochloride (EB2HCl) and its hygroscopic behaviour to be the major cause for instability of anti-TB fixed-dose combinations. Recently, our focus shifted to another critical issue with the same drug, *i.e.*, the isomeric quality of EB2HCl in the bulk drug samples and in single, two-, three- and four-drug combinations of anti-TB drugs. EB2HCl is known to exist in three diastereomeric forms, *viz.*, S,S, R,S and R,R. The activity of these forms was assessed as early as 1961 by Wilkinson *et al*. against an established infection with the human strain of *Mycobacterium tuberculosis* in mice[10], where ED_{50} (median effective dose in mg/kg/day administered for 14 days from day of infection) of S,S and R,S forms was established to be 45 and 500 mg/kg/day, respectively. The R,R form was found ineffective. The results were reproduced in *in vitro* antimycobacterial activity test[10]. In other reports, *(S,S)*-EB2HCl has been reported to be therapeutically active, while *(R,S)*-EB2HCl has been shown to be 16 times less active, whereas (R,R) form has been mentioned to be rather inactive and toxic[11-13]. Indications exist in literature on the possibility of the presence of *(R,S)* form in

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the pure drug, whereas the toxic (R,R) form is usually absent[10,12,14.]

The diastereomeric purity of the drug had been controlled through specific rotation tests prescribed in official compendia[15-18], but unfortunately the given tests cannot check the contamination of *(S,S)*-EB2HCl with the less active *(R,S)*-EB2HCl in fixed-dose formulations in the presence of coloured rifampicin[14]. For the purpose, a differential scanning calorimetry (DSC) method was developed, validated and reported by us recently in the Pharmacopeial Forum (USP)[14]. Lately, an HPLC method has been proposed in Pharmaeuropa[19] for the determination of (R,S)-EB2HCl in the monograph of EB2HCl drug substance, in which the impurity is limited to 1%. The recent edition of Indian Pharmacopoeia incorporates both DSC and HPLC tests to establish absence of less active *(R,S)* form in the drug substance[15]. There are no limits prescribed yet for the unwanted isomer in the pharmaceutical products containing EB2HCl.

Here we report the results of our studies on the presence of unwanted *(R,S)*-EB2HCl in bulk drug samples and commercial products available with local chemists, in a Directly Observed Treatment Short-course (DOTS) centre, and those supplied by Global Drug Facility (GDF). The samples were analyzed using the DSC method[14]. The results of a small number of samples, *viz*., 2 bulk drugs and 8 products, were reported by us earlier to justify the utility of the DSC method[14]. The complete outcome on almost 40 samples is presented in this paper to highlight the problem with respect to the bulk drugs and products manufactured/sold in India.

MATERIAL

(S,S)-EB2HCl was received as gift sample from Themis Medicare, Vapi, Gujarat, India. The *(R,S)*-form was prepared by the method reported in the literature[14]. The bulk drug samples were received gratis from various companies. The commercial formulations were procured from different medical shops in the local market, and a DOTS centre in the vicinity. A few products supplied by GDF to the institute for bioequivalence studies were also included in the investigation. All solvents used for extraction were of HPLC grade.

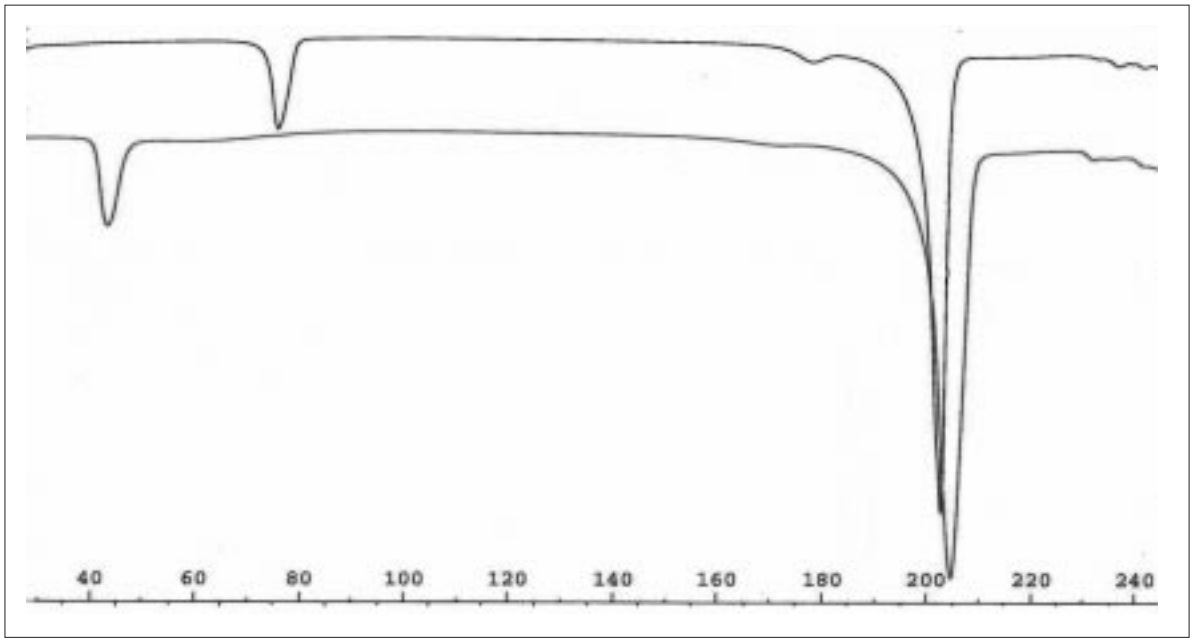

Fig. 1: DSC thermogram of *(S,S)*- EB2HCl (a) and *(R,S)*- EB2HCl (b)

EQUIPMENT

DSC analyses were performed using 821e model instrument from Mettler Toledo (Schwerzenbach, Switzerland). The same was operated using STAR software version 5.21 under Solaris operating system. Temperature axis and cell constant were calibrated using Indium, procured from the instrument manufacturer (Mettler Toledo, Schwerzenbach, Switzerland). The samples were exposed to a heating rate of 10 ºC/min over a temperature range of 25–250 ºC under nitrogen purging (80 ml/min) in 40 ìl pin-holed aluminium pans. Ultra pure water was obtained from a water purification unit (Elga Ltd., Bucks, England). **A r**otavapor (Buchi, Flawil, Switzerland) was used for solvent evaporation.

METHODS

Procurement of samples and products

Five Bulk drug samples and 35 formulations were procured in total. Of the 35 products, 15 were single-drug formulations containing EB2HCl alone, five were two-drug FDCs containing isoniazid and EB2HCl, 10 were FDCs of rifampicin, isoniazid and EB2HCl, four

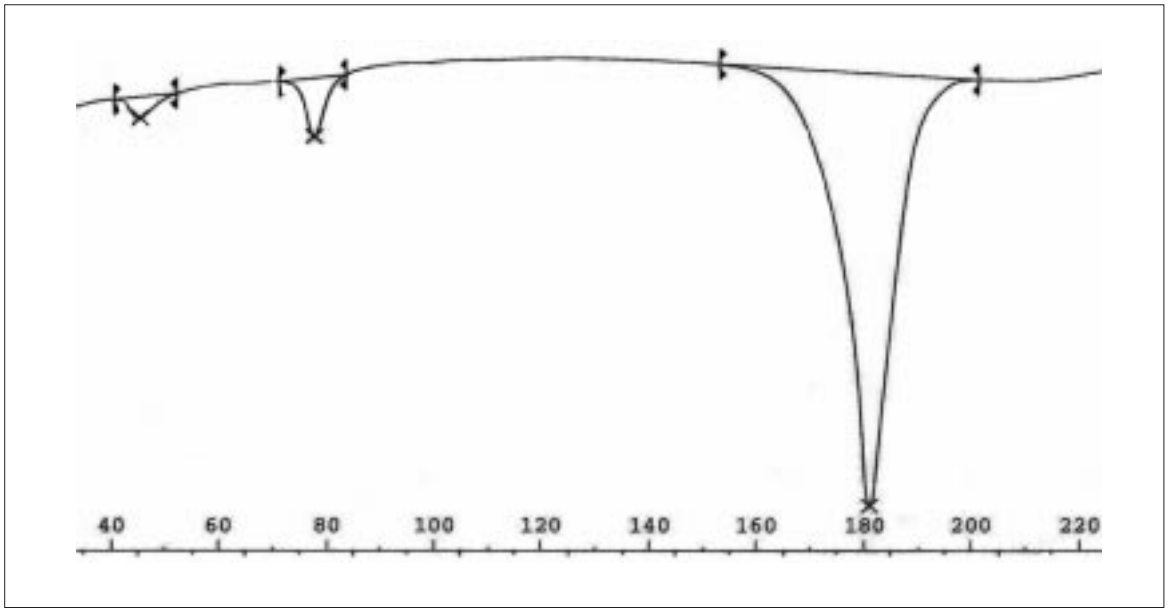

Fig. 2: DSC thermogram of EB2HCl bulk drug sample contaminated with *(R,S)*-

Table 1: Test report on EB2HCl bulk samples[#]

S.No.	Manufacturing date	Expiry date	Compendial status	% (*R,S*)- EB2HCl
1	September 2004	August 2009	BP	0
2	January 2001	December 2006	IP	0
3	January 2003	December 2008	-	19.2
4	August 2002	July 2007	BP	0
5	-*	-	-	0

*Sample was received without requisite information
[#]Samples were analyzed between March to June 2006

Table 2: Test report on EB2HCl formulations[#]

Sl. No.	Code for the manufacturer* (Source)	Type of formulation	Manufacturing date	Expiry date	Compendial status	% *(R,S)*-EB2HCl
1	A (Local market)	Single drug	August 2003	July 2006	IP	100.0
2	A (Local market)	Single drug	October 2003	September 2006	IP	93.5
3	B (Local market)	Single drug	September 2003	August 2006	IP	0.0
4	C (Local market)	Single drug	November 2005	October 2008	IP	48.5
5	C (Local market)	Single drug	April 2005	March 2008	IP	33.2
6	D (Local market)	Single drug	November 2003	October 2007	IP	0.0
7	E (DOTS centre)	Single drug	January 2005	August 2007	IP	97.4
8	F (DOTS centre)	Single drug	NR	NR	BP	0.0
9	G (DOTS centre)	Single drug	December 2003	November 2008	IP	0.0
10	H (Local market)	Single drug	December 2002	September 2005	IP	0.0
11.	H (Local market)	Single drug	April 2003	January 2006	IP	0.0
12.	I (Local market)	Single drug	July 2003	June 2006	IP	0.0
13.	J (Local market)	Single drug	February 2005	January 2007	IP	0.0
14.	G (Local market)	Single drug	April 2005	January 2010	IP	0.0
15.	K (Local market)	Single drug	May 2005	September 2008	IP	0.0
16.	A (Local market)	Two-drug FDC	April 2005	March 2008	IP	48.0
17.	A (Local market)	Two-drug FDC	December 2003	November 2006	IP	100.0
18.	A (Local market)	Two-drug FDC	August 2005	July 2007	IP	0.0
19.	G (Local market)	Two-drug FDC	May 2005	April 2007	IP	0.0
20.	K (Local market)	Two-drug FDC	February 2005	January 2008	IP	0.0
21.	G (Local market)	Three-drug FDC	September 2004	October 2006	IP	0.0
22.	G (Local market)	Three-drug FDC	December 2004	November 2006	IP	0.0
23.	L (Local market)	Three-drug FDC	November 2001	October 2003	IP	76.0
24.	G (GDF)	Three-drug FDC	July 2004	June 2006	USP	0.0
25.	M (GDF)	Three-drug FDC	November 2002	October 2006	BP	0.0
26.	N (Local market)	Three-drug FDC	November 2001	October 2003	IP	0.0
27.	O (Local market)	Three-drug FDC	June 2004	May 2006	IP	23.9
28.	O (Local market)	Three-drug FDC	March 2004	February 2006	IP	100.0
29.	O (Local market)	Three-drug FDC	August 2005	July 2007	IP	57.5
30.	O (Local market)	Three-drug FDC	June 2005	May 2007	IP	0.0
31.	A (Local market)	Four-drug FDC	June 2005	May 2007	IP	0.0
32.	A (Local market)	Four-drug FDC	June 2004	May 2006	IP	35.2
33.	G (Local market)	Four-drug FDC	June 2005	May 2007	USP	0.0
34.	G (GDF)	Four-drug FDC	August 2004	July 2006	USP	0.0
35.	P (Local market)	Five-drug FDC	May 2005	April 2007	IP	0.0

*Products with a common alphabet were from the same manufacturer
[#]Samples were analyzed between March to June 2006
NR – labeling was not readable

were four-drug FDCs containing rifampicin, isoniazid, pyrazinamide and EB2HCl, while one was five-drug combination containing pyridoxine, along with the four first-line anti-TB drugs. The products were collected randomly.

Analysis of samples

The samples were tested only for Diastereomeric impurity and no other compendial tests were done. The analysis was done by a DSC method reported by us earlier[14]. The method had proven to be specific, had good precision (%RSD being <1.5% for both intra- and inter-day studies) and was sensitive to the presence of R,S form up to 2% in the sample[14].

The bulk drug samples were subjected as such. The uncoated formulations were first triturated and the resultant powder was subjected to the DSC. In case of coated tablets, the coating was removed before trituration. For FDCs containing interfering excipients, the latter were separated by solvent extraction method, as described in the literature[14].

In all cases, accurately weighed samples were placed in pin-holed aluminum pans and thermograms were recorded between 25 ºC and 250 ºC at a rate of 10 ºC/min. The phase transition enthalpies for *(R,S)*-EB2HCl and *(S,S)*-EB2HCl were recorded at 42 °C at 77 °C, respectively. Following equations from literature[14] were used for the calculation of the relative percentages of *(R,S)*- and *(S,S)*-EB2HCl in a mixture:

% *(R,S)*-EB2HCl = [CF x M/(CF x M + D)] x 100
% *(S,S)*-EB2HCl = [D/(CF x M + D)] x 100

where, M and D are the phase transition enthalpies at 42 °C and 77 °C, respectively, and CF is the correction factor, with values of 1.114 and 1.000 for *(R,S)*- and *(S,S)*-EB2HCl, respectively[14].

RESULTS

DSC behavior of melting and phase transitions of EB2HCl

Figure 1 shows the typical DSC profiles for melting and phase transitions of EB2HCl. The characteristic melting endotherm of the drug is shown between 202-205 °C. The endotherms associated with polymorphic transitions appear much lower at 77 ºC and 42 ºC for (*S,S)* and *(R,S)* isomers, respectively. These distinct endotherms, which highlight the specificity of the method, were employed to determine the content of the two isomeric forms of the drug.

Screening of bulk drug substances

Of five API samples, four exhibited similar behaviour of melting and phase transitions (Table 1). As shown in Fig. 2, one batch showed three endotherms at 42±1 ºC, 75±1 ºC and 182±2 ºC for (*R,S)*-EB2HCl, (*S,S)*-EB2HCl and drug, respectively. The appearance of endotherm at 42 ºC, and depression of melting point from >200 ºC to 182 ºC confirmed the presence of diastereomeric impurity[14].

Screening of formulations

The data for formulations are listed in Table 2 and summarized in Table 3. A total of 11 formulations of the 29 products randomly procured from local chemist shops were found to be

Table 3: Summary of number of formulations found to contain the inactive isomer

Source	Total number of formulations	Number of formulations containing *(R,S)*-EB2HCl
Local market	29	11
DOTS center	3	1
GDF	3	0

substandard, and some of the products contained even up to 100 % of (*R,S)*-EB2HCl. Similarly, one among three formulations from DOTS centre was found to have ~97 % of the less active isomer. GDF supplies were free from the said impurity.

Hence, of the total 35 products from 16 manufacturers, 12 products were found to contain *(R,S)*-EB2HCl to an extent of up to 100 % (Table 3). Formulations from 11 manufacturers were of standard quality, while those of five had the substandard form. Of the 12 substandard products, five were single-drug formulations, two were two-drug FDC products, four were three-drug FDC products and one was four-drug FDC product. The problem was primarily restricted to IP labelled products, however, the BP and USP labelled products for export were not found to be contaminated.

DISCUSSION

The data in Table 2 shows that the problem existed primarily with products sold in local market and was also prevalent in a product being supplied under the DOTS programme. In comparison, the products from GDF were free from the undesirable form. Reports in literature indicate that (*R,S)*-EB2HCl and (*S,S)*-EB2HCl can be separated from each other by different approaches[10,20]. Therefore, the results in Table 2 suggest a possibility that some of the manufacturers of bulk drug substance are separating the two isomers, and are thereby maintaining the quality in local and export supplies. But it may be that some of them maintain the quality of the exported drug, but are not very strict with respect to material being sold to the local manufacturers of anti-TB formulations. In some cases, it may be even unintentional, due to the absence of proper methodology for testing of individual isomeric forms of EB2HCl in the compendial monographs, both in case of drug substance and the products.

The finding of this study is alarming because of the presence of up to 100 % of the therapeutically inactive form of EB2HCl in anti-TB products sold in Indian market and even those supplied through DOTS programme. The poor quality of anti-TB formulations may be contributory to the development of resistance of the drugs against the mycobacterium.

CONCLUSION

A bulk EB2HCl sample and several commercial formulations were found to contain the unwanted *(R,S)* isomeric form of EB2HCl. In some of the products, total drug was in the form of the inactive isomer, highlighting the gap in the quality control of anti-TB products in the country.

It directly foretells that there is a need of urgent steps to correct the situation. The regulatory agencies should show alertness and firmness to plug such loopholes, for the sake of improvement of the quality of anti-TB products. At their end, the international compendial authorities, including those from India, need to include a selective test for the presence of isomers of EB2HCl, of the kind developed by us[14] or proposed in Pharmaeuropa[19].

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GUJARAT STATE CONFERENCE

The 23rd Annual Conference on Tuberculosis and Chest Diseases of the Gujarat State TB Association was held in IMA Hall, Navsari on 22nd June, 2008 which was hosted by the Valsad-Navsari District TB Association. Dr. V.K. Arora, Vice-Chairman, Tuberculosis Association of India, attended the Conference. Dr. Arora thanked the office bearers of the Gujarat State TB Association and felicitated them.

Original Article

TREATMENT OUTCOME OF NEURO TUBERCULOSIS PATIENTS PUT ON DOTS - AN OBSERVATION STUDY FROM THE FIELD

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Summary

Background: Effectiveness of intermittent Short Course Chemotherapy for Neuro Tuberculosis has not been well studied. There are only few reported studies on this issue in the world literature under filed conditions. Neurologists all over India are reluctant to accept Directly Observed Treatment Short course for neuro tuberculosis since its introduction in India.

Aim: Assessing effectiveness of Revised National TB Control Programme (RNTCP - DOTS) regimens among neuro tuberculosis patients registered under the programme.

Methods: All the neuro tuberculosis patients referred to RNTCP for treatment were included in the study. Study population included only those patients diagnosed at higher centre and referred to RNTCP during the period Jan - Dec 2002, Alappuzha District. Diagnostic Algorithm as per RNTCP guidelines was strictly followed and treatment outcome and follow-up status were taken from tuberculosis register. No pediatric age group was included in the study.

Results: A total of 32 cases registered for DOTS regimen were included in the study, of whom 29 completed the treatment and all were asymptomatic at the end of treatment (85%). All patients received treatment as DOTS, but only 70% received actual DOTS. All patients were given nine months intermittent regimen as per RNTCP guidelines. Five patients died during the treatment (14%). This result shows that DOTS under field programme conditions are efficient in curing Neuro Tuberculosis.

Conclusion: Good result was obtained with intermittent short course chemotherapy under programme conditions in neuro tuberculosis. **[*Indian J Tuberc 2008; 55:199-202*]**

***Key words*:** DOTS, Neuro-tuberculosis, TBM, Intermittent Regimen

INTRODUCTION

Neuro-tuberculosis is the most serious form of tuberculosis. It needs more intensive and prolonged therapy. Even with prompt and adequate treatment, the mortality rate goes up to 27%[1]. It constitutes approximately 15% of extra-pulmonary cases or about 0.7% of all clinical tuberculosis[2]. CNS tuberculosis may be in the form of meningitis, intra-cranial tuberculoma and spinal tubercular arachnoidits and rarely tuberculous encephalopathy. Diagnosis is usually based on clinical presentation, CSF study and neuro imaging. CSF study remains the principle diagnostic tool in Tuberculous Meningitis[3]. CSF shows pleocytosis with lymphocytes, elevated protein ranging from 60% to 400 mg% or even higher, sugar between 20% to 40%. It is sterile on routine bacterial culture. Demonstration of tubercle bacilli by AFB staining or culture remains the most important step of CSF study but its yield is much low[4]. CSF may be normal in CNS tuberculoma and tubercular encephalopathy. Neuro imaging shows basal exudates, hydrocephalus, infarcts, tuberculoma, brain edema, etc. CT scan can also be normal. Conventionally, neuro tuberculosis is treated with initial intensive phase of four drugs – Isoniazid, Rifampicin, Ethambutol and Pyrazinamide followed by Isoniazid and Rifampicin daily for at least one year or even longer. Patients with even tuberculoma are showing good response to medical treatment, especially a Pyrazinamide containing regimen. There was no need of surgery for these cases [5]. The rate of hepato-toxicity in adults receiving Isoniazid is 1% and doubles

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with the addition of Rifampicin[6]. Outcome of CNS tuberculosis depends on the age of the patient, duration of illness, clinical stage at time of treatment initiation, the extent of arachnoiditis, vascular complication, hydrocephalus and increased intra-cranial tension. The incidence of residual neurological deficits, after recovery, varies from 10% to 30%[6].

With the introduction of Revised National TB Control Programme (RNTCP), Neuro Tuberculosis is categorized among extra-pulmonary seriously ill[8], recommending $2(HREZ)_3/4(HR)_3$ with extension of continuation phase for three more months (total nine months). For pediatric neuro T.B, RNTCP recommends substitution of Ethambutol with Streptomycin in the intensive phase. But neurologists and physicians are reluctant to accept the intermittent regimen, considering the seriousness of the condition and lack of published studies to prove the effectiveness of intermittent regimen in this situation.

With our best efforts, we could not find a single study in the literature proving the efficacy of fully intermittent short course therapy in Neuro TB. Thus the present study was planned.

AIM

Assessing effectiveness of RNTCP - DOTS regimen among neuro-tuberculosis patients registered under RNTCP.

SUBJECTS AND METHODS

All neuro tuberculosis patients registered for DOTS in all the four Tuberculosis Units (covering a population of five lakh each) of Alappuzha District during the period January 2002 to December 2002 were included in the study. DOTS therapy was given as per RNTCP guidelines[8]. Diagnostic algorithm and follow-up of RNTCP were followed. Data were collected from the TB register maintained in each Treatment Unit (TU). A detailed review of case history and investigation findings were made of those patients who reported for follow-up. A detailed examination of the patient was done during their review between 6 to 12 months after completing the treatment. A co-ordinated effort of Medical Officer - Tuberculosis Control and Senior Treatment Supervisors was ensured in the evaluation.

RESULTS

Thirty-two cases were registered in all the four Tuberculosis Units of Alappuzha district during the year 2002 (Jan – Dec). This constitutes about 8% of the total of 419 extra-pulmonary TB cases registered in the district during the period. Of the patients enrolled in the study, 17 were males and 15 females. The age distribution was from 16 years to 76 years. Majority of the cases (50%) belonged to the age group 31 to 50 years.

Twenty-six patients (81%) completed the course of treatment. Among them, only 15 were later available for further follow-up between six and 12 months after the completion of treatment. Others did not respond to our call letter and their present status is not known. Thirteen of them were referred from Medical College, Alappuzha and Kottayam and two from District Hospital. Decision to start ATT by neurologist or physician with post-graduate qualification was taken.

Majority of them presented with symptoms of headache, vomiting, fever and altered sensorium. CSF study was abnormal in all, except one. The total count varied from 70 to 660 with the mean value of 272. Lymphocyte predominance was seen in eleven cases (73%). A low sugar value below 40mg % was seen in only four cases (26%). Protein values ranged from 17 to 575 mg %. It was elevated in only 11pateints (63%). Routine Bacterial Culture was sterile in all the cases. But none was sent for AFB culture or staining. Chest X-ray was abnormal in three cases (20%). HIV screenings done in seven cases were negative. CT scan finding was suggestive only in three cases.

Of the 15 cases interviewed, only one had sequelae of hemi paresis and two were complaining of persistent mild headache. So, overall sequela in our study was negligible compared to many previous studies. There was no clinical evidence of relapse among these 15 patients.

Five patients died and one defaulted. All deaths were investigated. Among five deaths, for two cases, ATT was started empirically after surgery for intracranial space occupying lesions (SOL) by considering tuberculoma as one possible cause for space occupying lesion. Other two deaths occurred within first week of starting the treatment and the remaining one after three months' of treatment.

DISCUSSION

India is among the nations with high incidence of TB. Usually there are 20% of extra-pulmonary cases of whom 15% will be neuro tuberculosis. So in Alappuzha alone there were 419 extra-pulmonary cases put on DOTS in 2002. Thus an expected incidence of 63 cases of Neuro TB would have occurred during study period [2.] But the actual number of Neuro TB cases registered for DOTS was only 32 and four cases were registered for daily treatment because they were specifically requested by the referring Physician for daily treatment. Thus a total of 36 Neuro TB cases were referred to RNTCP in the district. This may be because of selective referral of patients to RNTCP only if patients are not affordable for the daily regimen from outside the programme . RNTCP started in Alappuzha only in 2001. Many referring physicians were unaware about regimens available from govt sector. There can be also initial screening of more serious forms (MRC grade 2 or 3) for daily regimens as these forms are having higher mortality[2,9]. 22 cases received DOTS from volunteers (Aganawadi workers) and 10 from health service staff. 70% cases received actual DOTS as per criteria for RNTCP internal evaluation (At least 20 out of 24 doses of Intensive phase ingested drugs in presence of DOT provider).

Even though RNTCP recommendation is for eight – nine months' treatment, two received treatment only for six months probably due to lack of awareness of this recommendation[10].

Four patients were converted to daily regimen. The reason noted for converting to daily regimen was that, three of them had clinical jaundice and one with persistent vomiting. Medical College Authority has made this alteration of regimen. There is a high incidence of hepatitis noticed in the study group and all three were 15 to 22 year age group. No other major side effect occurred necessitating change of regimen.

Eighty-one per cent treatment completion was obtained in our study, which is much higher than that in unsupervised (NTCP) regimen. A meta analysis of NTCP studies showed completion of only 50% [11]. High rate of completion seen in this study could probably due to easy availability of drugs, seriousness of disease and supervision of drug intake. The mortality rate was only 16%, which was much lower than the previously reported series. One of the known variables of mortality i.e, the stage of the disease at time of initiation of treatment could not be evaluated at the time of study [1,11,12].

There was only one defaulter after four days of treatment. He was later traced to have completed treatment from a private hospital. Thus the default rate was only 3% which is negligible when compared to that in unsupervised regimen which goes up to 50% [12]. In the present study, the survival with sequelae is only 9%. When comparing to previously published studies which shows mortality upto 75% and sequelae up to 85%, this data seems to be significant[13,14].

With the intermittent short course regimen, the total drug consumed by the patient is almost half that with the conventional daily regimen. The toxicity is less and cost of therapy is considerably low. So, this regimen can be universally recommended for all cases of tuberculosis including Neuro tuberculosis, especially in developing countries. Prospective studies on neuro tuberculosis should be undertaken covering all pitfalls of this study. A clear-cut diagnostic algorithm for diagnosis of neuro T.B. should be also included in the RNTCP guidelines and training modules.

CONCLUSIONS

1. **DOTS regime for Neuro tuberculosis is an effective regimen under programme conditions.**

2. Default rate is negligible for this intermittent short course chemotherapy.

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Original Article

LUPUS VULGARIS AND TUBERCULOSIS VERRUCOSA CUTIS (TBVC) – A CLINICAL, PATHOLOGICAL AND EPIDEMIOLOGICAL STUDY OF 71 CASES

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Summary

Background: The epidemiological aspects and diagnostic problems encountered in a rural set up are largely unknown. The present study on cutaneous tuberculosis encompassing clinical, pathological and epidemiological aspects was undertaken at Rajah Muthiah Medical college and Hospital (RMMC&H), a teaching hospital mainly catering to the health needs of a predominantly rural population from villages and hamlets around Chidambaram, a taluq headquarters, located in Cuddalore district of Tamil Nadu.

Material and Methods: During the period of study, 5744 cases (82%) of pulmonary tuberculosis and 1261 (18%) of extra-pulmonary tuberculosis were encountered. Cutaneous tuberculosis accounted for 117 (1.67%) of tuberculosis cases.

Results: Of the seventy-one patients with cutaneous tuberculosis, 39 had lupus vulgaris and 32 with TBVC. Lupus vulgaris was more prevalent with male pre-ponderance. The maximum incidence was seen in the second decade of life. Both LV and TBVC showed a male pre-ponderance, M: F ratio being 3:2 and 2:1 in LV and TBVC respectively. A majority of patients with LV (27 cases; 69.2%) and TBVC (31 cases; 96.8%) manifested with a single site of involvement. Lower extremities were more commonly involved among patients hailing from poor economic strata who were not habituated to the use of footwear while working out doors. Over crowding was also a contributing factor. The relationships between BCG vaccination and Mantoux test with cutaneous tuberculosis, association with pulmonary tuberculosis in addition to the underlying predisposing socio-economic factors are discussed. **[*Indian J Tuberc 2008; 55:203-209*]**

Key words: Lupus vulgaris (LV), Tuberculosis Verrucosa Cutis (TBVC), Scrofuloderma (SCF), Pulmonary Tuberculosis (PT)

INTRODUCTION

Tuberculosis continues to be a major public health problem in both developing and developed countries, more so with the advent of Human Immuno Deficiency (HIV) syndrome. Cutaneous tuberculosis constitutes a minor proportion of extra-pulmonary tuberculosis. Tuberculosis of the skin is caused by *M. tuberculosis, M.bovis* and under certain conditions the Bacillus Calmette Guerin (BCG), the attenuated strain of *M.bovis*.[1] Lupus vulgaris is an extremely chronic and progressive form of tuberculosis of the skin occurring in individuals with moderate immunity and a high degree of tuberculin sensitivity[2].

The epidemiological aspects and diagnostic problems encountered in a rural set up are largely unknown. The present study of clinical , pathological and epidemiological aspects of cutaneous tuberculosis was undertaken at Rajah Muthiah Medical college and Hospital (RMMC&H), a teaching hospital mainly catering to predominantly a rural population from villages and hamlets around Chidambaram, a taluq headquarters, located in Cuddalore district of Tamil Nadu.

MATERIAL AND METHODS

Seventy-one patients with cutaneous tuberculosis, 39 with lupus vulgaris and 32 with TBVC, attending the dermatology division of RMMC&H, between 1991 and 1998 were included in the present study. A detailed clinical examination

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was carried out in each patient, along with Mantoux test, relevant hematological, biochemical investigations, sputum examination and urine analysis. Roentgenograms of the lungs were taken to rule out associated pulmonary tuberculosis. Ultra sonographic [USG] examination of the abdomen was done when relevant. Blood was screened for both HIV and VDRL. Skin biopsy specimens from

Table: Summary of clinical features

Clinical data	Lupus vulgaris	TBVC
Incidence	39 patients (33.3%)	32 patients (27.4%)
Mean age of patients	23 years and 6 months	25 years and 3 months
M:F ratio	3 : 2 (approximately)	2 : 1 (approximately)
Male patients / female patients	25 males/ 14 females	21 males/ 11 females
Duration of illness	3 years and eleven months	4 years and 10 months
Positive Family history of Pulmonary Tuberculosis (PT)	9 patients (23 %)	11 patients (34.4%)
Co-existent PT	11patients (28.2%)	4 patients (12.5%)
BCG vaccination	16 patients (41%)	11 patients (34.4%)
Mantoux test PPD - Positivity	26 patients (72%)	29 patients (90.6%)
Mean ESR (in mm at end of 1st hour)	60mm at end of 1st hr	28mm at end of 1st hr.

Fig.1: Cutaneous Tuberculosis

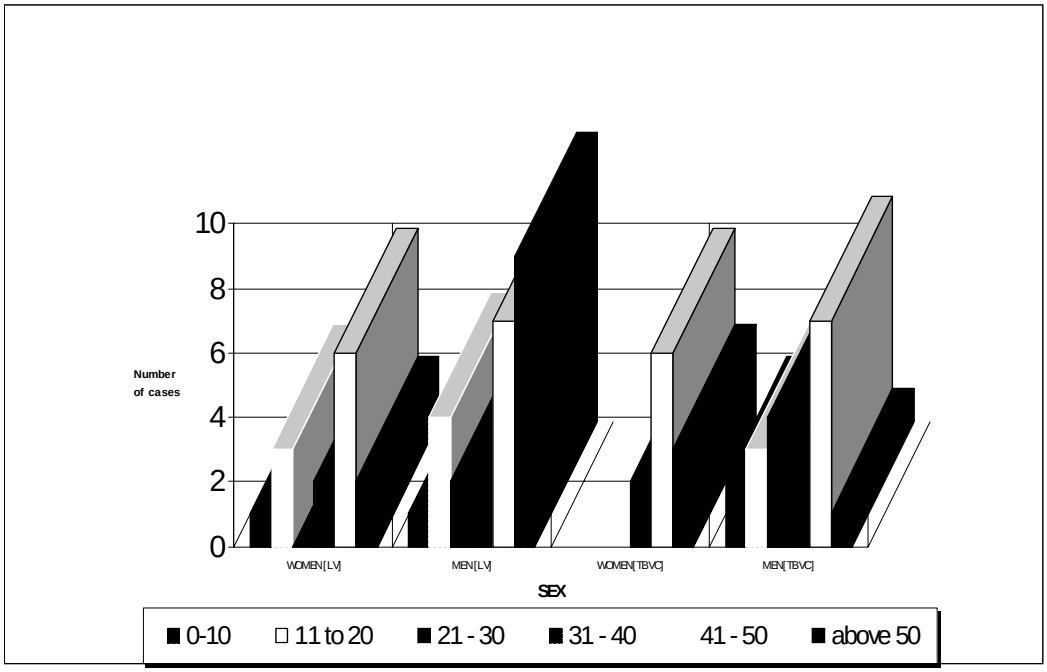

Fig.2: Lupus Vulgaris and TBVC - Age and Sex Incidence

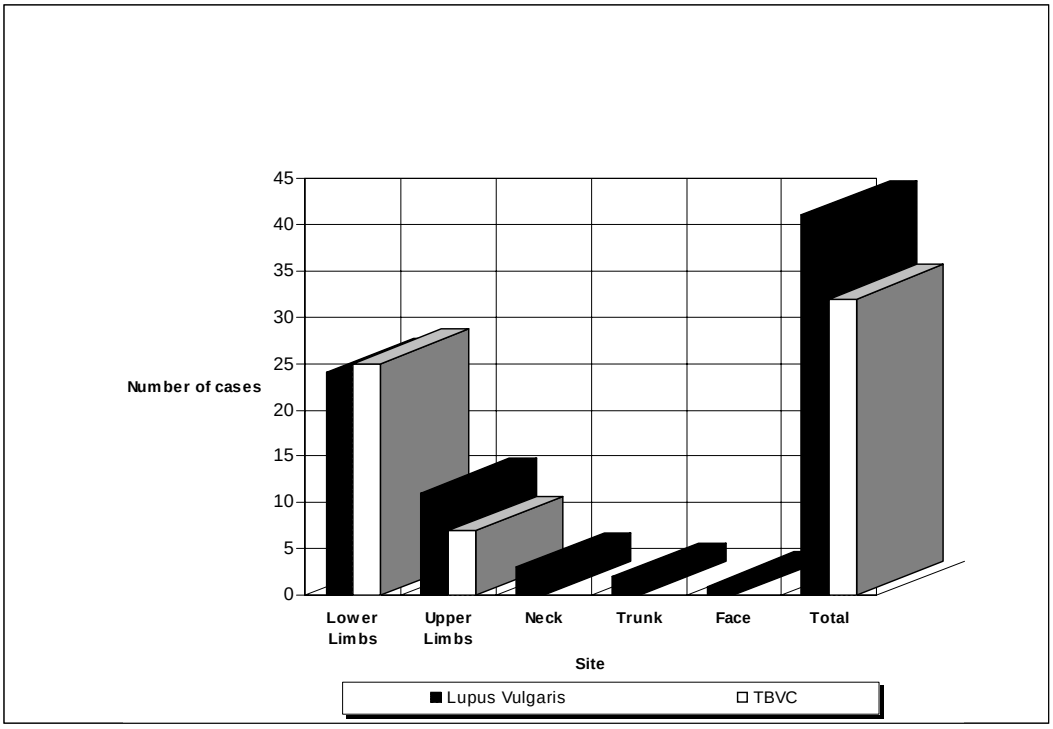

Fig.3: Lupus Vulgaris and TBVC-Sites involved

representative lesions were subjected to histopathological examination including ZN stain for AFB, KOH study to rule out fungal infections and inoculated into Lowenstein Jensen medium for the culture of AFB.

The general economic level at the time of study, the average wages of patients and their housing conditions were documented. Personal and socio-economic data like smoking, dietary habits and consumption of alcohol were recorded.

RESULTS

During the study period, pulmonary tuberculosis constituted 82% of TB cases while extra pulmonary tuberculosis accounted for 18% and cutaneous tuberculosis accounted for 1.67% (seventy-one) of tuberculosis cases, of which 39 cases (33.3%) were LV and 32 cases (27.4%) TBVC(Fig. 1).

The patients with LV showed great variation in their morphological features. Majority of the patients had plaques and nodules with the characteristic "apple jelly nodules" on diascopy. Hypertrophic lesions with exuberant proliferative growth at the active margins, circinate lesions with scarring at the center and spread at the periphery were also observed. Ulcerated and crusted lesions on face and sole were seen in two patients. Most cases of LV showed a tendency to formation of a thick scar. Majority of patients of TBVC presented with hyperkeratotic (verrucous) lesions.

Both LV and TBVC showed a male preponderance. The maximum incidence was seen in the second decade of life. The youngest patient with LV was two years old while the oldest was 70 years. The mean age for men and women with LV was 21 and 26 years respectively. Among patients of TBVC, the youngest patient was eight years old and the oldest was 70 years. The mean age for male and female patients was 28.5 years and 15.2 years respectively. A majority of patients manifested with a single site of involvement [LV 27 cases (69.2%) and TBVC 31 cases (96.8%)]. Involvement of lower extremities was most common in both LV (24.3%) and TBVC (78.1%). Two patients had co-existent LV and TBVC lesions. [Figs.2-3]

In patients with TBVC, the interval between the onset of the disease and the seeking of medical aid varied greatly from one month to 20 years with an average interval of three years and 11 months in case of LV and four years and 10 months in case of TBVC. Men sought treatment earlier than women. Pulmonary tuberculosis, diabetes mellitus, regional lymphadenopathy, carious teeth, Bitot's spots, icthyosis vulgaris, vitiligo and flourosis of teeth, dermatophyte infections and verruca vulgaris were associated with LV and TBVC.

A positive history of trauma preceding the onset of the lesions was present in twenty (62.5%) of patients with TBVC. Only 14 (43.75%) patients were using footwear outside their houses.

DISCUSSION

TBVC was originally termed verruca necrogenica by Wilks and Poland in 1862. Other synonyms employed for this condition are prosector's wart, post-mortem wart, anatomical tubercle, cadaver wart and warty tuberculosis, butcher's wart, lupus verrucosus, tuberculosis verrucosa cutis and tuberculosis cutis verrucosa.[3] Laennec published the first description of a prosector's wart in 1826, based on his own disease contracted in the autopsy room. Most cases of TBVC are due to exogenous re-infection in individuals with marked cutaneous hypersensitivity and good CMI.

The earliest description of lupus vulgaris was by Erasmus Wilson in 1865. An ulceration that tore into the flesh like the ravages of a wolf probably fitted the clinical description and explains the word "lupus" " which means wolf. The commonness of this condition in earlier times, accounts for the adjective -vulgaris, in lupus vulgaris.[4] Tuberculosis luposa and tuberculosis luposa cutis are other synonyms for this condition.[3]

LV is the commonest type of cutaneous tuberculosis in India and Europe[2, 5] similar to the

present study, while TBVC was more common in a large study from Hong Kong.[6]

In a majority of studies in India, cutaneous tuberculosis showed a higher incidence in men[5,7] which as in our observations. No particular predisposing factor could be attributed for the higher incidence in men, except that they run a greater risk of sustaining injury, since most of our patients were involved in heavy manual work.

In the present study, the maximum incidence was found below 20 years of age while the disease was reported at a slightly later age by other workers.[8, 9] However, in a study by Beyt et al, the average of the patients was 50 years. The youngest reported case of cutaneous tuberculosis was in two infants of four and eight weeks born to mothers with pulmonary tuberculosis,[10] while the oldest was in an 88 year old woman[11]. In the present study the youngest and oldest patients with LV were six years and 57 years old, while, the youngest and oldest patients with TBVC were of eight years and 70 years age.

Most of the patients sought medical help within one month, while the longest interval was 30 years. The shortest duration of the disease reported in case of TBVC is one week,[12] while the longest 43 years.[13] In our study, the shortest duration was one month and longest 20 years.

LV of 71 years duration in an 82 year-old man was documented[14]. In our study, the minimum duration was one month in a two year old child, while the maximum interval was 22 years in a 48 year-old male.

In our study, extremities, especially the lower limbs, were most commonly involved in both LV and TBVC, which is at variance with the other European reports, where face is the most common site of involvement by LV.[1]

TBVC lesions mostly occur on lower limbs [90%] while involvement of elbow in only one patient was reported earlier[15]. However, buttocks and knees were more often involved in Chinese boys, due to their habit of playing and squatting in the streets with open bottom trousers.[16] In the present study, a definite history of trauma preceding the onset of TBVC was forthcoming in 20 patients (62.5%). A majority of our patients 18 (56.2%) were not using footwear outdoors and were often bare footed. Being engaged in heavy manual work in the agricultural fields, they were more prone for frequent injuries. The resultant trauma might have provided a portal of entry to the AFB.

Occurrence of single or multiple lesions of cutaneous tuberculosis is described in literature as is the occurrence of one type of cutaneous tuberculosis in association with another type. Report of multiple lesions are available from other authors[17,2,18,19].The body apparently is able to control the outbreak to a limited number of lesions, about 50 is the maximum[20]. In the present study, multiple lesions were seen in only one patient of TBVC and in 12 patients (30.8%) with LV. A 15 year-old girl had nine lesions in the present study and she was Mx negative.

A group of workers are of the opinion that TBVC and LV should be classified together[17], while others[9] consider LV and TBVC as two separate entities with distinct variations in clinical, immunological and histopathological appearances. In our study, only two patients presented with lesions of both LV and TBVC.

The morbidity of LV patients from PT is 4-10 times higher than in the general population and in some cases, LV may be regarded as a symptom of another tuberculous disease running a serious course. LV could be associated with PT or tuberculosis of bones and joints in 10 -20% of patients[1]. In the present study, 11(28.2%) patients with LV and 4 (12.5%) of TBVC had co-existent PT. but there was no bone or joint involvement.

Generally, lymphadenopathy is not associated in TBVC, although it has been reported[21]., while lymphadenopathy was an accompaniment in 15 patients(46.9%) of TBVC cases , in 14 (35.9%) with LV.[1] The inguinal nodes (57.1%) were the most common group involved.

Though diabetes and tuberculosis are poetically termed "sister diseases", only one patient with LV had co-existent type II diabetes mellitus. However, she did not have any clinical or radiological evidence of PT. Similarly, HIV and tuberculosis are described as the "cursed duet". However, none of our patients were HIV positive.

The protective role of BCG vaccination against tuberculosis is controversial with claims of efficacy ranging from 0% in South India to 75% in Western countries.[22,23] Only 16 (41%) of patients with LV and 11 (34.4%) of TBVC patients received BCG vaccination while Mx test was positive in 26 (72%) and 29 patients (90.6%) in LV and TBVC respectively.

No correlation could be found between the Mx positivity, extent of the disease or previous BCG vaccination similar to other reports[5].

In HPE, none of the cases with LV or TBVC showed epidermal atrophy as reported by earlier workers[2,24]. Though not a common feature in LV, caseation was observed in two cases, while the granulomas were ill-defined in three cases.

In tuberculous skin disease with high levels of skin sensitivity, the number of bacteria within the lesions is small and it was hypothesized that in secondary tuberculosis due to a greater degree of immunity, only fewer number of bacilli will be found.[1, 25] This theory could probably explain the negative results of both culture and ZN stain in the present study. Since only a small percentage of cases have positive smear or culture, HPE diagnosis and clinical correlation are considered important.[16]

An optimum floor area per person in a household ranged from 30 – 50 sq feet, the recommended minimum optimum value being 5 - 100 sq feet.[26] Majority of our patients lived in over crowded, small houses. The average number in each household was eight and the available floor area per person was 30 sq feet, indicating over crowding. Association of over crowding and low socio-economic status with cutaneous tuberculosis was reported.[7] This is in concurrence with our observations, as the average monthly income of our patients was Rs. 750/-

In lower socio-economic environments, children become infected by playing and sitting on the ground contaminated with tuberculous sputum.[6] The presence of contact with an open case of PT may be relevant, especially in patients with LV and TBVC. An affirmative family history was available in 9 (23 %) of LV patients and 11 (34.4%) of TBVC patients, in the present study. It was hypothesized that where there is frequent contact with an infective adult, the chance of infection of a minute skin lesion is fairly high, whereas with larger cuts or injuries, the possibility of dust infection presumably with small numbers of tubercle bacilli increases.[27]

No correlation was found between incidence of LV/TBVC and personal habits like smoking and occasional consumption of alcoholic beverages. Multiple vitamin deficiencies were often encountered as our patients could not afford a regular balanced diet due to poverty.

The relative freedom of developed nations from mycobacterial disease is due to their prosperity. As stated by Grange (1980) " till the barriers of race, creed and nationality are broken down and until mistrust and strife are replaced by brotherly love , compassion and co-operation , the tyrannical reign of the 'king of diseases ' and the ' disease of kings ' will continue".[28]

Concerted efforts at improving the socio-economic status and creating awareness about health and hygiene among the population, besides providing primary medical care facilities, in the developing countries will go a long way in the eradication of the 'king of diseases'.

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STATUS REPORT ON RNTCP*

Revised National TB Control programme has continued to achieve its twin objectives of NSP case detection and NSP cure rate at the national level during the second quarter, 2008, indicating that the programme is moving in the right direction for consolidating and sustaining the achievements of the past several years. This has been possible with the dedicated and energetic teams in the states and districts.

RNTCP performance in second quarter 2008

During the second quarter, over 1.7 million suspects were examined, 254,127 sputum positive cases were diagnosed, and 412,766 TB cases were registered for treatment. The annualized total case detection rate is 144 cases per 100,000 populations. With a total of 170,100 new smear positive cases being registered for treatment, the new smear positive TB case detection rate (annualized) for the second quarter 2008 is 79%. In addition, 103,845 new smear negative cases, 61,273 new extra-pulmonary cases, 76,978 smear positive re-treatment cases and 23,348 re-treatment 'Others' were also registered for treatment in this quarter. The treatment success rate amongst the new smear positive PTB cases registered in the second quarter 2007 was 86%. The sputum conversion rate and cure rate among the new sputum positive cases were 89% and 84% respectively. Although the default rates among NSP (6.3%), NSN (7.8%) and re-treatment cases (15.3%) are showing a declining trend, the current rates continue to be an area of concern which the programme managers at all levels must focus upon.

Other major initiatives

1. The National level STOs and consultants bi-annual review meeting was held during the first week of April, 2008 to discuss technical and operational issues emerging out of the central

Population in India covered under DOTS and Total Tuberculosis Patients put on treatment each quarter

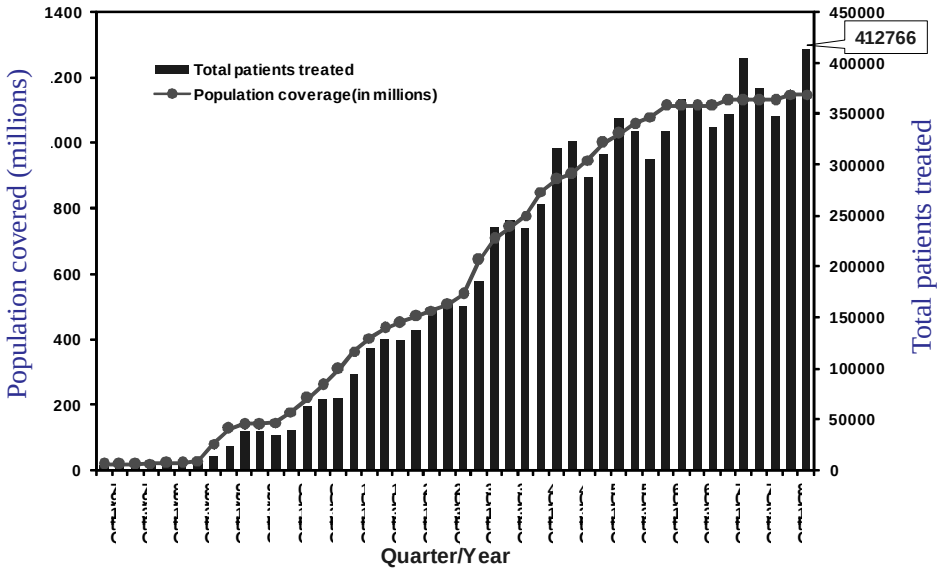

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Table: Performance of RNTCP Case Detection (2008 Second quarter), Smear Conversion (2008, First quarter), and Treatment Outcome (2007, Second quarter)

State	Population (in lakh) covered by RNTCP[1]	Suspects examined per lakh population	No of Smear positive patients diagnosed[2]	Total patients registered for treatment[3]	Annualized total case detection rate	New smear positive patients registered for treatment	Annualized new smear positive case detection rate (%)		No of new smear negative cases registered for treatment	No of new EP cases registered for treament	No. of smear positive re-treatment cases registered for treatment	3 month conversion rate of new smear positive patients	Cure rate of new smear positive patients	Success rate of new smear positive patients
Andaman & Nicobar	4	232	83	172	167	61	59	79%	48	41	19	86%	81%	81%
Andhra Pradesh	822	146	19614	28763	140	12897	63	84%	7811	3092	3791	91%	86%	88%
Arunachal Pradesh	12	233	330	669	223	234	78	104%	150	105	89	87%	89%	92%
Assam	299	141	6387	10711	143	4602	62	82%	3045	1328	983	90%	85%	87%
Bihar	938	93	12333	23041	98	9002	38	51%	7929	1736	2117	87%	75%	85%
Chandigarh	11	346	549	788	297	243	91	96%	143	278	76	94%	89%	90%
Chhatisgarh	236	120	3546	7262	123	2920	49	62%	2810	796	388	89%	82%	86%
D & N Haveli	3	153	68	94	144	33	50	63%	19	21	13	95%	92%	92%
Daman & Diu	2	337	53	53	113	13	28	35%	9	11	8	94%	63%	96%
Delhi	171	231	7261	14934	350	4213	99	104%	2391	5156	1859	90%	86%	86%
Goa	16	158	271	476	117	169	42	52%	92	133	51	89%	80%	83%
Gujarat	564	158	17599	20934	148	9331	66	83%	2634	2710	4614	91%	87%	87%
Haryana	238	168	6943	10425	175	4044	68	72%	1991	1747	1984	89%	85%	85%
Himachal Pradesh	66	256	2403	4023	246	1483	91	95%	723	918	632	92%	88%	90%
Jammu & Kashmir	124	163	2169	3732	121	1668	54	57%	651	900	408	92%	87%	90%
Jharkhand	300	114	5669	10478	140	4553	61	81%	3536	804	780	89%	82%	88%
Karnataka	574	174	10880	16768	117	6700	47	62%	3675	3078	2300	85%	77%	79%
Kerala	342	180	3705	6286	73	2864	33	67%	1208	1417	626	83%	80%	82%
Lakshadweep	1	88	1	1	6	1	6	8%	0	0	0	100%	100%	100%
Madhya Pradesh	693	107	14057	21875	126	8629	50	62%	6366	2491	3132	88%	83%	86%
Maharashtra	1069	124	19371	34985	131	13092	49	61%	8632	6279	4087	90%	83%	85%
Manipur	26	137	383	1173	179	281	43	57%	438	214	81	91%	80%	80%
Meghalaya	25	165	623	1229	194	408	64	86%	224	299	157	81%	84%	85%
Mizoram	10	240	279	693	283	207	84	113%	194	191	48	98%	94%	95%
Nagaland	22	133	400	857	157	332	61	81%	188	148	119	93%	89%	90%
Orissa	399	133	7843	13830	139	6205	62	73%	3268	2524	1165	88%	84%	87%
Puducherry	11	341	508	401	149	197	73	98%	65	83	50	89%	86%	86%
Punjab	266	154	6467	10686	161	4264	64	68%	2095	2206	1600	88%	82%	85%
Rajasthan	646	152	21915	32052	198	12602	78	97%	8821	3645	5869	91%	87%	89%
Sikkim	6	395	228	474	319	154	104	138%	86	136	63	86%	85%	85%
Tamil Nadu	664	223	12081	21695	131	8676	52	70%	5708	4337	2271	90%	84%	85%
Tripura	35	169	533	777	89	438	50	67%	135	118	70	92%	90%	92%
Uttar Pradesh	1909	155	48614	79219	166	34067	71	75%	22242	8739	10393	90%	85%	87%
Uttarakhand	95	180	2438	3806	160	1504	63	67%	909	615	580	89%	83%	86%
West Bengal	879	153	18523	29404	134	14013	64	85%	5609	4977	3207	88%	85%	86%
Grand Total	**11477**	**149**	**254127**	**412766**	**144**	**170100**	**59**	**79%**	**103845**	**61273**	**53630**	**89%**	**84%**	**86%**

1 Projected population based on census population of 2001 is used for calculation of case-detection rate. 1 lakh = 100,000 population

2 Smear positive patients diagnosed, include new smear positive cases and smear positive retreatment cases

3 Total patients registered for treatment, include new sputum smear positive cases, new smear negative cases, new extra-pulmonary cases, new others ,relapse,failure,TAD and retreatment others

level internal evaluations that were undertaken during the year 2007. The main focus of this review meeting was to further maintain and enhance the quality of DOT services with regular supervision and monitoring.

2. A joint donor review mission (JRM) of the RNTCP was undertaken from May 19-30, 2008. The mission team included representatives from Department for International Development (DFID), Global Fund against AIDS, Tuberculosis and Malaria (GFATM), United States Agency for International Development (USAID), World Health Organization (WHO) and the World Bank. The JRM conducted field visits in Gujarat, Maharashtra and Orissa and inter-acted with several officials at district, state and national levels. The mission concluded that the progress towards the project development objectives (PDO) and overall implementation remain satisfactory and appreciated the efforts made by the programme in addressing the disparities in performance that exist among states and districts.

3. A training of Master Trainers was conducted at National Tuberculosis Institute, Bangalore in May 2008 in order to expand the TB/HIV collaborative activities to the entire country as per the 'Joint National Framework for TB-HIV collaborative activities-2008'. The programme officers of both, NACP and RNTCP, from the states of Arunachal Pradesh, Assam, Bihar, Chandigarh, Jammu & Kashmir, Kerala, Madhya Pradesh, Meghalaya, Rajasthan, Sikkim and UP participated in the training. These master trainers will facilitate the trainings of the other programme managers and other staff at the state and district level as per the action plan prepared by them.

4. The 14th meeting of National Laboratory Committee of RNTCP was held at New Delhi in the first week of June, 2008 to review the status of accreditation process of Intermediate Reference Laboratories (IRLs) and medical college TB laboratories that have applied for the accreditation. The national reference laboratories have undertaken EQA-OSE visits to Jharkhand, Uttar Pradesh, Andhra Pradesh, Arunachal Pradesh, Assam. Nagaland and Manipur during the quarter.

   The IRLs of Andhra Pradesh and Delhi were accredited for *M TB* culture and DST during the quarter. With the accreditation of these two laboratories, there are currently four accredited IRLs. Another eight IRLs are likely to complete the process of accreditation shortly.

5. One hundred thirty seven MDR-TB patients have been put on Cat-IV treatment for the management of MDR TB by the end of second quarter 2008. The states of Gujarat and Maharashtra have expanded the DOTS plus services to a few more districts during this quarter. The national level DOTS-Plus training was held for the states of Delhi, Rajasthan and Kerala and these states along with Andhra Pradesh and Haryana are expected to start the DOTS-plus services shortly.

6. Revised National Tuberculosis Control Programme participated in the NRHM workshop for the finalization of the NRHM financial guidelines which was held May, 2008. The adoption of these financial guidelines by the programme divisions will ensure uniformity in financial management and reporting.

7. In order to understand the airborne infection control practices in the country, CTD along with experts from WHO-India and CDC, Atlanta, undertook field visits to various health facilities in Hyderabad, Kolkata and Delhi. This will help the programme in developing guidelines for infection control in our country setting.

8. A number of issues have been identified that need to be addressed for strengthening ACSM component, these include training for capacity building of STOs and IEC Officer, re-defining the role of communication facilitators by focusing on poor performing

districts. RNTCP is focusing on ACSM activities in order to expand the reach and quality of services to larger section of society through the network of civil society organization and community based organization. To do so emphasis is on strengthening the capacity of states and districts to develop need-based locally relevant interventions so that patient get services in a friendly environment, and patients and families are well informed and their motivation levels are high for completion of treatment.

Case Report

DISSEMINATED TUBERCULOSIS MANIFESTING AS CHRONIC PANCREATITIS

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***Summary*:** Pancreatic involvement in tuberculosis is known but uncommon. The clinical manifestation may vary from painless obstructive jaundice due to pancreatic mass (cyst or abscess) to fever of unknown origin. Here we report a case who initially presented as acute pancreatitis relapsing into chronic pancreatitis as an initial manifestation of disseminated tuberculosis. **[*Indian J Tuberc 2008; 55:214-216*]**

***Key words*:** Disseminated Tuberculosis, Pancreatic Tuberculosis, Acute and Chronic Pancreatitis

INTRODUCTION

Disseminated tuberculosis refers to concurrent involvement of at least two non-contiguous organ sites of the body, or involvement of the blood or bone marrow by tuberculosis process[1]. Tuberculosis is an extremely common disease in developing countries, though its incidence is on the rise in the Western world too! Pancreatic tuberculosis is a rare manifestation of such a common disease possibly due to protective pancreatic enzymes. We discuss below a patient who presented as acute pancreatitis, relapsing into chronic pancreatitis as an initial manifestation of disseminated tuberculosis.

CASE REPORT

A 23-year-old non-alcoholic female was admitted previously with history of episodic abdominal pain, fever, vomiting, along with tenderness in the epigastrium three months, prior to present admission. She was managed conservatively with provisional diagnosis of acute pancreatitis based upon markedly elevated serum amylase and lipase along with imaging evidence of pancreatitis. Ultrasound abdomen at that time had revealed ill-defined bulky and hypoechoic pancreas suggestive of pancreatitis with multiple space occupying lesions at porta suggestive of lymphadenopathy and splenomegaly. Contrast enhanced computed tomography (CECT) abdomen had shown focal pancreatitis along with retroperitoneal and mesenteric lymphadenopathy and splenomegaly. Patient was relieved for a short time and was re-admitted during present episode with history of intermittent low grade fever and abdominal pain radiating to back along with distension of abdomen of three weeks' duration. There was no history of jaundice, trauma, surgery, tuberculosis, or treatment with antitubercular drugs in past and patient also denied any history of contact with tuberculosis. On examination, her vitals were normal. There was no icterus, peripheral lymphadenopathy or pedal edema. Abdominal examination revealed tenderness in epigastrium, evidence of ascites and splenomegaly (3 cm below left subcostal margin). Respiratory examination was suggestive of left sided pleural effusion. A clinical possibility of chronic pancreatitis (in view of past evidences) along with disseminated tuberculosis was considered.

Her investigations revealed hemoglobin of 10.2 g/dl, total leucocyte count 6200/mm^3, differential leucocyte count $P_{64}L_{32}E_2M_2$, platelet count 3,26,000/mm^3 and erythrocyte sedimentation rate (ESR) was 40 mm in 1st hr. Other investigations including serum amylase, serum calcium, lipid profile, liver function tests with serum proteins, renal function test, blood sugar and urine examination were

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within normal limits. HBsAg, anti-HCV were negative and ELISA for HIV 1 and 2 was non-reactive. Mantoux test was positive (12x20 mm). Chest radiograph showed left sided pleural effusion. Ultrasound abdomen showed hepatosplenomegaly, dilated common bile duct (CBD) with narrowing at lower end, bulky head of pancreas and peripancreatic lymph nodes and ascites. Spiral CT abdomen showed bulky head of pancreas (Fig.) with prominent pancreatic duct with retroperitoneal and mesenteric lymphadenopathy, splenomegaly, left sided pleural effusion, ascites and omental thickening and likely radiological diagnosis of tuberculosis was suggested. CECT chest had revealed left-sided pleural effusion without any evidence of miliary tuberculosis/adenopathy. Magnetic resonance cholangiopancreatography (MRCP) revealed irregular bulky head of pancreas with cystic spaces suggestive of chronic pancreatitis with dilated tortuous main pancreatic duct, dilated CBD with stricture at lower end, mild dilatation of intrahepatic biliary radicals, splenomegaly, left pleural effusion and ascites. Upper GI endopscopy did not show any varices. Her ascitic fluid had total protein of 4 gm%, albumin 2.6 gm% and serum ascites albumin grading (SAAG) was 0.5 gm%. Total leucocyte count was 1800/mm^3 with 85% lymphocytes. On Gram stain, no organisms were seen, AFB stain, for mycobacterium tuberculosis was negative and culture was sterile. But polymerase chain reaction (PCR) for *M. tuberculosis* in ascitic fluid was positive. Pleural fluid was also exudative in nature. Diagnosis of disseminated tuberculosis with chronic pancreatitis was made and she was put on antitubercular therapy (RHZE) along with conservative treatment for chronic pancreatitis as there was no history of jaundice in past or at present episode, no symptoms of mal-absorption, liver function tests and blood sugar were normal. She showed gradual response in the form of marked

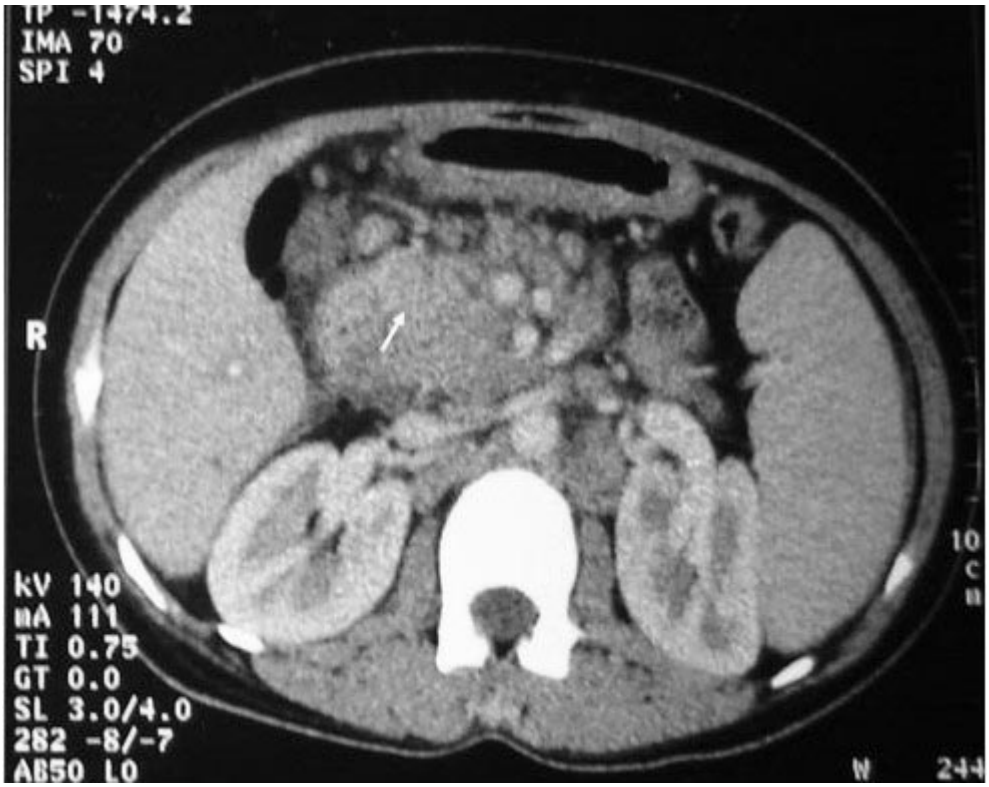

Fig.: Spiral CT abdomen showing bulky head of pancreas (arrow)

improvement with reduction in both intensity and frequency of epigastric pain, resolution of fever, ascites and pleural effusion over next three months. Ultrasound abdomen done during her follow-up had also shown gradual reduction in size of pancreatic head and she was doing well on follow-up.

DISCUSSION

This patient who had been previously diagnosed as acute pancreatitis presented as chronic pancreatitis along with hepatosplenomegaly, lymphadenopathy and polyserositis of tubercular etiology.

Abdominal tuberculosis affecting gastrointestinal tract, peritoneum, omentum, mesentery and its node and other solid intra-abdominal organs like liver, spleen is a common form of extra-pulmonary tuberculosis occurring in about 11-16%. Tubercular peritonitis constitutes 4-10% of all patients with extra-pulmonary tuberculosis[2].

Pancreatic tuberculosis is extremely uncommon[3] and occurs more often in immuno-compromised patients and miliary tuberculosis where the disease pattern can be variable[4]. Pancreas is supposed to be biologically protected from infection by *Mycobacterium tuberculosis* because of pancreatic enzymes. Pancreatic involvement is thought to be caused by direct spread from adjacent peripancreatic lymphnodes and also by hematogenous dissemination. Isolated case reports, which are available on presentation of involvement of pancreas in tuberculosis, include upper abdominal pain, pyrexia of unknown origin, obstructive jaundice mimicking pancreatic carcinoma, acute pancreatitis, pancreatic abscess refractory to antibiotics, massive gastrointestinal hemorrhage due to duodenal wall erosion, splenic vein thrombosis and non-specific symptoms with weight loss[5]. Mass lesion in pancreas due to tuberculosis are infrequently described[6-8]. Additional features of low attenuation peripancreatic and peri-portal adenopathies with peripheral rim enhancement on CT along with fine needle aspiration cytology wherever feasible usually supplement the diagnosis. Though a review of literature has revealed that a majority of cases are diagnosed on laparotomy either for constitutional symptoms along with mass or obstructive jaundice[9].

The advent of PCR has simplified the diagnosis of tuberculosis in situations where fluid or tissue samples can be obtained easily and it obviates the need for laparotomy. The polymerase chain reaction for *Mycobacterium tuberculosis* (TB-PCR) is a rapid and reliable method for the diagnosis of both pulmonary and extra-pulmonary tuberculosis with an overall sensitivity of 78.3% and a specificity of 100%. Because of the relatively low sensitivity of TB-PCR, clinical judgment remains the ultimate decision in the management of tuberculosis[10].

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Case Report

TUBERCULAR HEPATIC ABSCESS – A RARE PRESENTATION

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Summary: Hepatic tuberculosis is one of the rare forms of extra-pulmonary tuberculosis. The focal or nodular form presenting as tuberculoma or abscess is uncommon. Hepatic tuberculosis without involvement of lungs or other organs is even rarer[1,2]. We report a rare case of primary tubercular liver abscess without involvement of any other organ of body. ***[Indian J Tuberc 2008; 55:217-220]***

Key words: Hepatic Tuberculosis, Hepatic Abscess

INTRODUCTION

Hepatic tuberculosis is one of the rare forms of extra-pulmonary tuberculosis. Most cases of hepatic tuberculosis are associated with miliary tuberculosis, in which there is diffuse involvement of liver. It may also be secondary to pulmonary or gastrointestinal tuberculosis. The focal or nodular form presenting as tuberculoma or abscess is uncommon. Isolated hepatic tuberculoma without involvement of lungs or any other organ is perhaps the rarest form of tuberculosis[1-3]. The diagnosis is most often delayed or missed because of non-specific symptomatology and rare occurrence.

CASE REPORT

A-36-year-old man presented to our hospital with history of fever since two months, pain right upper abdomen and lower chest and loss of appetite since one month. Initially fever was high grade and was associated with rigors and chills but later on it was low grade and intermittent in nature. Pain in the right hypochondrium was dull in nature and there was no radiation to any other site. Patient did not complain of cough, expectoration, haemoptysis, breathlessness, loss of weight or any urinary/bowel symptom. There was no history of diabetes, hypertension or any other disease.

The patient was of an average built and had good nutritional status. General physical examination did not reveal any abnormality. Respiratory and cardiovascular examination was within normal limits. Abdominal examination revealed tenderness in right hypochondrium on palpation. Liver was enlarged four cm below the right costal margin. It was tender with sharp margins and a smooth and soft surface. The upper border was found to be in fifth inter-costal space on percussion. The spleen was not palpable and there was no ascities or any other palpable mass in abdomen.

Chest radiograph showed elevation of the right dome of diaphragm with blunting of right costophrenic angle (Fig. 1). There was no parenchymal lesion in chest x-ray. Ultrasonography

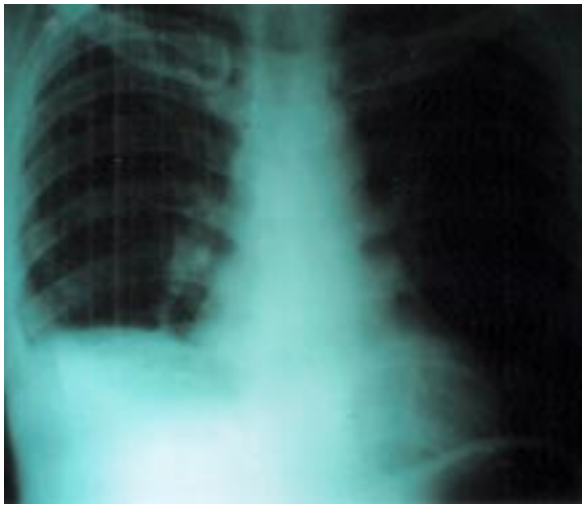

Fig. 1: X-ray chest PA view showing elevation of the right dome of diaphragm with blunting of right costophrenic angle.

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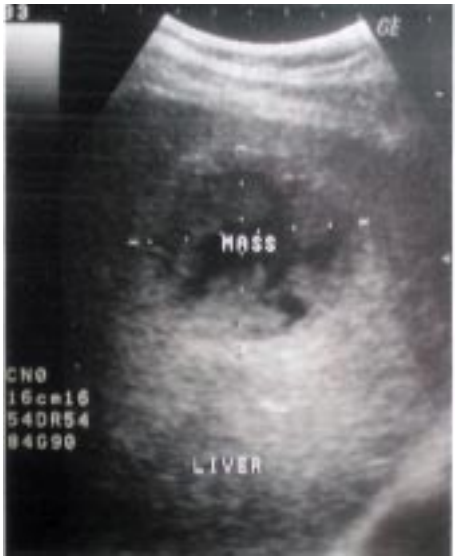

Fig. 2: Ultrasonography of abdomen, showing a mass measuring 64.1 x 57.7mm in right lobe of liver

of abdomen, which was done by private practitioner, showed a mass measuring 64.1x57.7mm with thick walls in right lobe of liver (Fig. 2). The patient was treated as a case of amoebic liver abscess by the private practitioner for about one month but without any relief.

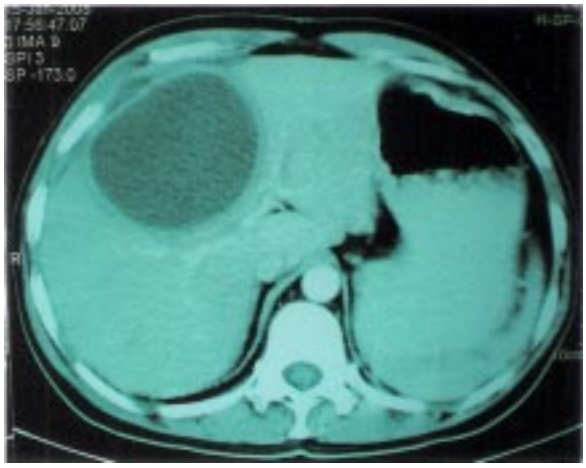

Fig. 3: CT scan of abdomen showing a hypoechoic mass measuring 89 × 89 × 75.6 mm in anterior segment of right lobe of liver.

On admission, the haemoglobin was 8 gm%, total leucocyte count was 6700/cu mm with 65% neutrophils, 33% lymphocytes and 2% monocytes. ESR was 87 mm in first hour (Westergren Method). Urine examination was normal and the stool examination was negative for

Fig. 4: ZN staining of the aspirated pus showing acid fast bacilli.

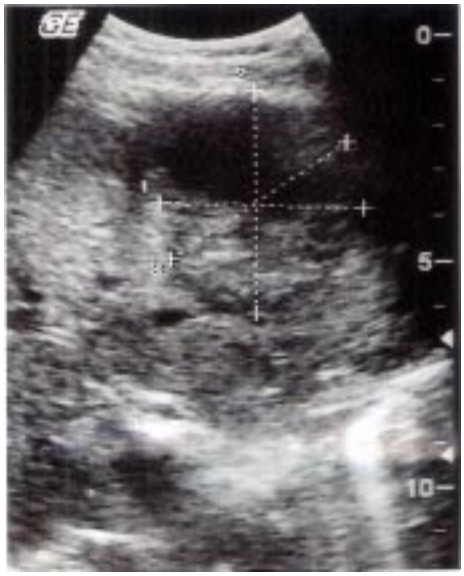

Fig. 5: Ultrasonography of abdomen three and a half months after ATT showing a mass measuring 44.4 x 39.2 x 45.9 mm

trophozoites and cysts of E. histolytica. Mantoux was negative. Liver function tests were within normal limits. Bleeding time (BT), clotting time (CT) and prothrombin time (PTI) were also within normal limits. Enzyme linked immunosorbent assay (ELISA) for HIV was non-reactive.

Fluoroscopy revealed that right dome of the diaphragm was raised with restriction of movements. Computed tomographic (CT) scan of abdomen showed a hypo-echoic mass lesion in anterior segment of right lobe of liver (Fig. 3). The lesion was 89x89x75.6 mm in size and on contrast study showed peripheral enhancement with central non-enhancing necrotic area. Spleen, pancreas, kidneys and intestine were normal and there was no free fluid in the abdomen.

CT guided needle aspiration of the lesion was done and about 150ml of brown coloured pus was aspirated. The pus was subjected to Gram and ZN staining, cytological examination and culture. Pus was found to be positive for AFB on ZN staining (Fig. 4) and negative for trophozoites of Entamoeba histolytica. Gram staining and culture for pyogenic organism was also negative.

Patient was started on RNTCP regimen CAT-1, to which patient responded well. Ultrasonography of the abdomen repeated after three and-a-half months of ATT showed decrease in the size of liver abscess (44.4 x 49.2 x 45.9 mm) with organization (Figure 5).

DISCUSSION

Hepatic tuberculosis is one of the rare forms of extra-pulmonary tuberculosis. Hepatic involvement has been reported in 10 to 15% of patients with pulmonary tuberculosis and it is a common finding in patients with disseminated tuberculosis[1,2]. Most cases of hepatic tuberculosis are associated with miliary tuberculosis, in which there is diffuse involvement of liver. The focal or nodular form presenting as tuberculoma or abscess (lesions larger than 2 mm) is uncommon[3] The prevalence of tubercular liver abscess is 0.34% in patients with hepatic tuberculosis. It was first described by Bestowe in 1858[4]. Approximately 100 cases of tubercular liver abscess have been described in the literature now[5] but primary hepatic Tuberculosis not associated with tuberculous foci anywhere in the body (as in the present case) is very rare, with fewer than 15 cases reported in the literature[6].

Reed *et al* described three morphological types of hepatic Tuberculosis: (1) miliary Tuberculosis of liver associated with generalized miliary tuberculosis, (2) primary miliary Tuberculosis of liver without involvement of other organs, and (3) primary tuberculous granuloma or abscess of liver[6].

Levine *et al* classified hepatic Tuberculosis as; (1) miliary tuberculosis, (2) pulmonary tuberculosis with liver involvement, (3) primary liver tuberculosis, (4) Tuberculoma and (5) Tuberculous cholangitis[7].

Hepatic tuberculosis is usually caused by pulmonary or intestinal tuberculosis. Tubercle bacilli reach the liver by way of hematogenous dissemination: the portal of entry in the case of miliary tuberculosis is through the hepatic artery whereas in the case of focal liver tuberculosis it is via the portal vein. Irrespective of the mode of entry, the liver responds by granuloma formation[3]. Secondary re-activation of the bacilli after hematogenous dissemination during primary infection is another mechanism by which the liver is affected[5].

The clinical diagnosis of tuberculous liver abscess had always been difficult. Usually symptoms and signs in this condition are non-specific. Constitutional symptoms in the form of fever, anorexia and weight loss are present in 55%-90% of the patients. Abdominal pain is present in 65%-87% of patients. Jaundice is uncommon in tuberculous liver abscess being present in 20%-35% of patients[3] and may be caused by extra or intra-hepatic obstruction[8].

Ultrasonographic finding of tubercular liver abscess is a hypoechoic mass lesion in liver. CT scan findings are hypodense lesion which shows

peripheral enhancement with central non-enhancing necrotic area[1]. However, the clinical and radiological features are non-specific and may mimic pyogenic or amoebic liver abscess or tuberculous pesudo-tumor.

The definitive diagnosis of tubercular liver abscess needs microbiological/pathological examination of the specimen from the abscess. Aspiration of the liver abscess under the guidance of USG/CT can provide a specific specimen for the histo-pathological examination and help in making a definitive diagnosis and to distinguish an abscess from neoplasm of the liver. The diagnosis depends on presence of caseating granulomatous lesion in liver biopsy and/or presence of AFB in such material[2]. Using needle biopsy specimen, epithelioid granuloma formation can be demonstrated in liver tuberculosis in 80% -100% of cases; caseation necrosis in 30% - 83% and AFB on smear examination in 0% - 59% of cases[3]. The present case was initially simulating amoebic liver abscess and it was only after aspiration that the diagnosis of tuberculosis was made possible by smear examination of the aspirated pus.

In summary, we have presented a rare case of tubercular liver abscess without involvement of the other organs. Clinical diagnosis of liver abscess is difficult because of the non–specificity of symptoms and signs. Fine needle aspiration of the abscess and histological examination of the specimen can help in making a definitive diagnosis. The present case highlights that tuberculous nature of liver abscess though rare, should be ruled out in cases of suspected pyogenic liver abscess before starting antibiotics so as to avoid delay in treatment as the prognosis of tubercular liver abscess is good.

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The Chief Minister of Delhi State Shiela Dixit felicitated

Dr. M.M. Singh, Vice-Chairman(OR), Tuberculosis Association of India with "eminent medical person award" for his dedicated services in tuberculosis field in Delhi on Medical Association's Foundation Day held on 10th August, 2008.

FIRST JOINT INTERNATIONAL CONFERENCE OF SOUTH-EAST ASIA REGION (THE UNION) AND 63RD NATIONAL CONFERENCE ON TUBERCULOSIS & CHEST DISEASES (SEAR-NATCON 2008)

The Tuberculosis Association of India

The *Tuberculosis Association of India* (TAI) along with the Union (SEAR) organized the First Joint International Conference of South East Asia Region (SEAR) and the 63rd National Conference on Tuberculosis and Chest Diseases (NATCON 2008) from **8th to 10th September, 2008** at India Habitat Centre, Lodhi Road, New Delhi-110003.

The Theme of the conference was **"TB, HIV and Lung Health in Resource Limited Countries"**.

Over 580 delegates from Bangladesh, Myanmar, Nepal, Pakistan, Bhutan, Sri Lanka, Norway, UK, USA, Germany and from all over India participated in this Joint International Conference of the Union (SEAR), and NATCON 2008. Eminent faculties from WHO, Union, FIND, BRAC, TB Drug Alliance, CTD, TRC, NTI, LRS Institute, PGI, Patel Chest Institute, ICMR, were invited, especially to make this congress a mega success. The team worked under the advice and guidance of the Organizing Chairman, SEAR NATCON 2008.

The Conference was inaugurated by the former President of India, Dr. A.P.J. Abdul Kalam, after the welcome address by Dr. V.K. Arora. The presidential and key note address was delivered by Dr. R.K. Srivastava, DGHS. Next the Patron SEAR-NATCON and President TAI, Dr S.P. Aggarwal, addressed the congress followed by the release of books written by Dr. V.K. Arora and Dr. V.K. Dhingra along with the Souvenir and fact sheets by Dr. A.P.J. Abdul Kalam. An HIV positive patient, Ms Celina Menezes, spoke with choked emotion to the gathering followed by presentation of awards. Chief Guest Dr. A.P.J. Abdul Kalam, deliberated in the "Scientific Inaugural Session" and spoke on the importance of tuberculosis and HIV control in resource limited countries and was emphatic when he said that we should do away with resource limitations while tackling health problems of such immense importance. He made the delegates take three TB oaths, namely: (a) Every delegate will go back and cure at least 100 TB patients in a year; (b) Each delegate will spread the message of early detection of TB among patients in their region; (c) Each and every delegate will go back and relieve the pain and suffering of these patients in their respective regions. The inaugural ceremony concluded with a vote of thanks by Dr. M.M. Singh, Chairman, SEAR, followed by the National anthem.

The scientific programme of the Conference was very interactive and included two pre-conference workshops on "Public Private Mix in resource limited countries" and "MDR TB" at New Delhi Tuberculosis Centre and LRS Institute respectively.

During the Conference, a total of 63 scientific papers and 61 posters were invited for presentation. A "Daily News letter" from the Conference secretariat and live updates of the Conference on our Website **(www.tbassnindia.org)** were the highlight of the Conference and it was another first for National Conference of Tuberculosis and Chest Diseases. Two prestigious orations were delivered; namely P.K. Sen Oration by Dr. Nils Billo and Lupin TAI Oration by Dr.Rajendra Prasad. They spoke on "The role of UNION in global lung health" and "MDR & XDR-TB: Problems and solution". Dr. Nils E Billo in his oration described about the activities of The Union in South East Asia Region namely, training programmes for medical and paramedical staff, technical and financial assistance in organizing conferences, workshops and field studies, especially involving NGOs. He stressed on the fact that resource limited countries should come forward with operational research proposals for financial assistance to the Union. Dr. Rajendra Prasad in his

oration described in detail the genesis, prevalence and impact of drug resistance to *M. Tuberculosis* among patients in the SEAR. He emphasized the need of providing facilities for DST and DOTS-Plus at a faster pace.

On the first day of the Conference, one workshop on "Tobacco and Lung health" and two symposia on "MDR & XDR-TB" and "Infection control strategies" were conducted by an experienced faculty. Talks on "PPM for TB: Blessing or Burden", "New vaccines for TB: A major global need" and "RNTCP response to MDR-TB in resource limited countries" were presented. The day ended with a clinical meeting at Gulmohar Hall followed by a dinner for the invited faculty.

The second day began with a symposium on "TB & HIV co-infection" in Hall 'A' and free paper session on "TB control strategies and epidemiological impact assessment" in Hall 'B'. Two panel discussions, "TB in migratory and floating population-programmatic challenges" and COPD were held in both the Halls simultaneously. Dr. V.K. Arora moderated the COPD panel discussion which had eminent doctors who deliberated on various aspects of diagnosis, management and prevention of COPD with special emphasis on resource limited countries. It was a very interactive session in which the delegates participated by putting up many questions like prognostic indicators of COPD, prevention and rehabilitation and role of NIV in acute exacerbations. Dr. M. Islam from BRAC also shared his experience of managing COPD in Bangladesh. This was followed by a talk on mycobacteriosis: clinical profile and symposia on "newer TB drug development", and "Advances in new diagnostic tests for TB." In Hall B, free paper sessions on "TB diagnostics and therapeutic issues" and "MDR & XDR-TB" continued along with a workshop on 'Bronchial Asthma'.

Poster presentations on Non-TB diseases also drew attention of the delegates. Scientific sessions progressed continuously without any break. Delegates took time from the stimulating scientific deliberations to visit the attractive stalls in the exhibition area and networked with other delegates at the Lounge area with Wi-Fi facilities. Meeting of executive committee of South East Asia Region (SEAR) of the The Union was held in Mahagony hall under the Chairmanship of Dr. M.M. Singh. Dr.Nils Billo of the Union and Dr. Nevin Wilson were present as observers. Dr. M.M. Singh gave a brief review of the activities of the South-East Asia Region which was appreciated by Dr. Nils Billo who said that despite financial constraints, the Region has done very well. He also said that the Union's technical and financial help will also be available in future. In the elections for the South East Asia Region, Sri Lanka was proposed as the Chairperson of SEAR. Dr. Kaluarachchi, who was representing Sri Lanka, promised that he will convey this decision and the final names of Chairperson of SEAR and Member Finance will be communicated subsequently. For the Vice-Chairpersonship, Bangladesh was proposed and Dr. Sakhawat Hossain representing Bangladesh declined the offer and the name of Dr. V.K. Arora (India) was proposed and approved. For the Rapporteur of SEAR, the name of Dr. Chaudhary Mohammad Nawaz was proposed and approved. After the scientific deliberations, gastronomic delights and other meetings, there was a banquet arranged by TAI at "Occasions", Pragati Maidan, New Delhi. Along with the banquet, there was a cultural programme.

The Conference progressed with renewed vigour on the concluding day with a symposium on "Childhood Lung Health" in Hall 'A' and Panel discussion by eminent faculty on "Bronchogenic Carcinoma" in Hall 'B'. This was followed by enthralling talks on "High dose INH therapy in MDR TB in resource limited countries" by Dr. S. K. Katiyar and on "Vaccination against TB" by Dr. Kumarswami. In Hall 'B', free paper session on "Non-TB pulmonary diseases" and some assorted papers continued along with a workshop on "Conducting clinical trials for development of new TB drugs". Miscellaneous poster presentations continued during the sessions. Hall 'A' had TAI oration on 'Progress towards MDG in SEAR countries" and some very interesting talks on topics like "Obesity and lung health", "Shortening TB treatment-TRC experience", "Role of surgery in tuberculosis in resource limited countries", "TB/HIV

collaborative activities", "Advocacy in TB control" and "Public private partnership in RNTCP" by eminent speakers.

Under Rule 3 (xiii) of the Rules and Regulations of TAI, Dr. K.K. Chopra, Dr. Shashidhar Buggi, Dr. Rupak Singla and Dr. Rajiv Ranjan were elected as representatives of the National Conference to serve on the Central Committee and will hold office till the next National Conference.

The congress concluded with a glittering valedictory function with mementoes presented by Dr. Nils E. Billo of the Union. Vote of Thanks was proposed by Shri M.P. Gupta after a speech by Dr. V.K. Arora and Dr. M.M. Singh.

Indian J Tuberc 2008; 55:224-230

FORUM

NATIONAL WORKSHOP ON PUBLIC PRIVATE PARTICIPATION (PPP) FOR TB CONTROL IN INDIA – A BRIEF REVIEW

INTRODUCTION

Controlling Tuberculosis (TB) is still important public health challenge in India. While most of the targets have been achieved under RNTCP (Revised National Tuberculosis Control Programme) at all India level, there are still inequities across states, gender, rural/urban areas, etc. Public Private Participation/Partnership (PPP), one of the strategies adopted by RNTCP, holds considerable potential to improve tuberculosis control in India. PPP is also supposed to achieve equity, improve access, availability and affordability and increase quality of services[1,2]. The Central TB Division published guidelines for the participation of the NGOs (2001) and private practitioners (2002), providing them opportunity to formally collaborate with the RNTCP[3-5].

A national level workshop was organized on TB on 23-24 January, 2008 by the Tata Institute of Social Sciences (TISS), Mumbai, in collaboration with the Maharashtra State Anti TB Association, Maharashtra Association of Anthropological Sciences, RNTCP and the Gorgas TB Initiative, University of Alabama at Birmingham, USA. The theme of the workshop was "Public Private Partnership for TB Control in India". The workshop reviewed the role of PPP in TB Control and identified current needs for research and training to strengthen it.

The workshop was attended by participants from WHO officials, representatives from NGOs, medical colleges, state/district level programme managers, private sector (individual practitioners, hospitals), research organizations and the corporate sector.

CONTENTS AND DELIBERATIONS

The workshop was inaugurated by Prof. S. Parasuraman, Director, TISS, and the welcome address was delivered by Prof. Shalini Bharat, Dean, School of Health Systems Studies, TISS. The chief guest Dr. S. Sahu, National Programme Officer (TB), WHO, India gave address on PPP – Concept and issues – Indian scenario. The sessions were conducted on Participation of NGOs, Corporate sector and Private Practitioners/Hospitals and also on Research in PPP. A series of case studies of projects, interventions and research studies were presented.

The topics discussed included challenges in expansion and sustaining PPP; successful models in different setups; involvement of Ayush practitioners; contribution of Medical Associations; lessons learnt from PPP in HIV/AIDS; barriers for private sector to actively participate along with possible solutions and alternative approaches; current needs for research and training to improve PPP. etc.

RECOMMENDATIONS

Specific recommendations (finalised by Group work and Panel Discussion) concerning involvement of NGOs, private sector and improving research were suggested as follows:

- The mechanism of **NGOs involvement** should be made simpler with regular review meetings at various levels. In current NGO schemes, additional activities like sputum collection and transportation can be included to improve the case holding and preventing delay in receiving report.

- **Private sector** is the first contact of health seeking for the patients, who value it as confidential. Thus there is a great need to

actively involve more of them in the programme. Different providers can be mapped and classified according to individual practitioners, system of medicine, size of hospitals, corporate, etc. to identify scarcely covered areas. Schemes may be based on different providers – Private Practitioners, Specialists, Hospitals, Medical colleges – separately for government and private. One to one peer sensitization instead of group sensitization will be more effective, which can be facilitated by IMA.

- There is a need to give more priority to **TB research**. It is not enough to know only how many patients are treated. There is a requirement of quantitative as well as qualitative data about the various schemes. Revision of various PPP schemes is also very difficult without any data or information from research. Sanctioning power of OR (Operation Research) proposals may be delegated at state level. Some possible research areas identified were like: comparison of different schemes geographically and temporally; problems of migrants, shift workers, etc.; stigma related research; need assessment of different sectors; behaviour related to spitting; equity in access to care, incentive structures, and regulatory mechanisms, etc. Documentation of current schemes, their experiences, lessons learnt is essential which can be done by external agency. Core group of TB researchers from recognized institutes all over India should be involved from inception of various schemes.

In addition, following general recommendations concerning future plans and sustaining programme were made.:

- It is essential to develop comprehensive policy document covering different schemes offered by RNTCP. The schemes should be function-based and there is a need to develop flexibility within the given framework of scheme. Regular revision and giving wide publicity to available schemes is necessary.

- There is a need to replace the word 'incentives' with either fees or cost of services or some other suitable word. Non-financial incentives can be introduced in different schemes like: Regular training programmes for capacity building, quality assurance of the treatment and updating knowledge and information; Recognition of services by staff; Felicitation of successful partners. If possible, the schemes may be institutionalized. Bringing out publications will give necessary recognition to their work. There should be regular appraisals. Appreciation and social recognition for good work will keep them motivated to perform better in future.

- Regular and timely funding to partners in the schemes is essential. Funding may be based on current price index so that inflation is taken into account. The field staff should not be burdened with out-of-pocket expense for field work.

- Possibilities for coordination in additional areas like TB-HIV and management of MDR and XDR-TB patients needed to be explored. As far as possible, DOTS centre should be made more accessible for the patients. Support to patients for nutrition, travel, lost wages etc. may also be considered.

- Celebrities and famous personalities should be roped in to increase the awareness and remove social stigma. Media utilization is important for awareness of community and provider. Community volunteers are required to see to it that patients complete treatment.

- Recommendations were also made to develop or adapt tools for training, implementation, monitoring and evaluation of PPP schemes.

Most of the models of PPP presented during this workshop have the potential to be replicated elsewhere in India. The recommendations made will be helpful for the revision of schemes by the Health Ministry and WHO.

Harshad Thakur, Mumbai,
Manoj Toshniwal, Pune,
Sheela Rangan, Pune and
Yatin Dholakia, Mumbai

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INFORMATION AND COMMUNICATION TECHNOLOGY: APPLICATION IN HEALTH SECTOR

Health as one of the fundamental human rights has been accepted in the Indian Constitution. The Indian health care sector constitutes:

- Medical care providers: physicians, specialist clinics, nursing homes and hospitals
- Diagnostic service centers and pathology laboratories,
- Medical equipment manufacturers,
- Contract Research Organizations (CRO's), pharmaceutical manufacturers,
- Third party support service providers (catering, laundry)

Before independence, the health care sector was in dismal condition with high morbidity and mortality rate and high prevalence of infectious diseases. Since independence emphasis has been put on primary health care and India has worked continuously to improve its health care system in the last several decades. Considerable progress has been made in expanding the public system and reducing the burden of disease. But the government funded facilities were not enough to meet the growing demand of population, whether it was primary, secondary or tertiary care, which necessitated the need for alternate source of funding in the health care sector.

Post liberalisation, in the 1980's the entry norms for private players in the health services industry were relaxed by the Government. The private health care facilities are owned and run by for-profit companies, non-profit or charitable organizations. The entry of private sector has opened a gamut of opportunities for India in terms of medical equipment, information technology in health services, BPO, telemedicine, medical and health tourism. Today the health care industry has emerged as one of the most challenging sector as well as one of the largest service sector industries in India with estimated revenue of about $ 30 billion (FY 2005) constituting 5% of the GDP. The Indian health services sector is estimated to be around Rupees 750 billion with hospitals accounting for more than half of this. The sector has had a growth of over 12% p.a. in the past four years and is estimated to grow by 170% by 2012.

Though the private sector has been responsible in bringing about the desired changes in the health industry, the health sector performance requires much improvement in comparison with other emerging economies, including most comparable nations in the region. Deficiencies persist with respect to access, affordability, efficiency,

quality and effectiveness, despite the high level of overall private and public expenditure on health.

To bring in the desired changes for a healthy growth of health care sector, a well-defined partnership between the government and the private sector is essential.

ICT (Information and Communications Technology) is an umbrella term that includes any communication device or application, encompassing: radio, television, cellular phones, computer and network hardware and software, satellite systems and so on, as well as various services and applications associated with them, such as video-conferencing and distance learning. ICTs are often spoken of in a particular context, such as ICTs in education, health care, or libraries.

The Government of India is convinced that building an information technology infrastructure for health will efficiently address all information needs of different stake holders (patients, government, hospitals, insurance companies, vendors and others) in the health care industry and will streamline health care activities through out the country and make India a viable health care destination.

"Information is a determinant of health"

Health care, an information-intensive sector, is one of the key areas that can benefit from the use of information technology. Information technology can play a larger role in addressing key issues that have been the concern of the health industry for many decades such as:

- Simplification of administrative processes
- Strengthening population-based public health systems
- Delivering health care services to the under-privileged sections of the society in a cost-effective manner

Information technology has the potential to correct inefficiencies by electronically storing and managing huge amount of information that can be used to accomplish multiple tasks and present health care providers with an opportunity to reduce expenses of administrative transactions and clinical procedures and enhance the processes.

IT plays a very significant role in synergizing stakeholders towards a common goal. There is a need to educate and empower different groups and players on the benefits of adopting modern technologies to get the stake holders on a common platform, to enable easy and smooth transition of information and data base and to help link them together to take effective action towards the goal '***health for all'.***

Information and Technology (ICT) applications in Tuberculosis

Tuberculosis (TB) has been curable for over 50 years but still kills nearly two million people annually. The drugs that can cure TB are cheap, powerful, and able to cure almost all new cases. But the epidemic is driven by an old problem—inefficient management practices that do not ensure that all infectious patients are completely cured. There's a new threat—the rapid spread of HIV can cause old, latent TB infections to break out in people who would otherwise probably never fall ill. Since an estimated two billion people today have latent TB infections, the spread of HIV can trigger a TB epidemic.

New approaches using computer technology offer better management of tuberculosis patients and allow early action to help patients who are not progressing, and make local, regional, and national authorities knowledgeable and accountable about what is happening in health facilities and among care givers in their areas. When followed correctly, the DOTS strategy quickly turns infectious patients into non-infectious patients, which breaks the cycle of transmission, thus protecting the patient's family and their community. The DOTS programme mandates careful monitoring, especially during the initial weeks of intensive treatment while the patient is still infectious. But just as important is monitoring after the period of intensive treatment while the patient is still on a less demanding drug regime. With better management information there can be few

excuses for infectious patients remaining ill and further spreading the TB germ. Just as importantly, nearly 100% of all new cases can be monitored so that drug-resistant forms of TB do not develop due to ineffective, repeated treatment of patients. Both foreign aid agencies and domestic governments benefit when field data is quickly integrated with a country's health ministry TB database. This improves the success of the TB fight, encourages the responsible use of money, and eliminates the delays and inefficiencies associated with traditional paper records.

The ICT will enable the country like India which is heavily burdened with TB to better achieve the WHO goals for treatment success and case detection rates. It also addresses social ecology issues, including community participation, this allows the doctor responsible for the district to view results for each individual patient, observe overall trends for each group of patients, and monitor the activities of the health workers themselves to see whose performance might indicate the need for more training or support. The resulting application allows health workers to collect data electronically for each diagnosed patient, while retaining the familiar format of the traditional paper DOTS form. Rural health workers with no previous computer experience become proficient within a few weeks.

In summary, the use of ICT tools in health sector particularly in a disease like tuberculosis where a lot of efforts are being put in, can be useful to :

• Inform the community, patients, health workers and doctors by making information available with the aim of increased transparency and accountability, providing information about the programmed facilities available.

• Increase access to government services and improve service delivery by giving proper education, in particular to poor and marginalized groups in remote communities, greater choices and faster delivery, and at the same time providing services that meet their needs.

Despite potentially large productivity gains, the health care sector lags far behind other sectors in an Indian economy in its expenditures and use of information technology.

- Personal health records (PHRs) and electronic health records (EHRs) are key components of needed technological advancements.

- Health information technology (HIT) is a promising tool for addressing the challenges of cost and access

To help achieve an optimal and efficient healthcare environment, the following issues need to be addressed:

- Simplification of administrative process
- Sharing of information between disperate systems
- Create and maintain population-based data
- Reduce data gathering and processing costs
- Standardization of health data; coding, reporting and transmission of data
- Standards for defining key stake holders – Patients, doctors, etc.
- Improving efficiency of clinical systems in the country
- Providing greater access to health care in a cost-effective manner
- Delivery of health-related information and services to remote locations

The ICT initiatives in the health care sector are divided in the following broad categories:

Telemedicine Based Solutions

Telemedicine based solutions assist the medical professionals in the following ways:

1. Electronic Medical Record (EMR) handling
2. Video-conferencing for consultation with specialists, tele-consultation
3. Graphical tools for annotating and analyzing medical reports

The following are some of the major initiatives in this category:

Mercury (http://www.cdacindia.com/html/medinfo/mercury.asp) Mercury is an integrated telemedicine software suite provided by CDAC (Centre for Development of Advance Computing). Mercury supports a host of functions including Electronic Medical records.

Internet Based Health care Solutions (Healthcare Portals)

Internet based health care portals are focused on information dissemination. Various efforts are on to build portals, which disseminate information about various diseases like AIDS, Polio, Tuberculosis, etc. Some of these portals also address the issues of how ICT is being applied to health care.

The following are some of the major initiatives in this category:

a. http://www.healthcare-informatics.com
b. http://www.hin.org.in/index.htm
c. http://indiatelemedicine.com
d. http://www.aarogya.com
e. http://www.doctoranywhere.com
f. http://www.indmedica.com

Health Care Data Collection

Some of the major initiatives in health care data collection are:

a. PDAs to be used to deliver health care in Indian villages:

A novel project in the Indian State of Andhra Pradesh will use mobile computing devices to help deliver the healthcare needs of rural people. Nurses and midwives from primary health centres in remote villages will visit villagers' houses carrying personal digital assistants (PDAs) to collect health-related data.

b Community Access to Sustainable Health (CASH):

CASH (Community Access to Sustainable Health) is a Media Lab Asia project for investigating how information technology can be used to improve rural health care in an economically sustainable manner. The CASH project targets primary health care workers in Indian rural areas. Each of these workers monitors and manages the health of several thousand people every month. Their responsibilities include infectious disease management, pre-natal care, family planning education and immunizations.

Challenges

The major **challenges** that need to be addressed for reaching out to the rural common man include (i) Assessment of Local Needs (ii) Connectivity (iii) Capacity and (iv) Sustainability besides the use of local language and need to improve prevailing infrastructure to elicit favorable response from the people.

Nishi Aggarwal and V.K.Dhingra
New Delhi Tuberculosis Centre

DOTS IN HIV POSITIVE PATIENTS

In the recently held SEAR-NATCON 2008 Conference at Delhi (8th to 10th September), a bold step was taken, when an HIV positive patient Ms. Celina Menezes narrated her experiences at the inaugural function. Her speech clearly showed how much discrimination, myths and misconceptions exist in public about HIV patients and lot of work is needed in this direction.

Her speech raised another very important issue if one tries to read in between the lines. Her biopsy proven tubercular lymphadenitis was treated with DOTS and RNTCP for full six months. After complete therapy, her biopsy was still positive for tuberculosis. What does it mean? It may indicate that especially in HIV positive patients, DOTS regimen is not adequate and there is need to strengthen the regimen or prolong its duration.

It is sincerely hoped that our policy makers will take the message hidden in Calina's treatment failure seriously and modify/prolong anti-tubercular therapy, at least in HIV positive individuals, lest it is too late.

Rajinder Singh Bedi
Patiala

Editor's comments:

Role of lymphnode biopsy in treated cases of tuberculosis is debatable and is inadvisable to assess the success of treatment schedule. Clinical response in the form of reduction in size and the change in the feel of gland (form) i.e. consistency is a better assessment tool along with follow up of the case.

ABSTRACTS

High risk of tuberculosis in health care workers in Romania

G. Sotgiu, A.S. Arbore, V. Cojocariu, A. Piana, G. Ferrara, D.M Cirillo, A. Matteelli, P. Castiglia, L. Ditiu, A. Spanevello, J-P. Zellweger, T. Mihaescu and G.B. Migliori. *The Int J Tub Lung Dis* 2008; **12:** 606-11

The objective was to assess whether health care workers (HCWs) have a higher risk of acquiring tuberculosis (TB) than the general population, and if TB incidence varies between departments, to develop adequate infection control measures. All records of TB cases among HCWs were reviewed by cross-checking laboratory and medical records (retrospectively, 1971-1996; prospectively 1997-2003, following the implementation of the first World Health Organization pilot project in Romania). Annual TB incidence rates among HCWs were calculated and compared with those of the general population; relative and attributable risk with 95% confidence intervals (CI) were calculated. Fifty TB cases were diagnosed in HCWs; 42% were nurses, 24% ancillary staff, 12% physicians, 10% laboratory staff, 10% administrative staff and 2% radiology technicians. The mean incidence of TB in Romania during the study period was 96.8 per 100,000 persons/year (95% CI 83.5-110.1); the mean incidence among HCWs was 942.8/100,000 persons/year (95% CI 726.3-1159.3, $P < 0.001$); comparing the two previous absolute risks, the mean relative risk was 11 (95% CI 8-14) and the attributable risk 846.

Assessment and evaluation of contact as a risk factor for tuberculosis in rural Africa

A.C Crampin, S. Floyd, B.M Ngwira, V. Mwinuka, J.N. Mwaungulu, K. Branson, P.E.M. Fine and J.R. Glynn. *Int J Tub Lung Dis* 2008; **12**: 612-18

The objective was to determine the effect of inaccurate recall on estimates of the proportion of tuberculosis (TB) cases attributable to contact with identifiable prior cases. It was a case-control study of laboratory-confirmed TB cases and community controls, comparing family, household and area contacts identified from a data base of TB cases with those named at interview. Estimation of prior contact as a risk factor for TB and identified factors associated with being a named contact. Ninety-five per cent of named contacts were known TB cases. The proportion of total identified contacts who were named at interview was 75%, and was similar for cases and controls. Cases were twice as likely as controls to identify prior contacts. Adding data base information did not affect odd ratios, but increased the proportion of TB cases attributable to prior contact. Smear-positive, male and human immunodeficiency virus (HIV) negative TB patients were more likely to be named by subsequent cases. Identifiable recent contact with known smear-positive cases accounted for 12.5% of the TB burden.

A five-year follow-up study of Revised National Tuberculosis Control Programme of India at Lucknow.

S.K. Verma, Sanjay Kumar Verma, Surya Kant, Santosh Kumar and R. Prasad.. *Ind J Chest Diseases & Allied Sciences* 2008; **50**: 195-97.

Revised National Tuberculosis Control Programme (RNTCP) was introduced in India in 1993, as a pilot project but the full-fledged programme was started in 1997. Since then, more than eight years have passed but to the best of our knowledge, no long-term follow-up study of patients at five years after completing treatment under DOTS is available. The objective was to determine the status of the tuberculosis (TB) patients after five years of completion of treatment under RNTCP. The study was carried out in Directly Observed Treatment, Short-course (DOTS) Centre, Department of Pulmonary Medicine, CSM Medical University, Lucknow. Patients of tuberculosis who were registered between October 1998 to October 1999

at the DOTS centre of CSM Medical University, Lucknow, were followed-up in their homes after five years of completion of treatment under DOTS strategy with the help of a health visitor. Outcome of 208 registered patients during the study period at the end of completion of their treatment' was: treatment success (cured+treatment completed)-187 (89.9%), default-11 (5.3%), death-9 (4.3%) and treatment failure-l (0.4%). On follow-up at five years, only 80 (42.8%) patients were traced, while 68 (36.4%) patients had migrated to other places and for 39 (20.8%) patients addresses could not be traced. The follow-up status of 80 patients (Cat. 1: 37, Cat. II: 15, Cat. III : 28) revealed that 73 (91.2%) were asymptomatic (Cat. I: 34, Cat. II: 12, Cat. III: 27), two had relapsed (one in Cat. 1 another in Cat. ll) and five patients had died (Cat. I: 2, Cat. II: 2, Cat. III : 1). Treatment under RNTCP is effective as revealed by the results at five years follow-up.

Evaluation of drug resistance in pulmonary tuberculosis patients at Sureyyapasa Chest Diseases Hospital, Istanbul, Turkey

T. Karagoz, P. Pazarli, O.Y. Mocin, D Duman, G. Duman, C Salturk and O. Unal. *Int J Tub Lung Dis* 2008; **12**: 631-35

The objective was to determine levels of *Mycobacterium tuberculosis* resistance to first-line drugs in patients with pulmonary tuberculosis (PTB). Between 1st January and 31st December 2005, all hospitalised PTB patients with culture-positive *M. tuberculosis* specimens and corresponding drug susceptibility tests (DST) for isoniazid (INH), rifampicin (RMP), streptomycin (SM) and ethambutol, routinely performed for every tuberculosis (TB) case at our centre, were included. Of a total of 1513 cases, 1277 (84.4%) were new and 236 (15.6%) were previously treated cases. Of the 1513 isolates, 290 (19%) were resistant to at least one of the drugs tested. Resistance among new and previously treated cases was 16.3% (209 of 1277) and 34.3% (81/236) respectively. Any SM resistance and any INH resistance were the most common drug resistance in new cases, while any RMP resistance was the most common drug resistance in previously treated cases. Multidrug resistance was detected in 3.2% (n = 41) of new cases and in 13.5% (n = 32) of previously treated cases.

Rapid drug susceptibility testing of mycobacteria by culture on a highly porous ceramic support

C.J. Ingham, A.B. Ayad, K. Nolsen, and B. Mulder. *Int J Tub Lung Dis* 2008; **12**: 645-50

Phenotypic, culture-based methods for drug susceptibility testing (DST) of *Mycobacterium tuberculosis* are relatively simple and may be particularly appropriate for resource-limited settings where tuberculosis (TB) is most prevalent. However, these methods can be slow and generate significant amounts of infectious waste. Low-cost digital imaging and a unique porous ceramic support for cell culture (Anopore) may offer opportunities to improve this situation. Objective was to test a rapid DST method based on fluorescence microscopy of mycobacteria grown for a few generations on Anopore. Mycobacteria were cultured with and without drugs, and the resulting microcolonies were heat-killed and stained with the fluorogenic dye Syto1. Microscopy, image-capture with a charge-coupled device camera and digital processing were used to quantify the inhibition of growth by drugs. Rapid DST for rifampicin and isoniazid was performed for clinical isolates. Mycobacteria could be cultured, killed, stained and imaged on Anopore. For DST, the Anopore method gave an accurate result in three days. This is an unprecedented speed for culture-based DST for this group of organisms and results in minimal infectious waste (<20,000 colony forming units). Analysis of mycobacteria by fluorescence and electron microscopy on Anopore also opens up research possibilities.

Manifestations of Pulmonary Tuberculosis in the elderly: A prospective observational study from North India

Dheeraj Gupta, Navneet Singh, Ravinder Kumar and Surinder K. Jindal. *Ind J Chest Diseases & Allied Sciences* 2008; **50**: 263-67.

There is scarcity of published literature on manifestations of pulmonary tuberculosis (PTB) among elderly patients in India. The aim of the present study was to compare the clinical,

radiological and laboratory manifestations of PTB among young and elderly patients.

This prospective study involved 100 human immuno-deficiency virus (HIV) negative patients with PTB. The demographic, clinical, radiological and laboratory manifestations were compared between young (n=50; under 60 years of age) and elderly (n=50; aged 60 years and above) with PTB. Elderly patients, in comparison to younger patients, tended to be heavier smokers and had more co-morbidities (40% *vs* 8%; $p < 0.05$). They presented more frequently with constitutional symptoms (except fever) and less frequently with respiratory symptoms. The mean duration of symptoms and rate of sputum smear-positivity for acid-fast bacilli was similar in both groups. Both the groups were similar with respect to physical examination and chest radiograph findings. Median values of erythrocyte sedimentation rate and total leukocyte count were significantly higher and lower respectively in the elderly patients. The presentation of PTB in elderly patients differs from that of younger patients by the predominance of constitutional rather than respiratory symptoms. A high index of suspicion is required to make a timely diagnosis of tuberculosis in the elderly.

Rapid diagnosis of *Mycobacterium tuberculosis* meningitis by enumeration of cerebrospinal fluid antigen-specific T-cells

M.M. Thomas, T.S.C. Hinks, S. Raghuraman, N. Ramalingam, M. Ernst, R. Nau, C. Lange, K Kösters, C. Gnanamuthu, G.T. John, B. Marshall and A Lalvani. *Int J Tub Lung Dis* 2008; **12**: 651-57.

The objective was to determine whether interferon-gamma (IFN-ã) secreting *Mycobacterium tuberculosis* antigen-specific T-cells are present in the cerebrospinal fluid (CSF) of patients with TBM and to evaluate the feasibility of CSF enzyme-linked immunospot (ELISpot) for the diagnosis of active TBM. It was a prospective blinded hospital-based study. The overnight ELISpot assay detected *M. tuberculosis* antigen-specific IFN-ã secreting T-cells in CSF from nine of 10 prospectively recruited patients with TBM, and zero of seven control patients with meningitis of other aetiology. This corresponds to a diagnostic sensitivity of 90% (95% CI 56-100) and specificity of 100% (95% CI 59-100). This pilot study demonstrates proof-of-principle for a new T-cell-based diagnostic test for TBM which is rapid, sensitive and specific.

Factors predictive of adherence to tuberculosis treatment, Valle del Cauca, Colombia

J.C.Mateus-Solarte and R Carvajal-Barona. *Int J Tub Lung Dis* 2008; **12**: 520-26.

Early diagnosis and treatment are fundamental to tuberculosis (TB) control. Nevertheless, the effectiveness of TB management continues to be influenced by treatment adherence. The objective was to determine which factors are predictive of adherence to TB treatment at the time of diagnosis in Colombia. A cohort of 300 patients newly diagnosed with TB was followed up over 26 weeks. Treatment adherence was measured by determining whether the patient took all or part of the 84 doses in the 26 weeks of treatment. A logistic analysis was carried out and the predictive power of the final variables was determined by means of a receiving operator curve analysis. A high incidence of partial completion of treatment (65.6%) was found. Significant associated factors were 1) living away from the family, 2) overcrowding at home (e”2 persons per bedroom), 3) lack of family support, 4) living >10 min away from the treatment facility and 5) not having used the services of the treatment facility before. Several factors can be measured on PTB diagnosis that would help identify those patients at higher risk for treatment non-adherence. The predictive value of each of these factors alone was weak, but if associated their predictive value was high.

Indian J Tuberc 2008; 55: 234

LIST OF REVIWERS

Agarwal, Nishi, *Delhi*
Arora, V.K. *Delhi*
Banerji, D. *Delhi*
Banavaliker, J.N. *Delhi*
Bedi, R.S. *Patiala*
Behera, D. *Delhi*
Chadha, V.K. *Bangalore*
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