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Editorial

TB CONTROL PROGRAMME – A WAY FORWARD

[*Indian J Tuberc 2008; 55: 113-115*]

Mycobacterium tuberculosis has been infecting the human race since the dawn of history. Archaeological evidence has established the association from Neolithic times. The insidious nature of the infection and its association with some of the brightest minds invested the disease with a mystical quality. The epochal discovery of Robert Koch that the disease is due to an infectious agent brought it into the realm of treatable conditions. The failure of the tuberculin therapy and the failure of early efforts to invent a specific chemotherapeutic agent left no alternatives but to use non-specific remedies with varying success. Those of us who started training in the 1950s would still remember the thoracoplasties, therapeutic pneumothoraces and pneumo-peritoneums that were performed to 'rest the lungs'. These along with the sanatoria went into oblivion with the introduction of streptomycin – the first antibiotic to have a proven antitubercular activity[1]. Very shortly after streptomycin was introduced acquired resistance was seen in *Myco tuberculosis.* Emergence of antibiotic resistance to single drugs was demonstrated *in vitro* as well as clinically when treatment failures and relapses occurred. Other effective drugs were discovered and a multi-drug regimen was shown to be more effective. The earliest combination therapy showed an improvement on the results of streptomycin monotherapy[2]. Short course chemotherapy based on the multi-drug regimes have become the order of the day along with Directly Observed Therapy (DOTS) [3]. The Indian programme has now covered the entire country and a careful appraisal has shown that the programme reduces the prevalence[4]. However, the Indian programme which promises much, is hamstrung by health systems. India has a large private health care system that is not too well organized or oriented to follow programme practises. For any success in the long run it is imperative that the sector is motivated to do right by the patients [5]. This community requires to be acquainted with and trained to fulfill the International Standards for Tuberculosis Care particularly the Standard for treatment (Standards 7-15) and public health responsibilities (Standards 16 and 17) [6]. This would be a massive effort, but, that alone will make a dent on the problem.

The first six standards deal with diagnostic aspects. While the larger laboratories would satisfy them, the vast majority of clinical laboratories would fall short of the requirement. In the absence of a nationally enforced regulatory mechanism governing laboratory practice, this would be difficult. This is another aspect that requires to be addressed. Thus, the organizational problems are immense but the promise is worth the effort of tackling them.

Imaging techniques along with clinical data would normally be used to establish the suspicion of tuberculosis. It is the demonstration and cultivation of the causative organism that establishes the aetiological diagnosis. Immunological tests have been shown to be useful in some situations. Likewise, biochemical tests, largely non-specific like adenine deaminase determination in plural fluids, have not gained wide acceptance. The paper by Kulkarni and Madrasi on the "Relationship of Nitric Oxide and Protein Carbonyl in Tuberculosis" in this issue may have preliminary information that could lead to another test. However, as indicated by the authors themselves the changes may not be specific to tuberculosis but more related to the tissue response.

The emergence of Multi-drug Resistant (MDR) and Extensively Drug – Resistant (XDR) strains of *Myco. tuberculosis* will certainly have an impact on the steady progress [7]. A paper presented at recent (9th) Sir Dorabji Tata Symposium by Rodrigues [8] viewed the issue from a tertiary care centre perspective and reported 9.3% XDR TB amongst their MDR isolates [8]. This figure is much higher than 3% of MDR seen in the community by Tuberculosis Research Centre, Chennai. Nevertheless, the problem is with us. Indian data appears to show that the community levels are not as high in some other parts of the world but certainly a cause for concern [9]. It is probably right to prepare for the eventual exaltation in numbers.

In the scenario of looming MDR and XDR tuberculosis the programme will need to be scaled up technologically. The most crucial aspects would be prompt diagnosis with information on the antibiotic susceptibility early in the treatment process. Recent advances in technology have made this possible. With quick accurate diagnosis, the numbers of smear negative tuberculosis would decrease and the euphemistic "therapeutic trial", with its implied procrastination, for tuberculosis to become a rarity. Thus the amount of unnecessary contamination of the environment would decrease. This may also decrease the rate of emergence of resistant organisms.

The three steps in aetiological diagnosis *viz*. Smear microscopy, culture and antibiotic sensitivity testing can be made more relevant to early patient care.

The current staining methods for tubercle bacilli are of quite low sensitivity requiring 5000-10000 bacilli/ml to be present in the sputum. The extra-pulmonary infections often contain much fewer organisms. The use of molecular biology techniques would improve the sensitivity. This is an area where technical advance can be expected. Molecular methods have been used for sputum samples but applicability in an endemic situation, as in India, will require careful development. The available kits/tests need to be evaluated and good ones made freely available. They could be more reliable in extra-pulmonary tuberculosis. If added to probes in a microarray format for antibiotic resistance genes, instant sensitivity results are possible in the future.

The normal Lowenstein-Jensen (LJ) medium based culture and sensitivity testing yields its earliest results around three weeks but usually after five weeks. The advent of the automated mycobacterial culture (BACTEC, etc) has improved the situation. Results could be expected a couple of weeks earlier but the technology is capital intensive and expensive. The Microscopic Observation Drug-Susceptibility assay has further improved the prospect of an early culture and sensitivity result [10]. The method is quite simple and can be practised in a reasonable bacteriological laboratory with good laboratory procedures. Specific additional capital equipment needed would be an inverted microscope. The consumables and safety cabinets have now-a-days become the norm in average microbiology laboratories. The author has witnessed the establishment of the method in a short time in an Armed Forces hospital. Technicians become proficient in the methodology with minimal training. The method can be made available across the country with benefit. In the Microscopic Observation Drug- Susceptibility method[10], culture and sensitivity results are available together by 10 days. The sensitivity and specificity was higher than in the LJ medium or the Automated method. While a few laboratories in India are set up for the test, it is time the method is practised more extensively. This can be taken up as a central programme integral to RNTCP.

In a country of subcontinental dimensions, the epidemiology of tuberculosis would be quite varied. A study of the entire country is needed. The first step would be to develop laboratories capable of performing molecular tests across the country and ensure steady and reliable performance. A number of methods for typing have been described [11]. It would possibly be advisable to start with IS6110 RFLP analysis and proceed to spoligotyping in all laboratories and other methods at larger laboratories across the

countries. Molecular techniques would be important to detect transmission of antibiotic resistant strains so that the outbreaks could be monitored and contained. An understanding of the transmission dynamics in different regions would assist in identifying actions that would decrease the disease load. The *Myco tuberculosis* genome has been shown to be remarkably conserved and the changes that occur with specific drug resistances consistent[12]. Molecular methods are ideal for tracking the resistant clones and enabling control measures. It is important that these aspects are developed along with strengthening of the DOTS programme.

In summary, tuberculosis control programme has achieved a lot and established considerable infrastructure. However, unless we take a technological leap, we will remain the top TB country for quite sometime. Not much has changed since the commentary [13]. "TB control - a long way to go".

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Original Article

EVALUATION OF DIFFERENT TYPES OF CHEST SYMPTOMS FOR DIAGNOSING PULMONARY TUBERCULOSIS CASES IN COMMUNITY SURVEYS

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Summary

***Background*:** Prevalence of tuberculosis (TB) is an important epidemiological index to measure the load of the disease in a community. A series of disease surveys were undertaken in rural community in Tiruvallur district in Tamilnadu, south India

***Objective*:** To investigate the yield of pulmonary tuberculosis (TB) cases by different symptoms status and suggest predominant symptoms for detection of cases in the community based surveys.

***Methods*:** Three disease surveys were conducted during 1999-2006, in a random sample of 82,000 adults aged ≥ 15 years to estimate the prevalence and incidence of pulmonary TB. All subjects were screened for chest symptoms and chest radiography. Sputum examination was done among those who were either symptomatic or abnormal on X-ray or both. Cases observed through symptom inquiry were included for analysis.

Results: In survey-I, 65.6% had cough of ≥ 14 days and yielded 79.1% of the total cases. In surveys II and III, symptomatic subjects with cough contributed 69.5% and 69.2% of the cases respectively. In survey I, 26.8% had symptoms without cough but with at least chest pain ≥ 1 month contributed 8.4% of total cases. The corresponding proportions in subsequent surveys were 29.3, 11.5%; and 23.4, 11.2% respectively. The number of symptomatics without cough and chest pain but with fever ≥ 1 month was negligible.

Conclusion*:** The relative importance of cough as a predominant symptom was reiterated. The yield of pulmonary TB cases from symptomatics having fever of ≥ 1 month was negligible. Fever may be excluded from the definition of symptomatics for screening the population in community surveys. ***[Indian J Tuberc 2008; 55: 116-121]

Key words: Prevalence, Chest symptoms, Tuberculosis, DOTS

INTRODUCTION

Tuberculosis (TB) is prevalent in India and continues to be a leading cause of death[1]. Its control programmes can achieve a high level of treatment success[2] and are associated with a decline in reported disease burden[3]. This is possible only if there is an effective TB control programme like the Directly Observed Treatment - Short Course (DOTS) aimed for higher cure and case detection. When the programme is successful, more cases will be detected and treated successfully. This will result in cutting the transmission in the community. Prevalence of the disease is estimated by undertaking epidemiological survey in the community and it involves researchers, trained field workers, X-ray units, X-ray films, sputum bottles, laboratory set-up and vehicles, etc,.

Different screening methods are employed for the detection of cases. First, the selected population is screened to identify persons with symptoms suggestive of tuberculosis and sputum specimens are collected from them. These specimens are processed using fluorescence microscopy[4] for acid fast bacilli (AFB) and cultured for *Mycobacterium tuberculosis* on Lowenstein-Jensen medium[5]. Alternatively, all persons are subjected to chest X-ray (CXR). These X-rays are read by independent readers who classify all persons as having shadows suggestive of TB, non- TB conditions or normal. Sometimes both methods are

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employed for the detection of TB. A case was defined as a person with a positive smear (>3 AFB) or culture irrespective of colonies or both.

Several TB surveys have been conducted in different pockets of the country. Some of these surveys[6,7] used mainly two screening methods namely, symptom inquiry and CXR. These tools considerably reduce the number of specimens to be collected and processed. A study[8] on the yield of cases by different screening methods showed that symptom screening picked up about two-third of the cases whereas CXR alone picked up more than three-fourth of the cases. With either method the prevalence was underestimated by one-third in the former method and about one-fifth in the latter method. Symptom elicitation is relatively inexpensive compared to CXR. In community surveys, the cost of mobile X-ray units, X-ray films, processing them and obtaining independent readings by at least two readers is very high. The yield of pulmonary tuberculosis cases by different chest symptoms was not documented in details based on a series of community surveys. It is essential to investigate the proportion of symptomatics by various symptoms status and yield of cases in order to suggest the symptoms that are fairly enough to employ in the community based surveys for detection of cases. The data collected from three disease surveys in the community conducted by Tuberculosis Research Centre (TRC) gave an opportunity to document the leading symptoms that yielded more cases.

This report summarizes the yield of cases employing different symptoms inquiry in three disease surveys and the relative merits of each symptom employed in screening the population for detection of cases.

MATERIAL AND METHODS

In 1999-2001, a baseline disease survey was conducted in a random sample of 50 villages and three urban units in Tiruvallur, south India by TRC soon after the implementation of DOTS strategy in the district. All subjects (aged ≥15 years) in the selected villages/units were registered by door-to-door census to cover the required sample size of 82,000 subjects. Two more repeat surveys (2001-2003 and 2004-2006) at every 2.5 years interval were carried out to estimate the prevalence of pulmonary TB and thereby to assess the epidemiological impact of DOTS strategy. The findings of the first survey have been already reported[7]. Two screening methods namely, symptoms inquiry and CXR (a mobile unit with mass miniature radiograph) were employed in these surveys. A symptomatic was defined as a person having cough of two weeks or more, chest pain of one month or more, fever of one month or more and/or haemoptysis at any time. Elicitation on history of treatment was also included as an additional criterion for detection of cases. Two samples of sputum specimens were collected from those who were symptomatic and/or abnormal on X-ray suggestive of TB and processed for identification of cases. The symptom elicitation was carried out by the trained field workers. To ensure quality, a supervisor independently interviewed 10% of adults screened for symptom. In the present exercise, the screening tool namely, symptom inquiry alone was considered for analysis and interpretation. The institutional ethics committee of the TRC approved

Table 1: Distribution of symptomatics and number of cases identified in three surveys

Surveys	No. Eligible	No. Examined (%)	No. of symptomatics (%)	No. of sputum examined (%)	No. of cases
Survey I	83425	75974 (91)	6417 (8.4)	6204 (97)	263
Survey II	85510	78222 (91)	8969 (11.5)	8546 (95)	243
Survey III	89454	81814 (91)	8794 (10.7)	8390 (95)	179

Table 2: Distribution of sputum positive cases by different symptom status

2a. Survey I

Symptom status	Sputum examined		Observed cases				
	No.	%				Total	
			S+C+	S-C+	S+C-	No.	%
Cough(C) - all	4073	65.6	103	89	16	208	79.1
Chest pain (P) (without C)	1664	26.8	5	12	5	22	8.4
Fever (F) (without C,P)	1	-	-	-	-	-	-
Haemoptysis (H) (without C,P,F)	120	1.9	1	1	1	3	1.1
History of treatment (without C,P,F,H)	346	5.6	17	11	2	30	11.4
Total	6204	100.0	126	113	24	263	100.0

2b. Survey II

Symptom status	Sputum examined		Observed cases				
	No.	%				Total	
			S+C+	S-C+	S+C-	No.	%
Cough(C) - all	4721	55.2	84	72	13	169	69.5
Chest pain (P) (without C)	2504	29.3	3	21	4	28	11.5
Fever (F) (without C,P)	24	0.3	-	1	-	1	0.4
Haemoptysis (H) (without C,P,F)	468	5.5	3	1	2	6	2.5
History of treatment (without C,P,F,H)	829	9.7	21	15	3	39	16.0
Total	8546	100.0	111	110	22	243	100.0

2c. Survey III

Symptom status	Sputum examined		Observed cases				
	No.	%				Total	
			S+C+	S-C+	S+C-	No.	%
Cough(C) - all	4897	55.7	53	57	14	124	69.2
Chest pain (P) (without C)	1886	23.4	3	11	6	20	11.2
Fever (F) (without C,P)	14	0.2	-	-	-	-	-
Haemoptysis (H) (without C,P,F)	522	6.3	2	1	1	4	2.2
History of treatment (without C,P,F,H)	1071	14.4	13	15	3	31	17.3
Total	8390	100.0	71	84	24	179	100.0

S+ = smear positive, S- = smear negative, C+ = culture positive, C- = culture negative

Table 3: Yield of cases according to interval between the onset of cough and its elicitation

Survey	Number of cases by duration						Total
	2 wks to < 2 m		2 m to < 12 m		> 12 m		
	No.	%	No.	%	No.	%	
Survey I	68	(32.7)	61	(29.3)	79	(38.0)	208
Survey II	44	(26.0)	49	(29.0)	76	(45.0)	169
Survey III	55	(44.4)	40	(32.3)	29	(23.4)	124

m = months, wks = weeks

the project and informed consent was obtained from all the participants in the study.

RESULTS

The population eligible for symptom elicitation, number elicited for symptoms, the proportion of symptomatics, the number of persons from whom sputum was collected and number of cases diagnosed in each survey (I, II, III) are given in Table-1. The coverage for symptom inquiry and sputum examination was above 90% in all surveys. The proportion of symptomatics in survey-I was 8.4% (6417/75974). It increased to 11.5% and 10.7% in the survey-II and survey-III respectively and difference was statistically significant.

The distribution of positive cases by symptom status is given in Table- 2a, 2b, 2c. In survey-I, of 6204 symptomatics as many as 4073 (65.6%) had cough of 14 days or more and yielded 208 (79.1%) of the 263 total sputum positive cases. In survey II, the proportion of symptomatics having cough of 14 days or more was 55.2% and contributed 69.5% cases. In survey III, the corresponding figures were 55.7% and 69.2% respectively. In survey I, there were 1664 (26.8%) symptomatics without cough but with at least chest pain of one month or more. They contributed 22 (8.4%) sputum positive cases. The corresponding proportions in surveys II and III were 29.3 and 11.5%; and 23.4 and 11.2% respectively. It could be seen that the number of symptomatics without cough and chest pain but with fever of one month or more was negligible and no case (except one case in survey-II) was diagnosed from these symptomatics. In survey-I, there were 346 (5.6%) persons who reported a previous history of treatment and they contributed 30 (11.4%) cases. The corresponding proportions in the subsequent two surveys were 9.7 and 16.0%; and 14.4 and 17.3% respectively.

The yield of cases according to the interval between the onset of cough and the time of elicitation of cough is given in Table-3. It could be seen that proportion of the cases yielded were 32.7, 29.3 and 38.0% from symptomatics who reported cough of 2 weeks to < 2 months, 2 months to < 12 months and ≥ 1 year respectively. In survey II, the corresponding proportions were 26.0, 29.0 and 45.0% and that in survey III were 44.4, 32.3 and 23.4% respectively. On an average, one- third of the cases were yielded from each category of symptomatics.

DISCUSSION

The findings of the three surveys showed the relative importance of cough as a predominant symptom employed in screening the population. In fact, two screening tools namely, symptom inquiry and chest radiography were used in all these surveys. In order to study the yield of cases by different symptoms (cough, chest pain, fever and haemoptysis including history of treatment), the cases diagnosed

by symptom inquiry were only considered for analysis. An earlier report[8] on yield of TB cases by employing these two screening methods in the first two surveys showed that the prevalence was under estimated by both methods; 54-66 (60%) of the cases were identified by symptom inquiry alone whereas 82% were identified using chest radiography in both surveys. In survey-III, a total of 277 cases were detected employing symptom inquiry and chest radiography as screening tools. The sensitivity of symptom inquiry was 65% (179/277) and that of CXR was 80% (222/277) showing that yield of cases was similar in all the surveys. Symptom inquiry is relatively simple and inexpensive compared to chest radiograph with exorbitant cost on CXR examination including mobile X-ray unit, film, processing the film and obtaining the readings from two independent readers. A correction factor (CF) of 1.5 (277/179) can be used to estimate the total prevalence of TB if symptom inquiry alone is employed. This has also been validated in the study[6] conducted by National Tuberculosis Institute, Bangalore and in our earlier report[8]. Our present study has shown that cough was relatively important and predominant symptom among the symptomatics as well as among cases as observed in all the three surveys. A TB prevalence survey[9] based on symptom inquiry in Raichur district of Karnataka showed similar findings. In that survey, of the 3685 symptomatics, 3193 (87%) had cough of 14 days or more and yielded 405 (92%) of the 440 sputum positive cases. In that survey, the additional contribution of persons with cough of less than two weeks (0.2%) towards sputum eligibility was negligible and hence it may not affect the calculation of the prevalence of the disease. In another study[10] in North Arcot district (now known as Kancheepuram district) of Tamilnadu it was shown that 61.4% (4932/8032) of the symptomatics reported cough of duration 14 days or more and 77% (211/274) cases came from those who had cough of 14 days or more with or without some other symptom. The relative importance of cough against chest pain for screening the population was reported by Gothi et al[6] and Baily et al[11]. The contribution of fever alone (without cough and chest pain) in identifying symptomatics and cases was negligible as observed in all the three present disease surveys similar to the findings in the earlier studies[9,10]. This showed that fever can, safely, be excluded from symptom inquiry in community surveys. The workload and the cost involved in collection of sputum from these symptomatics and processing the specimens in the laboratory can also be avoided. The study emphasized the importance of eliciting the previous history of treatment during symptom inquiry yielding substantial proportion of cases as observed in our study (11-17%).

In Revised National TB Control Programme (RNTCP), a symptomatic is defined as a patient having cough of three weeks or more with or without other symptoms. The importance of including quality check in the survey employing symptom inquiry was well demonstrated in an earlier report[12] by our centre. A multi-centric study[13] by our centre has demonstrated that inclusion of chest symptomatics with cough of two weeks or more has yielded a substantial increase in the number of sputum positive cases compared to symptomatics of three weeks or more as defined in RNTCP. This indicated the importance of identifying symptomatics employing cough of two weeks or more instead three weeks or more for diagnosis of TB. Among the 55561 adult outpatients screened, 2210 had cough of two weeks or more and yielded 267 (12%) smear-positive cases compared to 1370 with cough of three weeks and 182 (13%) cases. The estimated work-load of sputum microscopy in the laboratory using cough of two weeks or more, the number of smear per day was slightly higher costing about Rs. 130 (US$ 3) for every additional smear-positive patient detected. This as well as the effectiveness of this criterion on the provider point of view needs to be further assessed in a separate study.

There are a few limitations in this study. TB patients with Human Immuno-deficiency Virus (HIV) may have different symptoms from those without HIV. However, the prevalence of HIV among TB patients in this area was observed to be <1% (unpublished data) The findings of this study may not be applied to routine case detection, since the characteristics of the patients detected by DOTS

and those detected by the survey may be different. Patients with fever may visit health facility for care and may not get detected in survey.

CONCLUSION

The proportion of symptomatics in the community survey seemed to be stabilized to about 11% as observed in the last two surveys. As already reported in any other community surveys, the relative importance of cough as a predominant symptom was reiterated in this study also. The inclusion of fever in the definition of symptomatics yielded small proportion of symptomatics and negligible cases. In future surveys, fever may be excluded from the definition of symptomatics for screening the population in community surveys.

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Original Article

DOTS IN DRUG ADDICTS WITH TB : DELHI EXPERIENCE*

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Summary

Background: Drug abuse is on the rise. Drug addiction lowers the general immunity of the body. Tuberculosis is known to be one of the major infectious diseases with a high incidence among drug addicts. Treatment of drug addicts suffering from tuberculosis is a challenge to the treating physician.

Methods: An interventional prospective study which involved free de-addiction drugs and motivation along with free anti tubercular drugs under Revised National Tuberculosis Programme was undertaken among drug addicts. Sixty drug addicts suffering from tuberculosis, registered under RNTCP in SPM marg TB Clinic (Pili Kothi) between 2002-2007 and treated under DOTS along with de-addiction treatment by an NGO (Sharan) formed the study sample.

Objectives: Objectives of the study were :

a) To study the profile of drug addicts with tuberculosis
b) To assess the success results of DOTS in drug addicts with tuberculosis (along with de-addiction treatment).

Results: Extensive counselling for de-addiction and motivation of the study patients along with nutritional food supplements improved the compliance and adherence to treatment with equal success rates as in non-addict tuberculosis patients. The overall success rate in drug addicts was 83.3% . The default rate of 3.3% and failure rate of just 1.7% among study group were also within the permissible range of RNTCP (<4%).

Conclusion: DOTS along with supplementary intervention was observed to be quite effective in drug addicts with TB.

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Key words: Drug addicts**,** De-addiction, Tuberculosis, Success rates

INTRODUCTION

Drug abuse is defined as use of drugs in ways that are not medically approved because they cause strong feeling of euphoria or alter perception. Repetitive use produces wide-spread adaptive changes in brain leading to physical and psychological dependence. Drug addiction is a phenomenon of tolerance and psychological dependence and is defined as compulsive relapsing drug use despite negative consequences. Transition to addiction is determined by combination of environmental and genetic factors and only a fraction of dependent users may go on to become addicted[1].

Drug addiction is a phenomenon of tolerance and dependence on drugs. Drug abuse is on the rise. Alcohol and tobacco are the most commonly used substances. Other drugs used by drug addicts are Opium, Marijuana, Heroin, Smack, Cocaine, Methamphetamines and other club drugs e.g. Ectasy, GHB, LSD, PCP and Kelany. Tuberculosis is said to be one of the major infectious diseases with a high incidence in drug addicts[2]. Drug addiction lowers the immunity of body by decreasing killer cell activity, by decreasing gamma interferon production or by decline in interleukin production by B and T cells[3]. Deficient diet and life style changes indirectly increase the chance of development of disease by lowering the general immune status[4-7]. Prevalence of tuberculous infection among drug users was reported to be high (15 – 44%) and the prevalence of disease among them was observed to be 150 times higher than the general population in Iran[8].

The treatment of tuberculosis in drug addicts has many problems and is a challenging task for treating physician. Drug addicts usually fail to recognize and neglect the symptoms of cough and

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expectoration. They, thus, present themselves quite late to the treatment facilities. Even when diagnosed as tuberculous, these addicts also have a tendency not to adhere to treatment and hide their disease from their fellow addicts for fear that they may not be allowed to share with them drugs and thus have a great stigma not to reveal their disease and refuse to acknowledge the disease.

AIMS AND OBJECTIVES

Present study was undertaken with the following objectives:

- To study the profile of drug addicts with tuberculosis.
- To assess the success results of DOTS in drug addicts with tuberculosis with additional intervention of free de-addiction drugs, counselling and nutritional supplementation.

MATERIAL AND METHODS

Revised National TB Control Programme was implemented in SPM Marg, Pili Kothi area in November 1996. The allotted area covers congested old Delhi localities and has a number of patients who are drug abusers and addicts. A NGO '**Sharan**' which had taken up the de-addiction work in the area, in view of high number of drug addicts in Yamuna Bazar area, was involved in the

Table 1: Socio-demographic profile of Drug Addicts

Parameter		**Number (Total 60)**	**Percentage (100.0)**
Sex-all were males			
Age (In years)	15-24	11	18.3
	25-44	36	60.0
	45 and above	13	21.7
Educational Status	Illiterate	21	35.0
	Literate	39	65.0
Occupation	Unemployed	30	50.0
	Rag Picking	14	23.3
	Rickshaw Pulling	05	08.3
	Others	11	18.4
Place of their stay			
	Own residence	14	23.4
	Footpath	24	40.0
	Railway Station	02	3.3
	Bus Terminals	02	3.3
	Park	18	30.0
Duration of stay			
	< one year	38	63.3
	1-5 years	14	23.3
	6-10 years	04	6.7
	11-15 years	04	6.7

Table 2: History of Drug Abuse amoung study group

Parameter		Number (Total 60)	Percentage (100.0)
Duration of taking drugs	<6 months	06	10.0
	7-12 months	03	5.0
	13-18 months	05	8.3
	19-24 months	07	11.7
	25-30 months	09	15.0
	More than 30 months	30	50.0
Mode of using drug	oral	21	35.0
	Injecting	15	25.0
	Smoking	12	20.0
	Sniffing	07	11.7
	Chewing	05	08.3
Drugs used			
	Opium	27	45.0
	Pethidine	05	8.3
	Phenargan	04	6.6
	Fortwin	03	5.0
	Morphine	01	1.7
	Tidigestic	01	1.7
	Others	19	31.7

implementation of DOTS and de-addiction. The NGO Sharan has a few observation beds set up nearby and in Sharan Detox Centre in South Delhi consisting of 30 beds. The de-addiction protocol was carried out by the NGO and the supply of drug buprenorphine was also given free to the patients along with the supplementation of diet. Patients included in the study were residents of Yamuna bank, adjoining parks and pavements. They belonged to very poor and marginalized section of the society. Most of them were unemployed and had no source of income but had history of multiple drug abuse.

It was an interventional prospective study. All these drug addicts who were also suffering from tuberculosis and registered under RNTCP between 2002 to 2007 were included in the study. Drug addicts who were unfit for ambulatory DOTS treatment were, however, not registered and excluded. These patients were treated with DOTS regimen under RNTCP with proper categorization. They were also counselled for de-addiction by NGO Sharan, motivated and supplied drug buprenorphine free as a de-addiction programme schedule. In addition they were also given nutritional food supplements i.e. bread and eggs during each visit of drug collection in IP and also in CP. Motivation and re-motivation was done for these patients at regular intervals.

RESULTS

All the sixty drug addicts in the study population were males and majority belonged to 25 to 44 years of age group. In all 50 % were unemployed and 35% were illiterate. Majority had no place to stay. (Table1)

Out of these drug addicts, 50% were taking drugs for more than 30 months, 45% of them were

Table 3: Outcome of DOTS in drug addicts

Category	Cure/ completed	Died	Defaulter	Failure	Transfer Out	Still on treatment	Total
Cat-I	33(80.5)	02(6.9)	02(4.9)	01(2.4)	00(0.0)	03(7.3)	**41(100)**
Cat-II	15(88.2)	01(5.9)	00	00	01(5.9)	00	**17(100)**
Cat-III	02(100)	00	00	00	00	00	**2(100)**
Total	**50**	**03**	**02**	**01**	**01**	**03**	**60**
%	**83,3**	**5.0**	**3.3**	**1.7**	**1.7**	**5.0**	**100.00**

using opium. About 35% of them were using oral drugs and 25% of them were using in injectable forms. (Table 2)

Of the 60 drug addicts diagnosed to have tuberculosis, 43 (71.7%) were sputum positive. Category wise distribution was Cat I- 41 (68.4%), Cat II -17 (28.3%) and Cat III- 02 (3.3%). The outcome of these cases is shown in Table 3.

DISCUSSION

Treatment of tuberculosis in drug addicts is quite difficult and a challenging task. The socio-economic condition of drug addicts is often poor and whatever they earn they spend on drugs rather than food. They are often under-nourished and thus susceptible to development of disease. Their priority of spending is on the drugs to which they are addicted, even when suffering from tuberculosis, with consequent default of treatment. It is, therefore, of paramount importance that they should be given free drugs under supervision to enforce compliance. Indeed tuberculous drug addicts have higher default rates. These cases are, therefore, a source of transmission of infection to the healthy people. A study from Lucknow[9] reported that 10.6% did not comply with DOTS treatment and non-compliance was of the order of 23.9% in alcoholics and 47.4% among other drug addicts. Similar figure of 20% non-compliance was observed by Pulide Ortoga et al[10].

Present study deals with the treatment of these drug addicts with free TB drugs under Revised National Tuberculosis Programme with DOTS strategy. Besides these, patients were provided free de-addiction drugs and counselling at repeated intervals. Other interventional strategy was free nutritional supplements in the form of bread and eggs provided at the time of drug collection.

Nutritional support as given in the present study and other financial incentives for them may increase compliance to treatment. De-addiction advice, motivation and re-motivation during the treatment and psychosocial support from an understanding and dedicated worker facilitates the treatment and improve results. Involvement of local community and selection of outreach workers who provide social support, encourages the addicts to seek timely advice and improves compliance[11].

Flanigan et al[12] stated that DOTS is an effective approach for the treatment of tuberculosis among substance users and suggested to explore community based modified DOTS for persons with drug dependence. Of course de-addiction advice, psychiatric advice, repeat motivation and social support is necessary to

maintain adherence for successful outcome of treatment.

CONCLUSION

Directly Observed Treatment was observed to be quite effective in drug addicts with tuberculosis. De-addiction counselling and intensive motivation for adherence of TB treatment along with nutritional supplementation achieved excellent results in drug addicts with TB.

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Original Article

IS THE QUALITY OF LIFE DIFFERENT IN PATIENTS WITH ACTIVE AND INACTIVE TUBERCULOSIS ?

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Summary

***Objective*:** The aim of this study was to evaluate the quality of life (QOL) in outpatients with active and inactive tuberculosis, and to study the relations between QOL and demographic and socio-cultural chracteristics and variables concerning the disease and depression.

***Material and Methods*:** Included in the present study were 196 active and 108 inactive cases who attended Dispensary for Tuberculosis within a one year period, plus 196 healthy controls. In this study, questionnaire form, SF 36 quality of life scale and Beck Depression Inventory (BDI) were used.

***Results*:** It was determined that in all fields of QOL, scores of the control group were higher than those of the patient groups. QOL scores in physical and social functionality dimensions of inactive cases were higher than in active cases ($p<0.001$). As BDI scores increased in active and inactive cases, physical component summary (PCS) and mental component summary (MCS) decreased. As the treatment period increased in active cases, MCS increased. In active and inactive cases, marital status and accompanying diseases have an effect on the decrease of PCS scores ($p<0.05$). In patients with tuberculosis, the QOL of men, single, patients with a high level of education and those not having a disease that accompanies tuberculosis were found to be high ($p<0.05$). The QOL was negatively correlated with age and BDI, while being positively correlated with monthly income, daily sleep period and treatment period ($p<0.05$).

***Conclusion*:** It is stated that in inactive tuberculosis cases, as in active cases, QOL is deformed and demographic-socio cultural chracteristics, depression, daily sleep period, treatment period and accompanying diseases are factors that affect quality of life. **[*Indian J Tuberc 2008; 55: 127-137*]**

Key words: Tuberculosis, Inactive Tuberculosis, Quality of life, Depression

INTRODUCTION

Tuberculosis (TB) is a serious global health problem, as one-third of the world population is estimated to be infected with *Mycobacterium tuberculosis*, and eight milion new active cases occur annually[1].

Today on the one hand medicine is applied more technically and mechanically and on the other hand an effort is necessary not only for controlling the disease but also for increasing the quality of life of patients.

Quality of life (QOL), which can be defined as a person's perception of his or her physical and mental health[2], covers broad domains, including physical, psychological, economic, spiritual and social well-being[3]. The World Health Organization defines health as a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity[4].

TB affects all the predicted fields of quality of life, such as general health perception, corporal sense, psychological health, mental peace and functionality of physical and social roles[5-9]. Furthermore, in a limited number of studies, it has been shown that active tuberculosis, having drug side effects, social isolation and stigma from relatives, family members and friends, causing various symptoms such as hemoptysis, chest pain,

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fever, profuse sweating, weight loss and fatique, affects the QOL[10-12]. Nonetheless, for reasons of stigma from a social point of view, loneliness, sexual function disability, loss of income and uncertainity about the future and limitations in patients with inactive tuberculosis with special problematic areas, like anxiety and fear related to tuberculosis, dimension of life quality can be affected but this has not been studied as yet.

Because of the points-mentioned above, one of the main objectives of TB treatment is to improve the patient's general state of health. It is important to identify possible factors determining the quality of life of these patients. Some of these have been identified previously[8-11]. In patients with TB the effect of demogrpahic and socio-cultural factors on QOL was evaluated in a number of studies. Furthermore, depression and the number of hours' sleep/day are typical generic features of the chronic disease, and may also influence the quality of life. These factors have not been studied previously.

The aim of this study is to evaluate QOL of out patients with active and inactive tuberculosis, and to study the relations between QOL and demographic, socio-cultural characteristics, and variables related to the disease and depression.

MATERIAL AND METHODS

The study included groups of active and inactive cases who attended Dispensary of Tuberculosis in Kayseri, in a period of one year beginning on September 15, 2003, and a healthy control group.

According to WHO's case defining criteria regarding tuberculosis[13], our cases have been determined as active and inactive. Furthermore, active cases have been re-classified as new and relapse, depending on their history of previous treatment.

The active case-definition criteria were either proven by culture or with an abnormal radiograph and positive tuberculin test.

All of the 256 patients registered in the Kayseri Dispensary for Tuberculosis , in one year, were accepted into the study. Of these, 196 (76.6%) were included in the study according to our exclusion criteria.

According to our exclusion criteria; 60 (23.4%) patients were not eligible for the study for reasons such as being <16 years of age (8.6%), having a communication disability (9.2 %), death (3.1%), refusal (0.4%), existence of probable effects of diseases such as history of auto-immune diseases, malignancy, history of recent trauma or surgery, pregnancy and depression history of pre-tuberculosis (2.1 %).

Inactive TB was diagnosed when there was a history of a previous episode of tuberculosis and/ or associated with a positive reaction to tuberculin skin test, or negative bacteriological study findings.

One hundred and eight inactive cases who attended to the dispensary for a check-up were included in the study, by applying the exclusion criteria.

One hundred and ninety-six people, similar to the patient group in education, marital status, gender, and age who attended the Dispensary to find out whether they had been infected with tuberculosis were chosen as the healthy control group.

As a data collecting device, a questionaire form to know facts of stressors, effect of disease on patient, information related to disease, sleep period; and for personal information of the research group, the Medical Outcomes Study Short Form-36 (SF-36) and Beck Depression Inventory (BDI) were used. The questionaire was filled in through face to face interview.

SF-36 was constructed to survey the health status in the Medical Outcomes Study. The SF-36 was designed for use in clinical practice and research, health policy evaluations, and general population surveys[14]. The reliability and the validity for the Turkish population of the scale was carried out by Pinar[15]. The SF-36 Health Survey contains 36 items

that are scored in eight scales: Physical Functioning (PF), role limitations due to physical health problems (RP), body pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), role limitations due to emotional problems (RE) and mental health (MH). It also includes a single item that provides an indication of perceived change in health. For each scale, a score ranging from 0 (worst measured health) to 100 (best measured health) was calculated[14]. Additionally, scores were calculated for the physical health (PCS) and mental health (MCS) components of health related quality of life. A standardized algorithm was used to calculate the scores for the eight domains, and two dimensions of the SF-36 were transformed to norm-based scores with a mean of 50 and a standard deviation of 10[16,17]. Chonbach's á was computed to assess internal consistency reliability, 0.72 to 0.92 in patient groups and 0.64–0.82 in control groups for all eight domains. The survey was constructed for self-administration by persons 14 years of age and above and for administration by a trained interviewer in person or by telephone[14].

The reliability and validity of BDI were tested for Turkish people by Hisli[18]. In the present study, the value of Cronbach alpha of BDI was found to be 0.91 in active cases, 0.92 in inactive cases and 0.86 in individuals of control group. Each item on the scale is given 0-3 points. The highest point obtainable is 63. The cut off point of the scale is 17. Thus the disribution of the point in depression is as follows: depression at mild level is 11-17 points, depression at moderate level is 18-29 points and severe depression 30-63 points[19,20].

The study was approved by the Ethics Committe of Erciyes University and all patients gave their verbal consent.

Statistical Analysis

The data were analysed using the SPSS statistical package version 11.5 (SPSS Inc, Chicago, IL). Descriptive statistics included percentages, standard deviations, means and median. Chi-square test was used to compare the qualitative variables. Depending on the type of the variables, t, r, and F analyses were performed if it did not apply to normal distribution, the Kruskal-Wallis test and Mann Whitney-U were also employed. (post hoc) Tukey, one of multi-comparative tests, and/or Dunn's test were applied in order to determine which group the difference originated from. Pearson correlation co-efficient was calculated in assessing the relationship between the variables. Multiple linear regression analysis was performed. The minimum acceptable level of significance was set at $p<0.05$.

RESULTS

The demographic-socio-cultural characteristics of individuals forming the research group can be seen in Table 1.

There was no significant difference between active and inactive cases and control group in respect to age ($F=2.235$, $p= 0.108$), gender ($\div^2=3.570$, $p=0.168$), education ($F=1.619$, $p=0.099$) and marital status ($\div^2=2.034$, $p= 0.729$).

It has been proved that 52 (26.5%) of the active cases and 37 (34.3%) of the inactive cases had a disease accompanying TB. The most frequent of these diseases were diabetes mellitus (8.2%), and hypertension (7.7%) and chronic obstructive lung disease (5.1%) in active cases, and hypertension (11.1%), chronic obstructive lung disease (7.4%) and diabetes mellitus (7.4%) in inactive cases.

It was found that 59.2 % of the active cases had been taking treatment for 1-3 months. It was seen that 45.4% of the inactive cases had the disease 1-5 years before and 25.0% 11 or more years previously.

It has been proved that active cases gave responses to their illnesses, such as 75.5% acceptance, 43.4% grief, 28.6% fear, pessimism, anxiety and anger. In our study it was seen that 56.3% of the new cases, 62.5% of the relapses, and 75.0% of those who stopped their treatment for a while and then re-started experienced one or more stressors. It has been seen that the new cases had family problems (34.3%), cases with a relapse had trouble within the family (50.0 %), and those who had stopped their treatment for a while and re-started

had problems at work or in their education (66.7%).

It was also seen that in active cases, the disease had effects on individuals such as changes in the habit of sleep: appetite 57.0%, 40.3% being in denial, 35.2% giving up their habits and effects on the relations of the individual with the environment such as 16.3% having stigmatized, 10.7% being excluded by society, and 5.6% having problems with family relationships.

QOL results according to variables

In all fields of QOL except the BP dimension, the control group scores were significantly higher compared to patient groups ($p<0.05$).

Among the PF and SF dimensions, the inactive cases'scores were higher when compared to active cases ($p<0.001$) (Table 2).

It was found that scores of males were significantly higher than those of females in active cases PF and SF dimensions of SF 36 and in individuals forming the control group in all dimensions, except SF, in inactive cases in PF, BP and RE dimensions ($p<0.05$).

The scores were the highest in unmarried cases and lowest in widowed cases in the active group in all dimensions of SF 36, in inactive cases except RE and in the control group in all dimensions except BP ($p<0.05$).

Table 1: Socio-Demographic Profile of cases included in the study

Variables	GROUPS					
	Active TB Cases		Inactive TB Cases		Control	
	N (196)	% (100.0)	N (108)	% (100.0)	N (196)	% (100.0)
Gender						
Female	82	41.8	37	34.3	89	45.4
Male	114	58.2	71	65.7	107	54.6
Age ($\bar{X}\pm SD$)[a] (min-max)	40.76 ±16.59 (16-71)		41.05±14.75 (16-73)		38.27±11.90 (17-70)	
Marital Status						
Single	43	21.9	21	19.4	41	20.9
Married	138	70.4	82	75.9	145	74.0
Divorced-Widowed	15	7.7	5	4.6	10	5.1
Education						
İlliterate-literate	38	19.4	21	19.5	22	11.3
Primary school	89	45.4	59	54.6	91	46.4
Middle school	20	10.2	7	6.5	30	15.3
High school	38	19.4	16	14.8	41	20.9
University	11	5.6	5	4.6	12	6.1
Monthly income (min-max)[b]	257 USD (73-1.468 USD)		220 USD (73-1.468 USD)		268 USD (73-1.468 USD)	

$\bar{X}\pm SD$: [a] Values are presented as mean ± standard deviation
[b] **Min-max:** minumum-maximum values.
USD – US Doller

Table 2: The scores of Quality Of Life of cases and control groups taken into study

SF 36 Health Status Dimensions		GROUPS			Statistical assessment	
		Active TB (n=196)	Inactive TB (n=108)	Control (n=196)	χ^2	P
Physical Functioning	$\bar{X} \pm SD$	66.70±26.52[a]	75.37±23.52 [b]	86.40±12.90 [c]	63.319	<0.001
	Med.(min-max)	75.0 (0-100)	82.5 (0-100)	90.0 (35-100)		
Physical Role Limitations	$\bar{X} \pm SD$	33.93±40.07[a]	42.59±41.62[a]	65.05±37.00 [b]	56.478	<0.001
	Med.(min-max)	25.0 (0-100)	25.0 (0-100)	75.0 (0-100)		
Pain	$\bar{X} \pm SD$	58.74 ±31.52	57.84±31.42	64.09±24.60	4.273	0.218
	Med.(min-max)	61.0 (0-100)	61.0 (0-100)	62.0 (0-100)		
General Health Perceptions	$\bar{X} \pm SD$	50.45±23.32[a]	47.85±26.21[a]	62.22±19.39 [b]	33.257	<0.001
	Med.(min-max)	52.0 (0-100)	47.0 (0-97)	63.5 (10-97)		
Vitality	$\bar{X} \pm SD$	45.03±25.13[a]	44.07±25.47[a]	54.36±21.01 [b]	19.309	<0.001
	Med.(min-max)	45.0 (0-100)	45.0 (0-100)	55.0 (0-100)		
Social Functioning	$\bar{X} \pm SD$	60.43±28.68[a]	67.36±29.34 [b]	72.64±23.48 [b]	19.075	<0.001
	Med.(min-max)	62.5 (0-100)	75.0 (0-100)	75.0 (0-100)		
Emotional Role Limitations	$\bar{X} \pm SD$	40.65± 39.91[a]	42.21±40.06[a]	53.74±42.06 [b]	10.016	0.007
	Med .(min-max)	33.3 (0-100)	33.3 (0-100)	66.7 (0-100)		
Mental Health	$\bar{X} \pm SD$	55.65±21.17[a]	53.11±22.33 [ab]	58.94±19.53[ac]	6.137	0.046
	Med.(min-max)	56.0 (0-96)	52.0 (8-100)	60.0 (0-100)		
Physical component summary	$\bar{X} \pm SD$	41.79±10.06[a]	43.63±9.89[a]	48.74±6.21 [b]	32.603	<0.001
Mental component summary	$\bar{X} \pm SD$	38.35±10.60[a]	38.43±11.42[a]	42.45±9.98 [b]	8.883	<0.001

$\bar{X} \pm SD$: Values are presented as mean ± standard deviation.
Med.(min-max): median with minumum-maximum values.
χ^2= Kruskal Wallis Chi Square
Similar letters show that the groups are similar and different letters show that the groups are different

Table 3: The relation between the dimensions of SF-36 health status and the characteristics of socio-demographic and those related to the illness and beck depression score in active, inactive and control groups (pearson correlation analysis)

Active Cases	**PF**	**RP**	**BP**	**GH**	**VT**	**SF**	**RE**	**MH**	**PCS**	**MCS**
Age (n=196)	r = -0.405**	r = -0.254**	r =-0.102	r = -0.321**	r = -0.286**	r = -0.248**	r = -0.029	r = -0.161*	r = -0.345**	r = -0.219**
Monthly income (n=181)	r = 0.120	r = 0.084	r =0.111	r = 0.092	r = 0.054	r = 0.067	r = 0.096	r = 0.197**	r = 0.097	r = 0.130
Sleep/day (n=196)	r = 0.148*	r = 0.097	r =0.180*	r = 0.135	r = 0.171*	r = 0.169*	r = 0.082	r = 0.105	r = 0.184**	r = 0.129
Duration of therapy/month (n=196)	r =- 0.080	r = 0.209**	r = 0.111	r = -0.016	r = 0.045	r = 0.137	r = 0.042	r = 0.031	r = 0.035	r = 0.155*
BDI (n=196)	r=-0.536**	r=-0.584**	r=-0.487**	r=-0.654**	r=-0.699**	r=-0.621**	r=-0.531**	r=-0.696**	r=-0.601**	r=-0.764**
Inactive Cases										
Age (n=108)	r = -0.445**	r = -0.340**	r =-0.183	r = -0.217*	r = -0.243*	r = -0.204*	r = -0.063	r = -0.159	r = -0.374**	r = -0.209*
Monthly income (n=97)	r = 0.195*	r = 0.138	r =0.132	r = 0.115	r = 0.242*	r = 0.036	r = 0.038	r = 0.064	r = 0.193	r = 0.097
Sleep/day (n=108)	r = 0.194*	r = 0.143	r =0.146	r = 0.220*	r = 0.216*	r = 0.243*	r = 0.046	r = 0.283**	r = 0.175	r = 0.267**
Duration of illness recover (n=108)	r = 0.050	r = -0.152	r= - 0.117	r =- 0.076	r =- 0.136	r = 0.125	r =- 0.133	r = -0.096	r = 0.011	r = -0.027
BDI (n=108)	r=-0.554**	r=-0.618**	r=-0.602**	r=-0.733**	r=-0.727**	r=-0.662**	r=-0.488**	r=-0.739**	r=-0.676**	r=-0.795**
Control group (n=196)										
Age (n=196)	r = -0.416**	r = -0.131	r =-0.134	r = -0.120	r = -0.104	r = 0.075	r = -0.035	r = -0.063	r = -0.295**	r = -0.013
Monthly income (n=181)	r = 0.089	r = 0.147*	r =0.043	r = 0.093	r = 0.090	r = 0.154*	r = 0.066	r = 0.046	r = 0.119	r = 0.122
Sleep/day (n=196)	r = 0.021	r = 0.125	r =0.011	r = 0.043	r = 0.129*	r = 0.068	r = 0.076	r = 0.143*	r = 0.015	r = 0.165*
BDI (n=196)	r=- 0.164*	r=-0.303**	r=-0.347**	r=-0.412**	r=-0.526**	r=-0.374**	r=-0.430**	r=-0.546**	r=-0.299**	r=-0.563**

***p<0.05 , ** p<0.01**

Physical functioning (PF), role limitations due to physical health problems (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), mental health (MH), Physical component summary (PCS), Mental component summary (MCS), Beck Depression Inventory (BDI)

In addition, there was a parallel increase with education level in the mean scores of PF, SF and PCS in active cases; PF, RP, GH, SF, RE, MH, PCS, and MCS in the control group; PF, BP, PCS, and MCS in inactive cases ($p<0.05$).

In all dimensions of SF 36, the mean scores of the active and inactive cases with accompanying

Table 4: Evaluation of variables that may affect **Physical component summary** and **Mental component summary** in active and inactive cases with multiple linear regression analysis

	B	P
Active group (n=196) Physical component summary		
Beck Depression Inventory	-0.453	<0.001
Marital Status 1.Single 2.Married 3.Divorced/Widowed	-2.745	0.008
Accompaniment diseases 1.Existent 2.Non-existent	5.389	<0.001
Inactive group (n=108) Physical component summary		
Beck Depression Inventory	-0.476	<0.001
Marital Status 1.Single 2.Married 3.Divorced-Widowed	-3.643	0.013
Accompaniment diseases 1.Existent 2.Nonexistent	4.750	0.001
Active group (n=196) Mental component summary		
Beck Depression Inventory	-0.697	<0.001
Duration of therapy	0.402	0.012
Inactive group (n=108) Mental component summary		
Beck Depression Inventory	-0.736	<0.001

The independant variables of multiple linear regression analysis include age, gender, marital status, educational status, family type, sleep/day, having a disease in the past, having an accompanying disease to tuberculosis, duration of treatment, duration of disease and Beck Depression Inventory score. The variables that were significant as a result of the evaluation of multiple linear regression analysis were shown in table 4.

diseases to tuberculosis were lower. A significant difference was found according to the condition of having a disease accompanying tuberculosis among the mean scores of PF, BP, GH, VT, MH, PCS, and MCS in inactive cases; and in PF, RP, GH, VT and PCS in active cases ($p<0.05$).

The average score of BDI in active cases was 17.51±11.54, that of inactive cases was 17.43±12.34, and 9.08±5.39 in the control group. BDI average scores of active and inactive cases were significantly higher than the control group ($F= 43.55$, $p<0.001$). Among the active cases, there was mild depression in 19.4 %, medium in 26.5 % and severe in 18.4 %. In the inactive cases, these values were 25.0 %, 22.2 % and 19.4 %, respectively.

It was found that there was a negative significant relation between the BDI and all dimensions of SF 36 in the active, inactive and control groups ($p<0.05$) (Table 3).

As the patient's age increases there was significant decrease in PF and PCS scores of the control group in all dimensions of QOL in inactive cases except BP, RE and MH and BP and RE dimensions of SF 36 in active cases ($p<0.05$) (Table 3).

As the monthly income increases, there was significant increase in MH dimension scores of active cases, PF and VT of inactive cases and RP and SF of the control group ($p<0.05$).

It was also found that as the duration of daily sleep increased, there was significant increase in the scores of health dimension of PF, BP, VT SF and PCS in active cases; PF, GH, VT, SF, MH, MCS in inactive cases; and VT, MH and MCS in the control group ($p<0.05$) (Table 3).

There was a positive significant relation between the duration of treatment and RP, and MCS in active cases ($p<0.05$) (Table 3).

According to multiple linear regression analysis, as the BDI score increased, MCS and PCS decreased in both active and inactive cases. As the duration of the treatment increased in active cases, MCS increased. In active and inactive cases the marital status and accompanying diseases reduced PCS scores (Table 4).

DISCUSSION

In the present study, it was found that the scores of the control group in all dimensions of SF-36 were higher than those of active and inactive cases with TB. Wang et al[10], Marra et al[11] and Dion et al[12] have reported in their studies that quality of life of patients with tuberculosis is negatively affected in active pulmonary TB, and active TB respectively. The results of our study of the active cases are consistent with the literature. For the first time, the present study showed that in inactive cases, QOL decreased similarly to that in active cases, whereas in inactive cases, QOL scores in dimensions of PF and SF were higher than those of active cases. The fact that the QOL of cases with inactive TB is better in the dimension of PF may have been more physical effects on people because of the symptoms such as cough, loss of appetite, fatigue, weight loss, fever and night sweats of active TB cases[21-24]. However, no symptom was seen in inactive TB. In the studies performed on active cases, Marra et al[11] has shown that tuberculosis disrupts the social functioning and markedly affects situations such as social activities and human relationships. The results of the present study and the isolation active tuberculosis cases experienced during treatment may explain the disruption in social functioning of QOL in active cases.

It was found that as the age of the patients increases, the QOL decreased significantly, consistent with the literature in dimensions of BP and RE of SF-36 in active cases, and in inactive cases all the dimensions except BP, RE and MH, however, in the control group in dimensions of PF and PCS (25) ($p<0.05$).

In their study, Rajeswari and Muniyandi[7] reported that the health recognition of 82 % of new cases who were ≤ 45 years or less was positive. In the present study, in contrast to the literatüre, in inactive cases the decline of QOL in several areas, as well as ageing, may depend on a decrease in

physical abilities appearing with growing older, retrogression in cognitive functions and daily activities, slackness in social relationships, worsening economic situation, and living alone, in addition to social relief systems being inefficient, and other physical problems appearing with old age. Added to these factors is the fact that there is an increase in negative effects of tuberculosis with ageing.

In the present study, it was concluded that the scores of the men were significantly higher than those of the women in the dimensions of PF and SF of SF 36 in active cases, in all dimensions, except SF in control group, and in the dimensions of PF, BP and RE in inactive cases ($p<0.05$). In several studies performed in England, it has been suggested that the negative effects of TB on QOL are greater in women than in men[8]. In their study, Liefooghe et al[26] stated that both male and female tuberculosis patients faced many social and economic problems, and female patients suffered more. However, Duyan et al[9] did not find relationship between age and the QOL of the patients with TB. The fact that QOL scores appeared to be low in the women of both the TB and control groups, in the present study could be explained by social roles and restrictions regarding sex, and could also be related to the physiological structure and hormonal differences of the women.

It was found that the QOL scores are high in unmarried cases but low in widowed cases. The marital status in active and inactive cases decreased the PCS. Being a widow or widower is an important factor that decreased QOL. This condition may also be related to socio-economic difficulties in addition to a negative attitude to the widowed, especially in the culture of developing countries. On the other hand, being a widow or widower through separation due to sickness or being abandoned may also be a determining factor.

The present study showed that the higher the education level, the higher the QOL is. The findings of the present study correlate with those of Duyan et al[9]. The increase in the education level could be related to the increase of self-confidence, a better approach to the negative stance such as sickness and being stigmatized, and possibly a better economic situation or social state, and a better social acceptability level of a person.

Research results indicate that patients of lower income status have a lower perception of QOL. The findings of the present study correlate with Duyan et al[9]. It has been reported that poverty has a great role in spread of the disease, it is impossible to prevent tuberculosis from spreading as long as poverty is not eliminated. For this reason, the quality of life will be wholly affected[27]. We believe that the increase in monthly income is related to the fact that patients feel better and can cope more easily with the difficulties caused by the illness, are able to maintain their high living standards, do not have to work overtime, and thus the individual does not lose his confidence and people do not feel so desperate.

It was determined that active and inactive cases with a disease accompanying TB have lower QOL than those who do not, and that it has a negative effect on PCS scores. In cases with additional physical diseases, the QOL can be affected negatively because of factors such as pain, physical restrictions concerning the sickness, obligation to take more medicine and possible side effects, worsening of self-perception, and expectations of the future.

In active cases, a statistically significant relation was found between the period of treatment and RP dimension ($p<0.05$). In active cases, the longer the period of the treatment is, the more MCS increases. The increase of the treatment period may be related to the decrease of negativity the sickness has caused, the patient's feeling of recovering and the improvement of the patient's perception of QOL.

The increase in the duration of daily sleep may cause an increase in the QOL in active and inactive groups. Sleep problems express themselves in daily living, causing difficulties in cognitive performance (learning, concentration and memory problems) mood swings and emotional distress, poor performance at work and during leisure activites, and in creating a lack of general physical and mental well-being[28,29].In chronic illnesses, the relationship between sleep and the component MH, VT, SF of quality of life is reported as in our study as well[29].

Sleep problem severity and its association with health relation to quality of life reveals a distinct pattern such that dimensions of mental health from anxiety and depression, to VT, RE and SF may be impacted[29]. The disadvantages caused by tuberculosis may effect quality of life by reducing sleep quality and duration in our patient groups.

The average BDI of active and inactive cases was found to be significantly higher than that of the control group. In the literature, inactive cases were not distinguished in the limited number of studies on assessing depression in TB. Generally it is reported that depression occurs as a result of tuberculosis, and it is emphasized that it is the result of isolation caused by being chronically ill and in quarantine or stigmatized, and is especially seen more frequently in older people[6,8,30]. In addition to the fact that TB is a chronic disease, it requires a long period of treatment and some anti-tuberculosis drugs causes depression as side effect, plus the physical insufficiency caused by the illness which may lead to a loss of the productive power, because the stigma and psycho-social difficulties could form circumstances for several psychological disorders such as depression to develop[31].

In the present study, it was found that as the severity of depression increased, the average scores of all dimensions of SF-36 health status decreased significantly in the active, inactive and control groups ($p<0.05$). In the active and inactive cases, as the BDI score increased, MCS and PCS decreased. Depressive disorders impair health-related quality of life[32,33]. In addition, a large number of studies have documented that depression is associated with impairment and disabilities in role functioning[34,35]. In general, in TB cases it has been reported that there are psychological reactions to a wide range varying from relief to fear and from depression to anger[6,7]. As it reduces motivation, decreases the feeling of learning and succeeding, causes a psychological disorder and difficulties in carrying out social roles, depression could affect the QOL of an individual negatively considerably. However, poor QOL is some times seen as a consequence of depression. On the other hand, poor QOL scores may also be precursor to depression[32,33].

The present study suggests that the QOL of inactive TB cases deteriorates in a similar way to active cases, and that demographic–socio-cultural characteristics, depression, the period of daily sleep, the treatment period and accompanying diseases are factors that affect the quality of life.

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Original Article

RELATIONSHIP OF NITRIC OXIDE AND PROTEIN CARBONYL IN TUBERCULOSIS

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Summary

Background: Tuberculosis (TB) is a highly contagious disease caused by *Mycobacterium tuberculosis*. The bacilli replicate within the macrophages and can remain dormant for years; activated macrophages show immunity against these bacilli.

Material and Methods: A prospective study was carried out in newly diagnosed TB patients (n=70) before their anti-tuberculosis treatment and in normal control subjects (n=35). Serum level of nitric oxide was estimated by Moshage method, 1995 and Bories and Bories method, 1995 and protein carbonyl by Levine method, 1990. Pearson's correlation (r) and Fisher's 'z' test was performed on the obtained results.

Results: In our study, serum nitric oxide and protein carbonyl levels were significantly increased ($p<0.001$) in TB patients as compared to normal control group. Positive correlation was seen in pulmonary TB ($r = 0.8892$, $p<0.001$) [Fisher's 'z' transformed = 0.7901 to 0.9430] and extra-pulmonary TB ($r = 0.8330$, $p<0.001$) [Fisher's 'z' transformed = 0.6918 to 0.9128]; 'r' and Fisher's 'Z' was significantly different from zero (two sided $p<0.001$).

Conclusion: The mean serum nitric oxide and protein carbonyl levels were concomitantly increased and positively correlated with each other in patients with pulmonary TB and extra-pulmonary TB. The changes in the level of nitric oxide and protein carbonyl are a reflection of increased defence mechanism and free radical activity in tuberculosis. **[*Indian J Tuberc 2008; 55: 138-144*]**

***Key words*:** Free radical, Nitric oxide, Protein carbonyl, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is a chronic granulomatous disease caused by Koch's bacilli called *Mycobacterium tuberculosis* (M.TB). The lung is the portal entry of M.TB and provides a congenial environment for this slowly replicating pathogen. The infection is established in alveolar macrophages of the distal alveoli[1]. M.TB can exploit complement receptors through multiple mechanisms to bind and enter into macrophages[2]. Local macrophages are activated when bacillary antigens processed by macrophages; stimulate T-cells to release a variety of mediators and proteins. This immune reaction covers not only macrophages and lymphocytes but also pleural mesothelial cells[3]. Nitric oxide ($NO^{\bullet}$) synthesized by inducible nitric oxide synthase (iNOS) in activated macrophages is an important host defence mechanism; mediates "non-specific" immunity. $NO^{\bullet}$ contributes to the inflammatory response; leading to tissue leakage and damage, thereby increasing vascular permeability[4]. Induction of iNOS by cytokines and/or endotoxin during inflammatory infectious processes that produce abundant amount of $NO^{\bullet}$ for extended period in many cells like macrophages, neutrophils, smooth muscle cells, etc. The potential mechanisms by which $NO^{\bullet}$ and other reactive nitrogen intermediates (RNI) affect antimicrobial activity are protean, modification of bacterial proteins and lipids at microbial surfaces, deamination of bacterial DNA and direct interaction with accessory protein targets; resulting in enzymatic inactivation or other protein malfunctions to initiate intracellular mycobacterial killing[5]. Two stable end products of $NO^{\bullet}$ metabolite namely nitrate (NO_3) and nitrite (NO_2) as NOx can be easily detected by photoelectric means[6].

Oxidative changes to proteins due to $NO^{\bullet}$ can lead to diverse functional consequences such as inhibition of enzymatic activities, proteolysis and altered immunogenicity[7]. Activated macrophages

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may release lytic enzymes and RNI. It also secretes cytokines like interleukin 1 (IL-l), tumour necrosis factor (TNF), and gamma interferon (IFN-). Because of the low pH and anoxic environment, M.TB cannot develop in macrophages and persists for extended periods. Protein carbonyl (aldehydes, ketones) serves as a useful marker for assessing oxidative stress *in vivo*. There is now a fair amount of evidence to indicate a role of NO· and RNI in TB[8]. Hence, we planned to estimate serum NO· and protein carbonyl to know their relationship in newly diagnosed cases of pulmonary TB and extra-pulmonary TB.

MATERIAL AND METHODS

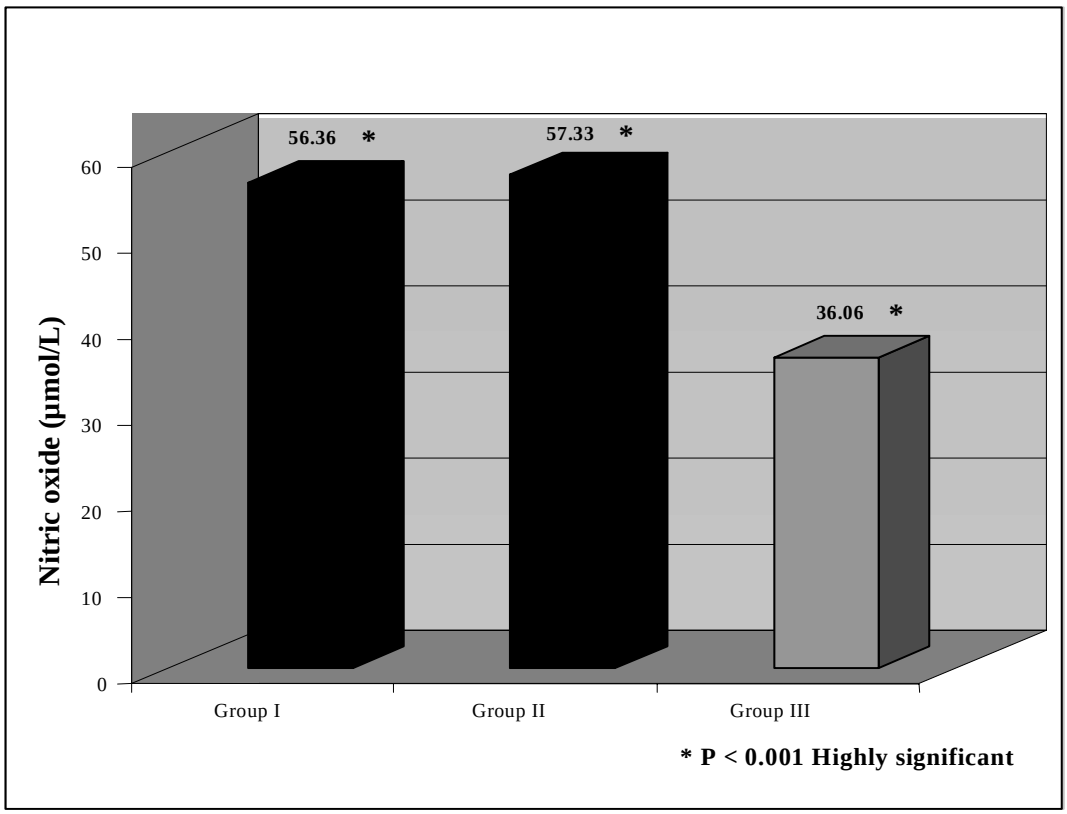
The study was undertaken in 70 newly diagnosed patients with pulmonary TB and extra-pulmonary TB (52 male and 18 female) attending the Out Patient Department and DOT centre at Government Medical College and Hospital, Miraj as well as P.V.P General Hospital, Sangli; selected before anti-tuberculosis treatment. Thirty-five normal subjects were included as controls.

The study was conducted during August 2005 to December 2006, in accordance with the approval and regulations of Medical Ethical Committee of the institute.

The patients with chronic diseases, bronchiectasis pregnancy, human immuno-deficiency virus (HIV) infection, smokers, etc. were excluded from the study. None of the patients had taken corticosteroids within three months before the study.

Patients were divided into two groups on the basis of diagnosis. The subjects were distributed into three groups and in each group 35 subjects were studied.

Group I – Pulmonary tuberculosis (n=35)
Group II – Extra-pulmonary tuberculosis (n=35)
Group III – Normal control subjects (n=35)



Group I- Pulmonary tuberculosis Group II- Extra pulmonary tuberculosis Group III- Controls

Fig. 1: Serum Nitric oxide level in control group and Tuberculosis patients

Group I - Pulmonary tuberculosis Group II - Extra-pulmonary tuberculosis Group III - Controls

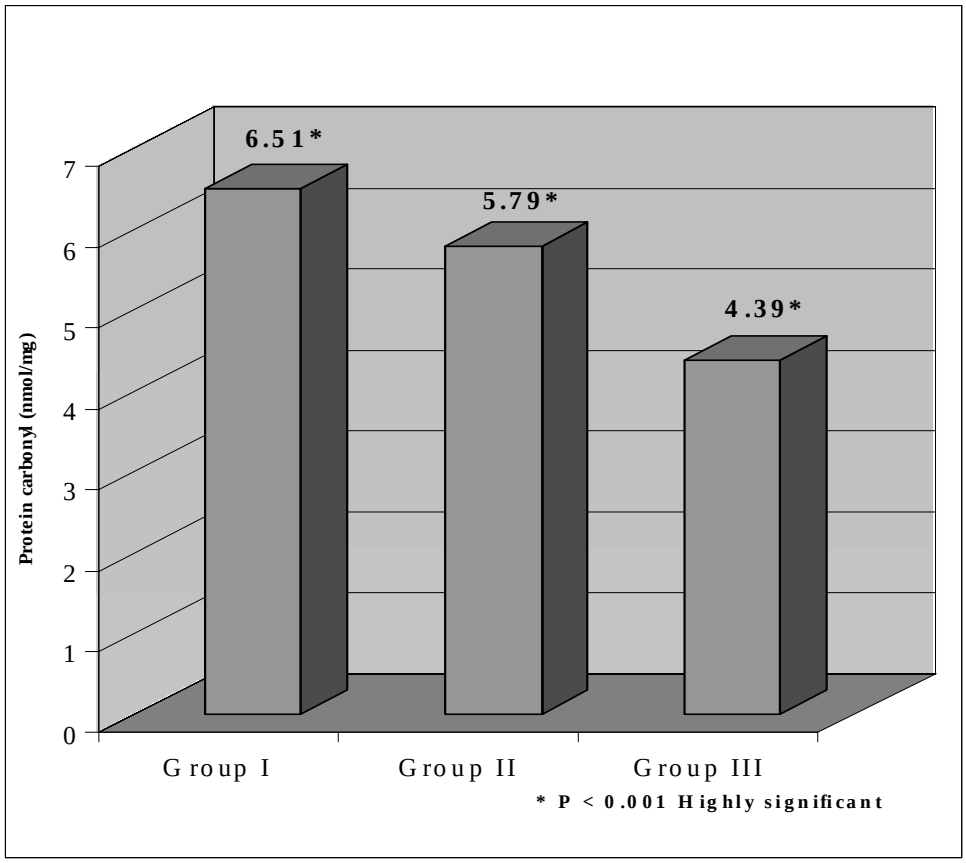
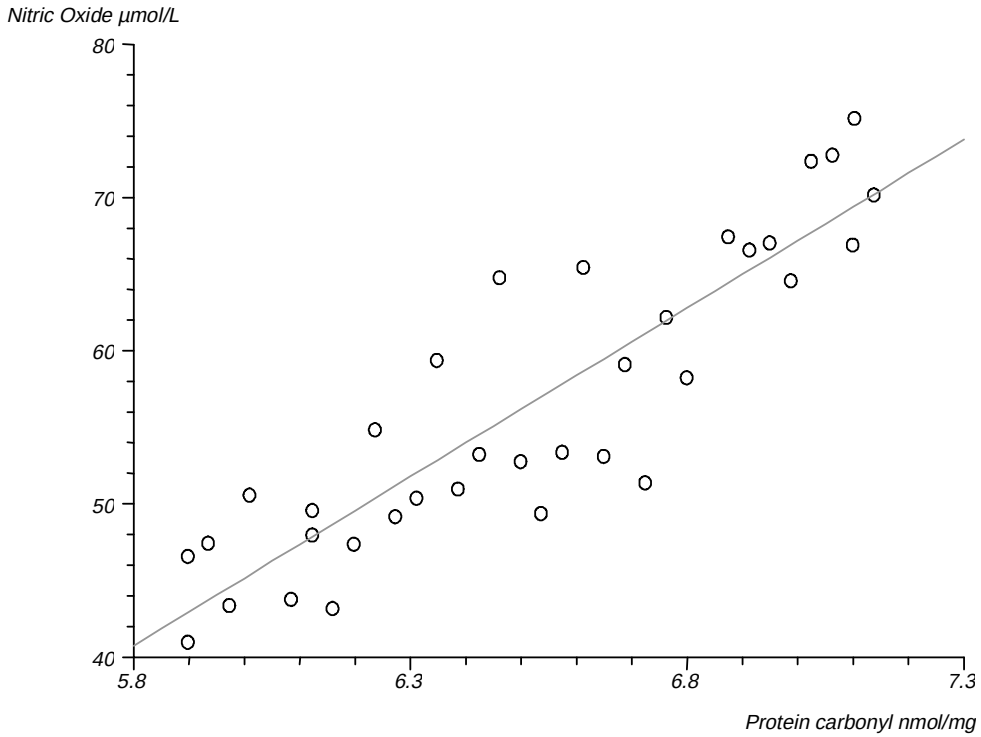


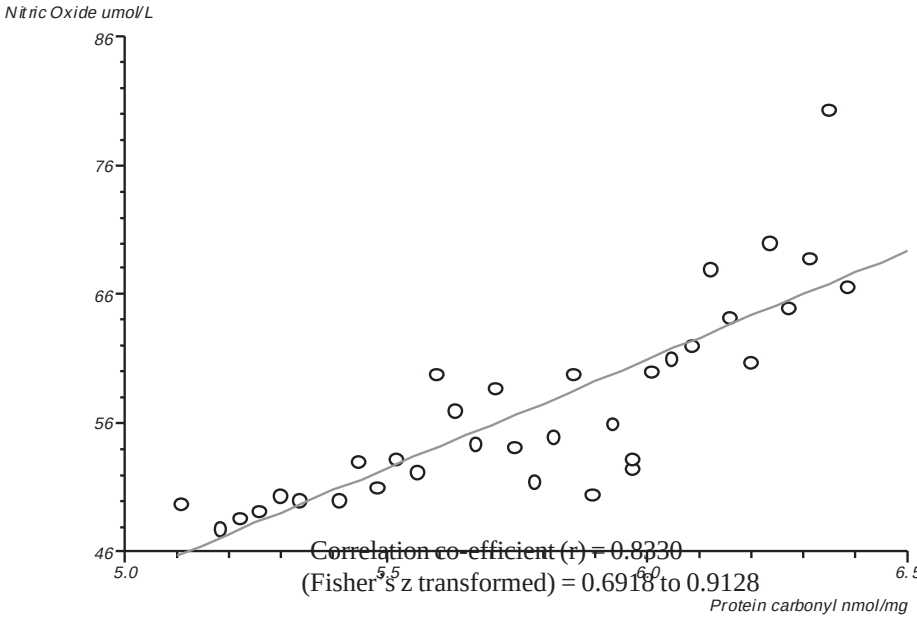
Fig. 2: Serum protein carbonyl level in control group and Tuberculosis patients.

Table: Serum NOx and Protein carbonyl levels in Extra-pulmonary TB patients and normal control group.



Correlation co-efficient (r) = 0.8892 Two sided p< 0.001
(Fisher's z transformed) = 0.7901 to 0.9430

Graph 1: Scatter diagram of serum nitric oxide and protein carbonyl levels in pulmonary tuberculosis.



Correlation co-efficient (r) = 0.8330 Two sided p< 0.001
(Fisher's z transformed) = 0.6918 to 0.9128

Graph 2: Scatter diagram of serum nitric oxide and protein carbonyl levels in extra-pulmonary tuberculosis.

Extra-pulmonary TB cases were sub-divided into pleural TB, Abdominal TB, Lymph node TB, Central Nervous System (CNS) TB, Skeletal TB and Disseminated TB as per the guidelines of American Thoracic Society, 2000.

The age range of patients was 17 to 70 years. The mean age of male subjects was 37.27 ± 10.98 years, while female subjects were 37.38 ± 8.65 years.

Blood sample from all the subjects was collected and non-icteric and non-lipemic serum was selected for analysis. Serum was separated within one hour by centrifugation at 1200 rpm for 5 min. Serum nitrite ($NO_2É$) and nitrate ($NO_3É$) as NOx levels were estimated by Moshage method, 1995[9] and Bories and Bories method, 1995 [10]. The method was standardized by using the known concentrations of NO_2 É and $NO_3É$ in the procedure. Protein carbonyl level was estimated by Levine method, 1990[11]. Statistical analysis of all the data was done by 'Z' test, Pearson's correlation co-efficient and Fisher's 'Z' test. All values are expressed as mean ± standard deviation.

RESULTS

In our study, mean serum NO˙ level in newly diagnosed patients with pulmonary TB (56.36 ± 9.67 µmol/L) and extra-pulmonary TB (57.33 ± 7.50 µmol/L) was significantly increased ($p<0.001$) as compared to normal control group (36.06 ± 1.93 µmol/L) [**Fig. 1]**.

Serum protein carbonyl level in pulmonary TB (6.510 ± 0.39 nmol/mg) and extra-pulmonary TB (5.788 ± 0.369 nmol/mg) was significantly increased ($p<0.001$) as compared to control group (4.390 ± 0.20 nmol/mg) [**Fig. 1]**. On careful observation over mean value of the biochemical parameters, it is seen that there is a concomitant increase in the levels of NO˙ and protein carbonyl in patients with pulmonary and extra-pulmonary TB as compared to control group [**Figs.1 and 2].** NOx level showed minimal higher values in an extra-pulmonary TB than pulmonary TB and control group but the protein carbonyl level showed lower values in an extra-pulmonary TB than pulmonary TB [**Figs.1 and 2].**

Statistical analysis

NO˙ and protein carbonyl levels were calculated by Pearson's correlation and Fisher's 'Z' test, showed positive correlation in pulmonary TB ($r = 0.8892$, $p<0.001$) [Fisher's 'z' transformed = 0.7901 to 0.9430] [**Graph 1**] and extra-pulmonary TB ($r = 0.8330$, $p<0.001$) [Fisher's 'z' transformed = 0.6918 to 0.9128] [**Graph 2**]. Correlation co-efficient (r) and Fisher's 'z' transformed was significantly different from zero and found to be statistically highly significant (two sided $p<0.001$) in patients with pulmonary and extra-pulmonary TB as compared to control group [**Graphs 1 and 2**]. Normal distribution (z) test of NO˙ and protein carbonyl levels showed standard normal deviate (z) = 30.4875.

DISCUSSION

Free radicals are likely to be of equal potential importance as damaging agents in the pathogenesis of TB. NO˙ has been implicated in number of pathologies like circulatory shock, stroke, inflammation etc. M.TB infects and replicates within macrophage; induces cytokines that initiate the inflammatory response in the lungs and can persist for many years in TB[12].

In our study, we have made an attempt to estimate serum NO˙ and protein carbonyl levels in control group and patients with newly diagnosed TB. Serum NO_2 É and NO_3 É as NOx concentration were estimated as a stable end products of NO˙ metabolism. In the present study, serum NOx level was significantly increased ($p< 0.001$) in newly diagnosed patients with pulmonary and extra-pulmonary TB as compared to normal control group [**Fig. 1**]. The potential mechanisms of the tuberculocidal effect of NO˙ are modification of bacterial proteins and lipids; modification of bacterial DNA; direct interaction with accessory protein targets resulting in enzymatic inactivation or other protein malfunctions; and induction of macrophage apoptosis leading to intracellular mycobacterial

killing[13]. Host cells produce NO˙ and inflammatory cytokines to control intracellular replication of M. TB, as part of mycobactericidal and immunoregulatory mechanisms. M.TB infected human macrophage and neutrophils produce NO˙, which converts L-arginine to L-citrulline by iNOS, which is involved in the inhibition of M.TB. Thus, serum concentration of NO˙ metabolites namely NO_2É and NO_3É - NOx may be increasing due to increased NO˙ production.[14]

Serum Protein carbonyl level was significantly increased ($p< 0.001$) in patients with pulmonary and extra-pulmonary TB as compared to normal control group [**Fig. 2**]. NO˙ rapidly reacts with molecular oxygen and superoxide anion to form peroxynitrite, which on further reaction with tyrosine residue from protein forms nitrotyrosine. Peroxynitrite and nitrotyrosine together are called as reactive nitrogen intermediates (RNI). RNI has damaging effects on proteins converting them into protein carbonyls. Peroxynitrite has cytotoxic and genotoxic effect[15]. Introduction of carbonyl group in proteins makes them susceptible to degradation, by proteolytic enzymes leading to deficiency of proteins. The proteins may aggregate together; some proteins may become susceptible to degradation and this modification can cause many pathological conditions. Oxidatively modified proteins are not repaired and must be removed by proteolytic degradation, and a decrease in the efficiency of proteolysis will cause an increase in the cellular content of oxidatively modified proteins, hence shown to increase in the disease process[16].

The mean value of the biochemical parameters showed concomitant increase in the levels of NO˙ and protein carbonyl in patients with pulmonary and extra-pulmonary TB as compared to control group. [**Figs. 1 and 2].** NOx level showed minimal higher values in an extra-pulmonary TB than pulmonary TB and control group, on the contrary protein carbonyl level showed lower values in an extra-pulmonary TB than pulmonary TB [**Figs. 1 and 2].** Out of extra-pulmonary TB cases, higher values were seen in Pleural TB and Dissiminated TB than Skeletal TB, Abdominal TB and CNS TB. Positive correlation between NO˙ and protein carbonyl was seen in extra-pulmonary TB ($r = 0.8330$, $p<0.001$) **[Table No.1], [Graph 2].** In pleural TB, accumulation of large amount of fluid showed increased amount of NO˙ producing cells; reflecting a host defence mechanism as compared to pulmonary TB. Arginase-NO˙ production pathway is involved in the pathogenesis of tuberculous pleural effusion. Reduced arginase activity may cause arginine accumulation, which may then lead to increased NO˙ synthesis by immune and mesothelial cells, reflecting a host defence mechanism[17]. Most patients with disseminated disease also have pulmonary involvement, these include upper lobe infiltrates with or without cavitation, pleural effusion, and pericardial effusion, hence showed elevated levels due to multiorgan involvement[18]. The human tuberculous lungs have increased expression of iNOS and nitrotyrosine in the inflammatory zone of granulomas and in pneumonitis areas. The principal cell in which NOS isoforms and nitrotyrosine were found was the alveolar macrophages and its derivatives, epithelioid macrophages and multinucleated giant cells and they showed abundant expression in pulmonary TB patients. Our results are consistent with the previous studies[19].

On statistical evaluation, correlation between NO˙ and protein carbonyl in pulmonary and extra-pulmonary TB showed positive correlation in pulmonary TB ($r = 0.8892$, $p<0.001$) [Fisher's 'z' transformed = 0.7901 to 0.9430] [**Graph 1**] and extra-pulmonary TB ($r = 0.8330$, $p<0.001$) [Fisher's 'z' transformed = 0.6918 to 0.9128] [**Graph 2**]. Correlation co-efficient was significantly different from zero and found to be statistically highly significant (two sided $p<0.001$) in patients of pulmonary and extra-pulmonary TB. This is clearly indicated that the elevated level of NOx increases the protein oxidation; indeed the protein carbonyl increases hence there is tight relationship between NOx and protein carbonyl seen in TB patients. An oxidative modification of proteins means formation of carbonyls (aldehydes, ketones) on the side chains of amino acids e.g. All (Lys, Arg, Pro, Thr). This modification can cause many patho-physiological conditions in inflammatory diseases like TB. Oxidative modification of enzymes can have either

mild or severe effects on cellular or systemic metabolism, depending on the percentage of molecules that are modified and the chronicity of the modification.[20]

In conclusion, the mean serum nitric oxide and protein carbonyl levels were concomitantly increased and tightly correlated with each other in patients with tuberculosis but the level of nitric oxide in extra-pulmonary TB is higher and protein carbonyl is lower than pulmonary TB. The changes in the levels are a reflection of defence mechanism and increased free radical activity in TB. Alarming signals of TB infection warrant global attention for more extensive research and need rapid outcomes to control the massive rate of infection in the present situation.

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Indian J Tuberc 2008; 55: 145-148

STATUS REPORT ON RNTCP*

The programme in the first quarter of 2008, has once again nearly achieved its twin objectives for new sputum positive case detection and treatment success. At the National level, the annualized new sputum positive (NSP) case detection rate for first quarter 2008 stood at 52 per lakh population (69%) and the cure rate at 84 % for the first quarter 2007 patient cohort. With this, as the programme consolidates its achievements of the previous years, it is progressing satisfactorily on its path towards achieving the Millennium Development Goals.

RNTCP performance in Q1 2008

During the quarter, over 1.7 million pulmonary TB suspects were examined and 0.22 million sputum positive TB cases were diagnosed. A total of 368,969 TB cases were registered for treatment, of which 147,778 were new smear positive pulmonary TB (NSP) cases, 97,909 were new smear negative pulmonary TB (NSN) cases, 53,057 were new extra-pulmonary TB (EPTB) cases, and 69,890 were re-treatment cases. The annualized total case detection rate is 129 per lakh population. Treatment success rate amongst the NSP cases registered in the first quarter 2007 was 86.1%, for NSN cases 90.4%, new EP-TB cases 93.4% and for smear positive re-treatment cases it was 69.3%.

TB-HIV Collaboration

As a follow-up on the results of the periodic HIV survey in TB patients and the CPT pilot conducted in 2007, NACP and RNTCP have revised the "National framework of joint TB/HIV Collaborative activities" in February 2008. Under the revised framework, an 'intensified TB/HIV package of services' has been introduced for states with a higher burden of HIV. The key interventions to be undertaken under the package are: a. Routine offer of VCT to all TB patients; b. Decentralized delivery by RNTCP of CPT for HIV-infected TB patients; c. Referral of all HIV-infected TB patients for ART; and d. Detailed recording and reporting on access to HIV care of HIV-infected TB patients. The package will be initially implemented in nine States, viz. Andhra Pradesh, Goa, Karnataka, Maharashtra, Manipur, Mizoram, Nagaland, Pondicherry and Tamil Nadu.

Recording and Reporting

The RNTCP recording and reporting system was revised during the quarter, and the new revised records and reports are being used across the country. All the states were pro-active in taking up these new revised records and reports, and submitting the first quarter 2008 reports in the new reporting formats.

The RNTCP recording, reporting and data management is done using the Epi-Centre Software. The existing version of Epi-Centre was developed way back in 1999, using Epi-Info and Epi-Map in the DOS environment. With the advancement in popularity and user-friendliness of Windows-based applications and the gradual phasing out of DOS-based software, the need for migrating Epi-Centre into a Windows-based platform had become a necessity for RNTCP. To address this issue a Windows version of Epi-Centre, which had been developed and successfully pilot tested in the states of Chhattisgarh, Gujarat, Rajasthan, Tamil Nadu and West Bengal in 2007, was introduced in the remaining states of the country during this quarter.

Collaboration with NRHM

Appraisal of the respective state Project Implementation Plans (PIP) for the 2008-09, was conducted during this quarter by the National Rural Health Mission division jointly with the disease control programmes, including Central TB Division, NRHM mission directors and state representatives from all 35 states and UTs. Approval for RNTCP

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Table: Performance of RNTCP Case Detection (2007 Fourth quarter), Smear Conversion (2007, Third quarter), and Treatment Outcome (2006, Fourth 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 retreatment 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	218	79	153	149	58	56	75%	38	40	9	94%	88%	90%
Andhra Pradesh	822	153	18362	28754	140	12222	59	79%	8593	2979	3703	93%	86%	88%
Arunachal Pradesh	12	218	260	579	193	189	63	84%	156	86	78	91%	80%	82%
Assam	299	114	5017	8903	119	3781	51	67%	2564	1066	771	90%	85%	86%
Bihar	938	83	10524	19814	84	7594	32	43%	6816	1359	1916	88%	77%	85%
Chandigarh	11	365	439	588	221	204	77	81%	98	164	72	92%	85%	87%
Chhatisgarh	236	118	3277	6888	117	2666	45	56%	2748	757	401	89%	83%	86%
D & N Haveli	3	144	68	103	157	37	56	71%	30	21	7	86%	88%	88%
Daman & Diu	2	388	41	66	140	18	38	48%	16	6	9	88%	76%	94%
Delhi	171	233	6037	12117	284	3403	80	84%	2171	3819	1542	91%	86%	86%
Goa	16	208	291	527	129	171	42	53%	140	122	63	91%	74%	74%
Gujarat	564	163	14948	19419	138	8692	62	77%	2578	2667	3844	92%	87%	87%
Haryana	238	170	5668	8206	138	3032	51	54%	1599	1368	1585	90%	85%	86%
Himachal Pradesh	66	261	2090	3407	208	1261	77	81%	719	666	533	92%	87%	88%
Jammu & Kashmir	124	166	1853	3251	105	1412	46	48%	569	757	385	92%	88%	89%
Jharkhand	300	106	5011	8591	115	3843	51	68%	2775	628	671	89%	83%	88%
Karnataka	574	185	10701	17124	119	6523	45	61%	4050	3111	2372	85%	76%	77%
Kerala	342	208	3806	6301	74	2824	33	66%	1239	1514	534	83%	82%	85%
Lakshadweep	1	103	2	6	35	2	12	15%	1	1	1	100%	100%	100%
Madhya Pradesh	693	107	11298	19570	113	7119	41	51%	6410	2257	2545	88%	82%	85%
Maharashtra	1069	139	19285	35806	134	13299	50	62%	9246	6258	3933	90%	84%	86%
Manipur	26	154	303	1059	161	211	32	43%	425	195	64	87%	84%	85%
Meghalaya	25	142	533	1138	179	359	57	75%	218	273	144	89%	85%	85%
Mizoram	10	214	238	546	223	169	69	92%	140	154	45	93%	92%	93%
Nagaland	22	102	260	591	108	227	42	55%	186	87	56	91%	91%	91%
Orissa	399	132	7140	12496	125	5444	55	64%	3057	2305	1049	88%	82%	87%
Puducherry	11	341	389	327	122	146	54	73%	45	90	36	87%	83%	83%
Punjab	266	166	5636	8640	130	3477	52	55%	1705	1615	1393	90%	82%	85%
Rajasthan	646	143	16773	26441	164	9523	59	74%	7993	2912	4788	92%	87%	89%
Sikkim	6	287	176	375	253	109	73	98%	87	82	48	92%	82%	82%
Tamil Nadu	664	223	12081	22392	135	8735	53	70%	6199	4595	2125	89%	83%	85%
Tripura	35	168	498	710	81	381	43	58%	114	120	76	91%	87%	91%
Uttar Pradesh	1909	142	40094	64521	135	27205	57	60%	18855	6534	9173	91%	84%	86%
Uttarakhand	95	185	2272	3132	132	1266	53	56%	770	411	520	90%	83%	86%
West Bengal	879	161	16902	26428	120	12176	55	74%	5559	4038	2892	90%	85%	86%
Grand Total	**11477**	**149**	**222352**	**368969**	**129**	**147778**	**52**	**69%**	**97909**	**53057**	**47383**	**90%**	**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

activities and budgets to the states was done during the appraisal.

Intermediate Reference Laboratories (IRLs) and Quality Assurance of Sputum Microscopy

During the quarter, the programme has achieved a major landmark with the accreditation of the Intermediate Reference Laboratories in Gujarat and Maharashtra. These laboratories will now provide quality assured culture and DST facilities for the diagnosis and management of MDR-TB patients enrolled under the RNTCP DOTS-Plus activities in the respective states. The 13th meeting of the National Laboratory Committee of RNTCP was held at New Delhi in February 2008. The status of the accreditation process of IRLs and other medical college TB laboratories, which have applied for accreditation, were reviewed in detail by the committee. Another eight IRLs are in the process of accreditation at present. The National Reference Laboratories have undertaken on-site evaluation visits to Assam, Haryana, Karnataka, Kerala, Tamil Nadu and West Bengal in this quarter as a part of the external quality assessment process.

RNTCP's DOTS-Plus activities for the management of MDR-TB cases

The MDR-TB treatment services, which have been initiated under RNTCP DOTS-Plus services in the states of Gujarat and Maharastra, are progressing well and during the quarter, an additional 49 MDR-TB patients have been initiated on treatment. By the end of the quarter, a total of 111 MDR-TB patients were on RNTCP Category IV treatment. The lessons learnt at these sites are being used effectively for the scaling up of the Category IV services to other parts of the country. While the pioneer states of Gujarat and Maharashtra are ready to expand the Category IV services to other districts of their respective states, seven other states, namely Andhra Pradesh, Delhi, Haryana, Kerala, Rajasthan, Tamil Nadu and West Bengal, are in advanced stages of preparation for rolling out of the RNTCP DOTS-Plus Category IV services. This is in line with the RNTCP plan for scaling up DOTS-Plus Category IV services across the whole country by 2009-10. The National level DOTS-Plus training for the states of Andhra Pradesh and Haryana was conducted at Ahmedabad in February 2008, and the two states will commence the management of MDR-TB patients shortly. However, the programme fully considers that the greatest responsibility is to prevent the emergence of MDR-TB through implementation of quality DOTS services.

Advocacy Communication and Social Mobilization activities

The media agency presented the script for the new TV and radio spots, which were suggested to be modified. The work plan for field level activities and public events was discussed and the World TB Day activities were organized in collaboration with the Delhi State Government. Radio publicity and print advertisement was followed by social mobilization activities in different localities of Delhi. World TB Day was observed with varied activities being undertaken across the country. A meeting of the IEC Advisory Group was held in January 2008 to share the work-plan of the media agency, and also to discuss the observations of the World Bank Mission team from December 2007.

Strengthening NGOs and PPs Involvement

A "National Consultation on Revision of the RNTCP NGO/PP Guidelines" was held on 29-31 January 2008 at the Lala Ram Sarup Institute for TB and Respiratory Diseases, Delhi, with the objectives of reviewing the progress in involvement of NGOs and PPs in RNTCP since the formulation of the RNCTP schemes and to share experiences, identification of constraints and suggestions for improvement in the present RNTCP NGO/PP schemes. The Consultation was attended by over 100 participants who included programme managers (for example STOs and DTOs of areas where NGOs/PPs have been active in RNTCP), professional bodies e.g. IMA, and NGO representatives both from NGOs within the programme and outside of RNTCP. Representatives from other Government programmes such as NACP, Malaria Control Programme and Blindness Control Programme, also participated in the deliberations. The suggested

modifications to the existing schemes and introduction of newer schemes, e.g. the purchasing of culture and DST services from laboratories in the non-public sectors, establishing sputum collection centres and schemes for 'urban slums', have been finalized and are presently under consideration for approval by the Ministry of Health and Family Welfare, GoI.

Indian Medical Professional Association Coalition against TB (IMPACT): The IMA has supported the formation of a coalition of professional bodies against TB at the National level , known as IMPACT, which met on the 23rd of March 2008. Participants at the meeting endorsed the ISTC in their personal capacity, and they ensured to obtain the endorsement of the ISTC by their respective associations in the coming months.

The programme is virtually achieving the global targets of treatment success and case detection and this needs to be sustained. However, the default rates, especially amongst Category II smear positive cases, accelerating the pace of rolling out of RNTCP DOTS-Plus services for the management of MDR-TB, and the strengthening of ACSM activities are areas of focus for the programme. The programme managers at all levels are closely monitoring the trends in performance, working towards establishment of IRLs and focusing on developing needs-based ACSM activities, in order to improve the quality of RNTCP services.

Case Report

SCAPHOLUNATE DISSOCIATION: A RARE PRESENTATION OF TB WRIST IN A CASE OF MULTI-FOCAL SKELETAL TUBERCULOSIS

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Summary: Tuberculosis rarely involves wrist joint and is usually diagnosed in arthritic stage. Early presentations are easily confused with traumatic event and commonly missed. We describe a case presenting with scapholunate dissociation initially, which later progressed to full blown arthritis. Similar presentation has never been documented.

[Indian J Tuberc 2008; 55: 149-152]

Key Words: Tuberculosis of wrist, Scapholunate dissociation

INTRODUCTION

TB wrist has an insidious and indolent clinical course[1,2]. It usually presents with local swelling, pain, warmth and numbness of the fingers, with limited systemic inflammatory manifestations in an elderly individual[3]. A patient would rarely present before the disease has progressed to arthritis[4]. The chronic and indolent course and non-specific clinical manifestations of the disease often lead to failure in making a prompt diagnosis[3].

CLINICAL RECORD

A 13-year-old girl, presented to us with pain and deformity in left wrist with a discharging sinus on volar side. She had earlier consulted a primary care physician for pain and swelling of the wrist joint about 14 months ago. Radiographs showed scapholunate dissociation (Fig. 1) and she was given a plaster slab for eight weeks suspecting a traumatic event. She was not relieved of symptoms and presented to us with progressive increase in

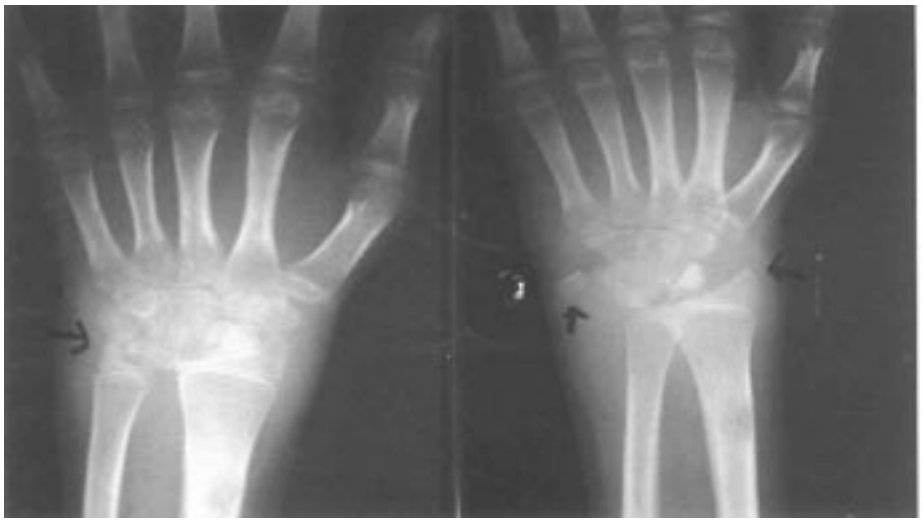

Fig. 1: Initial radiographs showing scapholunate dissociation

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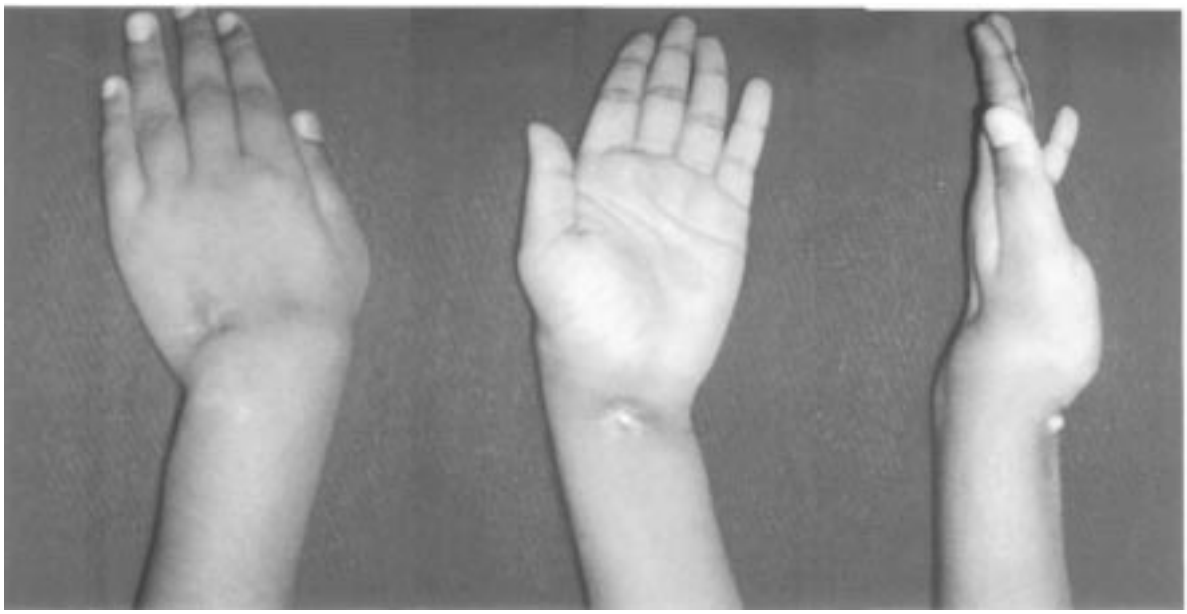

Fig. 2: TB wrist in late arthritis having reverse dinner-fork deformity with a sinus on volar side.

deformity and discharging sinus for the last three months.

Patient was malnourished and had an associated loss of weight and appetite also. On examination, she had reverse dinner fork deformity and a discharging sinus on the volar aspect of the wrist with limitation of all ranges of motion (Fig. 2). Any attempted movement was painful. Axillary lymph nodes were enlarged. She had similar discharging sinuses over dorsum of right foot, anteriorly over right lateral end of clavicle and

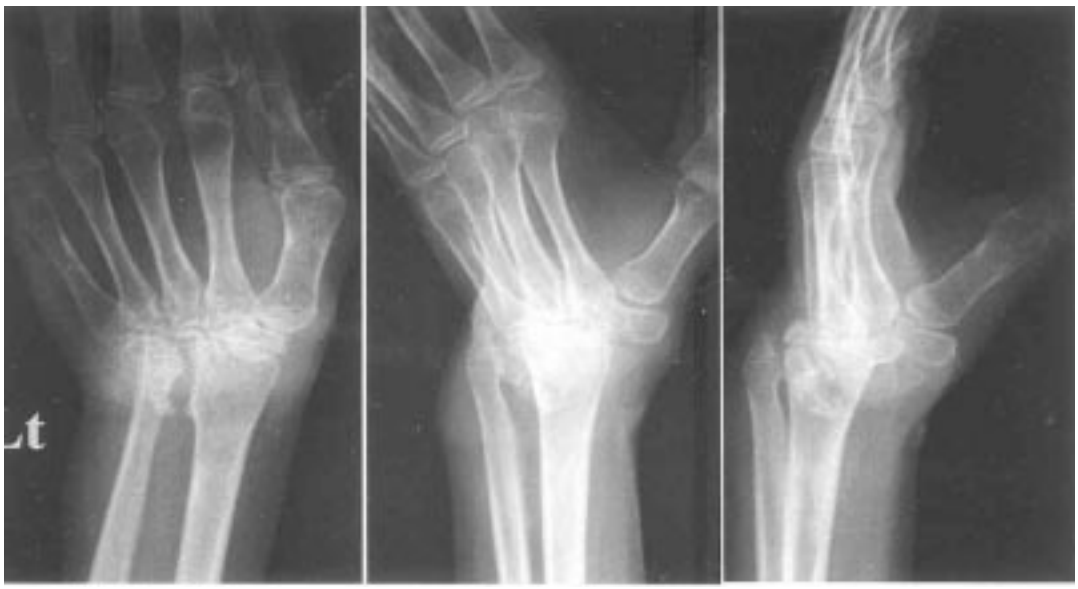

Fig. 3: Radiographs of TB wrist in late arthritis with destruction of carpus and volar translocation

posteriorly over acromion. The radiographs of the wrist showed destruction of distal radius, ulna and all the carpals. None of the carpals could be identified due to totally disorganized joint though these appeared to have translocated volarly (Fig. 3). There were lytic lesions seen also over lateral end of right clavicle, right acromion and another lytic lesion with sequestrum in first metacarpal of right foot. Blood investigations were as follows: Hemoglobin-9.2 gm%, TLC- 6200/mm^3, DLC-P68 L29 E2 M1, ESR-42mm in first hour. Chest X-ray was normal. Biopsy from the ulcer margins showed epithelioid cells with necrotizing granulomas.

A diagnosis of multi-focal skeletal tuberculosis was made. The four drug antitubercular treatment was started (Isoniazid, Rifampicin, Pyrizinamide, Ethambutol). Her general conditions improved. Sequencial ESR showed gradual return to normal level. All discharging sinuses started healing by three weeks and got healed completely in six weeks.

Arthrodesis of the wrist was performed after six weeks using iliac bone graft. Patient continued on drug treatment till 18 months.

DISCUSSION

Tuberculosis of peripheral joints in general, and of the wrist in particular, are uncommon presentations of extra-pulmonary tuberculosis[5]. Wrist osteoarticular TB accounts for, one per cent of all cases of skeletal TB[6]. Besides, the insidious and indolent presentation, the lack of detailed description of TB wrist in literature limits clinicians' understanding and awareness of this disease entity[3]. Both tubercular tenosynovitis and skeletal tuberculosis involving carpals are quite rare. 30–50% of patients initially present with history of undocumented trauma. Early lesions are easily missed radiographically[7]. Diagnosis is rarely established in a patient before the stage of arthritis. An initial X-ray presentation like in our case compounds the difficulty in making a diagnosis.

The common sites of primary osseous focus are the os-capitatum or the distal end of radius. The disease may also start in synovium but very soon gets disseminated to involve the whole carpus[4]. In our case, the disease appears to be synovial type, initially affecting the scapholunate ligament, which later on progressed to involve the whole carpus.

The combination of juxtaarticular osteoporosis, peripherally located osseous erosions, and gradual narrowing of the joint space ("Phemister's triad") is characteristic of tuberculous arthritis.[7] These features are the result of the formation of granulation tissue in an inflammed synovium. This pannus erodes cartilage and bone, leading to demineralization. Tuberculous infection does not produce proteolytic enzymes, and so the joint space tends to be preserved for a considerable time[7]. Demineralization, marginal erosions and slight diminution of joint space are well-described early signs in TB wrist[4], but presentation like scapholunate dissociation has never been documented.

Establishing the diagnosis is difficult in TB wrist. Culture positivity rate is 80% for synovial fluid and 90% for synovial tissue[8]. Biopsy is of particular importance in determining organism sensitivities in areas in which drug resistance is common[9]. Polymerase chain reaction (PCR) for *M. tuberculosis* may increase the diagnostic rate[10].

Anti-tubercular chemotherapy and splintage is treatment of choice, but helpful when diagnosis is established early. Since most patients present late with arthritis and deformity, they usually require wrist arthrodesis as done in the present case.

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Case Report

AN UNUSUAL CASE OF A PLEURAL EFFUSION WITH AN ABDOMINAL MASS

Preetam R Acharya[1], Rameshchandra Sahoo[2] and Poornima Baliga[3]

(Received on 10.12.2007. Accepted after revision on 22.4.2008)

***Summary*:** A 38-year old man presented to us with a left sided pleural effusion. Pleural fluid was aspirated and analysis revealed it to be an exudate with predominant lymphocytes and an elevated ADA level. He was discharged on anti-tuberculous treatment. Patient returned with re-accumulation of pleural fluid. Computed tomography done in our institute picked up not only parenchymal disease in the lung which was not evident on chest radiographs but also picked up an abdominal mass in the left renal fossa. Pathological examination of excised mass revealed its tuberculous nature. The repeated recollection of pleural fluid was attributed to a "paradoxical response"; the patient was reassured and his anti-tuberculous treatment continued. Recognition of the fact that evidence of tuberculosis at distant sites may occasionally be needed to substantiate the diagnosis of tuberculous pleural effusion in a difficult and bacteriologically "negative" case prompted us to report this case. **[*Indian J Tuberc 2008; 55:* 153-156]**

Key words: Tuberculous Pleural Effusion, Paradoxical Response, Incidentaloma

INTRODUCTION

Establishing Tuberculosis as the cause of pleural effusion can be difficult at times. The diagnosis of Tuberculous Pleuritis is commonly made from observation of granulomas in pleural biopsy specimens or a culture positive for *Mycobacterium Tuberculosis* from pleural tissue or pleural fluid. However, the diagnosis can be uncertain or missed in "bacteriologically negative" cases. Proof of co-existing pulmonary tuberculosis or getting evidence of the presence of mycobacterium at other extra-pulmonary sites may indicate dissemination and establish sufficient grounds for institution of anti-tuberculous treatment in an otherwise microbiologically ½ negative½ case.

CASE REPORT

A-38-year old man presented to us with left sided pleuritic chest pain and exertional breathlessness (Medical Research Council Grade I) for last seven days. He also had cough with minimal expectoration for a month. He denied having had haemoptysis, fever, chills or night sweats. On review of systems, the patient reported that he had lost some weight since last one month. He had no past history of respiratory disease and was a non-smoker. Family history for pulmonary tuberculosis was positive in an elder sibling who had completed a course of anti-tuberculous treatment 15 years back.

Respiratory system examination was suggestive of a left sided pleural effusion. Chest radiograph revealed a moderate left sided pleural effusion with contra lateral tracheal shift and no evidence of any parenchymal abnormalities (Fig.1). Routine blood investigations like haemogram, ESR, fasting blood glucose, total bilirubin, transaminases and creatinine were all within normal limits. Human immuno-deficiency virus (HIV) ELISA was negative. Three samples of sputum examined for AFB by Ziehl-Neelsen method were negative. Thoracentesis was done and serosanguinous fluid aspirated. Pleural fluid was an exudate (Protein: 7.1 gm/dl) with a leukocyte count of 4,800 cells/cumm and a lymphocyte differential of 95 %. Pleural fluid examination by Gram stain and ZN stain were negative. AFB culture of the pleural fluid sample did not show any

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mycobacterial colonies at the end of eight weeks of incubation. Cytological examination of pleural fluid was negative for malignant cells. Pleural fluid adenosine deaminase (ADA) levels were elevated (patient value: 122.61 iu/L, normal: up to 36.0 iu/L). A provisional diagnosis of tuberculous pleural effusion was made and the patient discharged on a four drug antituberculous regimen consisting of Isoniazid, Rifampicin, Ethambutol and Pyrazineamide (HERZ).

Over a period of next four weeks, our patient did not show any improvement. A chest radiograph taken at follow-up at this point showed re-accumulation of pleural fluid. A closed pleural biopsy was inconclusive. Pleural fluid carcinoembryonic antigen (CEA) was normal (1.7). Pleural fluid was re-aspirated and a contrast enhanced computed tomography of chest was advised. This revealed calcified nodular opacities in apices of both the lungs. Additionally, a hypo dense

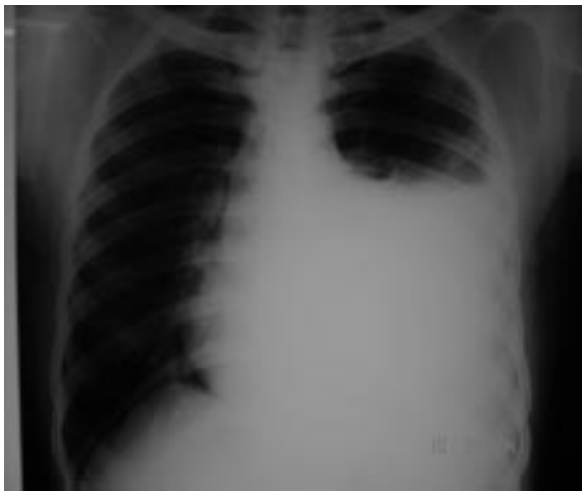

Fig. 1: Chest radiograph showing left sided effusion

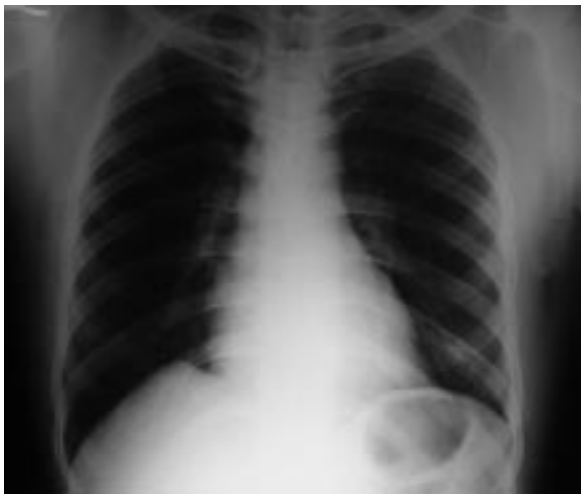

Fig. 3: Chest radiograph at treatment end.

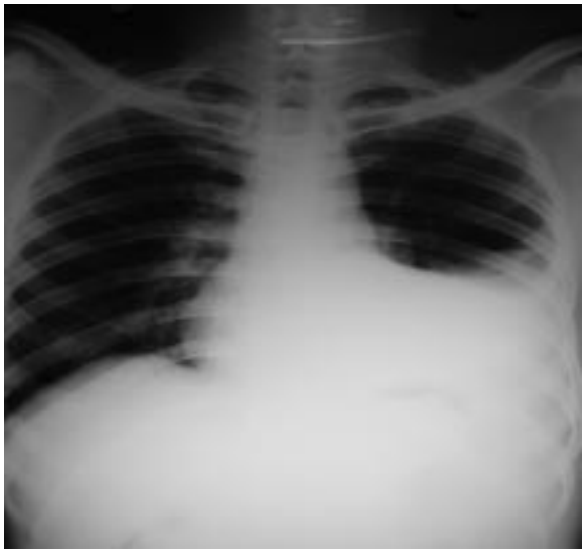

Fig. 2: Follow-up chest radiograph at 12 weeks

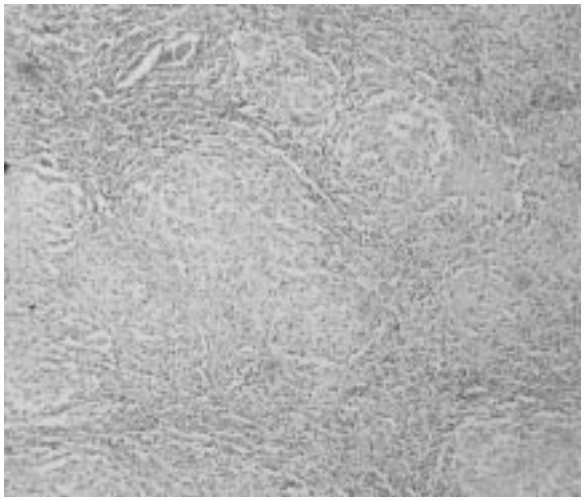

Fig. 4: Image showing granulomas consisting of epitheloid cells and Langhan's giant cells (H & E X10)

enhancing mass lesion with a few areas of hyper intensity was seen to arise from the upper pole of the left kidney. CT guided biopsy and FNAC was done from the mass which showed only necrotic material.

Because of the rapid re-accumulation of pleural fluid despite regular anti-tuberculous treatment, a decision was taken to surgically explore the abdomen and excise the mass to rule out a malignant etiology. Surgical exploration revealed a pale brown mass measuring approximately 8×7×4 cms not involving the kidney. The mass was excised in its entirety. Histopathological examination revealed caseating granulomas consisting of epitheloid cells, Langhan's giant cells and mature lymphocytes suggesting tuberculosis (Fig.4).

The presence of caseating granulomas in the excised mass in addition to the pleural fluid characteristics helped us to substantiate our initial diagnosis of tuberculous pleural effusion. Patient was asked to continue his anti-tuberculous drugs. Follow-up at regular intervals and serial chest radiographs (Fig.2, Fig.3) have not revealed any further re-accumulation of pleural fluid.

DISCUSSION

Pleural effusions can occur in any form of pulmonary tuberculosis. It is a well-known fact that neither the clinical features nor any of the imaging modalities are of much help in the diagnosis of a tuberculous pleural effusion. Co-existing parenchymal disease detected radiographically in about one third of the patients with an effusion serves as a marker of active pulmonary tuberculosis. Computed tomography of chest may show lymphadenopathy, pulmonary infiltrates or cavitation not seen on chest radiographs; which although non-specific, may help to distinguish tuberculous pleurisy from other causes like malignancy[1].

The onus of proving tuberculosis as a cause of pleural effusion rests on microbiological (smear/ culture), and histological analysis of aspirated pleural fluid and biopsied pleural tissue. Mycobacteria are seen in pleural fluid only in 10 - 20 % of cases whereas a culture though positive in 25 - 50 % of the cases takes a minimum of 6-8 weeks by conventional methods to be of any clinical utility. Pleural biopsy will show granulomas in the parietal pleura in 50 – 80 % of patients and if cultured will grow mycobacterium in 55 – 80% of the cases[2]. High levels of pleural fluid ADA (The reported cut-off value for PADA varies from 47 to 60 U/l) may be helpful in distinguishing tuberculous effusions from malignant effusions. Several reports have suggested that an elevated pleural fluid ADA level predicts tuberculous pleuritis with a sensitivity of 90 to 100% and a specificity of 89 to 100%[3]. However, controversy surrounds the use of elevated pleural fluid ADA as a diagnostic aid for tuberculous effusion[4].

Treatment with anti-tuberculous drugs is the mainstay of management of extra pulmonary tuberculosis. The term "paradoxical response" refers to enlargement of old lesions or unexpected appearance of new lesions during anti-tuberculous therapy. Re-crudescence of fever, enlarging adenopathies, worsening of pulmonary infiltrates, pleural effusion, ascites and appearance of intracranial tuberculomas have all been described. An incidence of 16% of paradoxical worsening of tuberculous effusion following the start of anti-tuberculous treatment has been observed[5,6]. Such a paradoxical worsening can occur in both HIV uninfected and infected starting TB therapy. The syndrome poses a diagnostic challenge since the apparent clinical deterioration may raise the suspicion of drug resistant tuberculosis, non- compliance to prescribed regimen or presence of a concomitant disorder unrelated to TB. These patients generally need no alteration in their drug regimen.

An incidentaloma is a tumor (-oma) found by coincidence (- incidental). The widespread use of ultrasound, CT and MRI has resulted in the incidental discovery of asymptomatic adrenal masses. Adrenal incidentaloma is not a single pathological entity and the differential diagnosis includes adenoma, adrenocortical carcinoma, phaeochromocytoma, metastases, Cushing's

syndrome, primary aldosteronism etc.The incidental adrenal masses may also be infiltrative disease, fungal and tuberculous granulomas , hemorrhage and lesions that masquerade as adrenal but arise from adjacent organs (e.g. kidneys, pancreas, gall bladder, spleen, lymph nodes). The adrenal gland is also a common site for metastases from the breast, lung, renal, melanoma, lymphoma[7]. Tuberculosis may affect many of the endocrine glands the commonest being the adrenal gland; acute tuberculosis adrenalitis producing mass-like enlargement of the gland[8]. Ultrasonography and computed tomography do not always differentiate between adrenal and extra-adrenal masses and between malignancy and non-malignancy; surgical excision therefore seems to be desirable in such cases[9].

In our patient, CT thorax was requested for purpose of evaluating lung parenchymal abnormalities. The upper abdominal cuts in the CT helped us to pick up the incidental adrenal mass. Unfortunately, transcutaneous needle biopsy of adrenal mass proved to be inconclusive prompting us to subject the patient to exploratory laparatomy with excision of the mass in its entirety. Histological examination of the excised mass showed features suggesting tuberculosis. **Considering the pleural fluid characteristics i.e. exudate with lymphocytic predominance and a high pleural fluid ADA levels, the diagnosis of tuberculous pleural effusion was substantiated. In retrospect, the increase in effusion size on anti-tuberculous treatment may be attributed to Immune reconstitution syndrome – a syndrome of paradoxical worsening known to occur during treatment with ATT. Our assumption is strengthened by the fact that the patient has completed treatment and has had no recurrence of the effusion on follow-up.**

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Short communication

ANNUAL RISK OF TUBERCULOSIS INFECTION IN CHENNAI CITY

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Summary

Aim: To study the proportion of children infected with *Mycobacterium Tuberculosis* in Chennai city.

Methodology: A cluster sampling methodology was adopted to select an estimated sample size of 7000 children from five corporation zones selected systematically from ten zones of the city. A total of 7098 children aged 1-9 years were subjected to Mantoux and test read; 1897 (27%) from slum area and 5201 (73%) from non-slum area.

Results: The prevalence of infection among children without BCG scar was estimated to be 10.5 % (ARTI of 2.0%) and was similar to that among children irrespective of scar status. The prevalence of infection was higher among children in slum areas (11.1%; ARTI 2.1%) compared to non-slum areas (8.9%; ARTI 1.7%); but the difference was not statistically different.

Conclusion: The tuberculosis situation in Chennai as measured by risk of infection was higher in urban city area than rural areas and comparable to that found in other cities as reported from earlier studies. This information can be used as baseline information for monitoring the epidemiological trends in Chennai city in future. **[*Indian J Tuberc 2008; 55: 157-161*]**

Key Words: Tuberculosis, Annual Risk of Infection.

INTRODUCTION

The first country-wide survey was conducted by the Indian Council of Medical Research during 1955-1958[1] to estimate the prevalence of TB. Based on the findings of this survey, an .estimate of the burden of TB in India of 3.5 million bacillary cases and 14 million smear negative Chest X-ray abnormal cases suggestive of TB was made at the time of introduction of RNTCP in 1997[2]. A repeat survey of TB, similar to this survey, is not operationally convenient and economically feasible mainly due to the heavy expenditure involved in subjecting the persons to chest radiography. As an alternative, tuberculin surveys and the computed Annual Risk of Tuberculosis Infection (ARTI) provide the indirect method of assessing the extent of tuberculosis in the community[3]. These studies usually conducted among children aged 1-9 years are less expensive compared to TB morbidity prevalence surveys and repeated tuberculin surveys measure the trend of the disease and impact of TB control measures. For this reason, a national sample survey[4] on ARTI was conducted during 2000-2003 and it has provided valid information on the prevailing epidemiological situation of TB in different zones of India. It has also provided an overall estimate of ARTI (1.5%) at national level. The proportion infected was found to be higher in urban areas compared to rural children. In the south zone[5], the proportion infected was 8.8% (ARTI of 1.6%) in urban and 4.7% (ARTI: 0.8%) in rural population groups. The urban population selected for the south zone included children from peri-urban area of Chennai city and not aimed at measuring the infection in the city. Moreover, epidemiological information on TB in the city is very limited. So, it was proposed to conduct a tuberculin survey in Chennai city to provide a precise estimate of prevalence of infection and ARTI.

MATERIAL AND METHODS

Assuming the prevalence of infection to be 10% (the prevalence obtained for the urban area in south zone of India[6]), the sample size was estimated

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Table: Estimated prevalence of infection among children

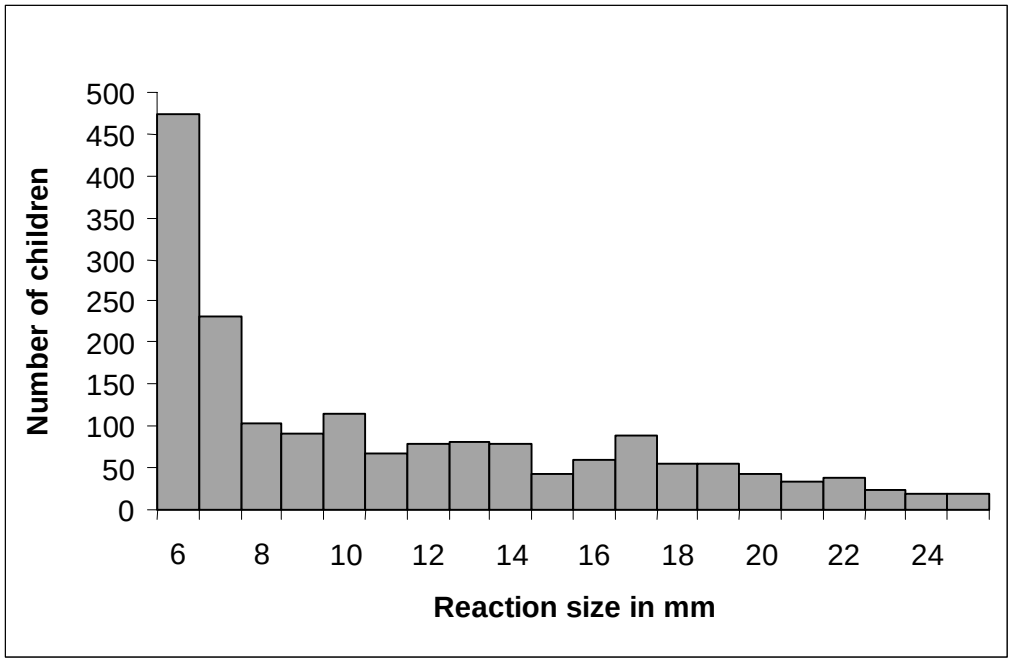

Fig: Distribution of reaction sizes among children aged 1-9 years

to be 900 for a precision of 20% at 5% significance level. Assuming BCG coverage of 70%, test/read coverage of at least 90% and a design effect of two for cluster sampling, the sample size was projected to be 7000 children. A stratified cluster sampling methodology was adopted with proportional allocation to select the sample. First, a systematic random sample of five zones was selected from the ten zones in the city. Next, a 50% random sample of wards was selected and the sample size was distributed among the selected wards proportional to the size of the ward. Subsequently, a random sample of streets was selected from each selected ward in the ratio of slum ('slums' are in any respect unfit for human habitation) to non-slum population (1:3) of the city.

The survey was conducted during the period April-November 2006. A tuberculin testing team consisting of a census taker, tester and supervisory staff visited the zone and sought the co-operation of the zone officials for the study. All children aged 1-9 years in the selected streets were registered after getting the written consent from the parents/guardian of the children. The presence or absence of the BCG scar was ascertained from each child by examining the upper part of the left arm. All children were tested with 1TU of PPD RT 23 with Tween 80 on the volar aspect of the left arm. The reading team, consisting of a reader, secretary to the reader and supervisory staff, visited these children after 72 hrs of testing and read the reaction sizes taking the maximum transverse diameter in mm using a transparent scale. All the information was recorded on individual card for each child, and formed the study meterial. The data generated were scrutinized by keying twice and further corrected for the errors.

The analysis was carried out among three groups, i.e,. those without BCG scar (unvaccinated), those with BCG scar (vaccinated) and those irrespective of BCG scar. The prevalence of infection was estimated using the mirror image technique[7]. The ARTI of children was computed using the formula $1-(1-P)^{1/a}$, where P is the prevalence of infection and 'a' is the mean age of the children. The chi-square test was used to test the difference between the proportions.The 95% Confidence Interval (C.I) was also estimated for each estimate. The statistical significance was set at $p < 0.05$.

RESULTS

Of 7354 children tested, reaction was read in 7098 (96.5%) children. The frequency distribution of reaction sizes of these children is given in figure. The mode at the right hand side is fairly located at 17mm. Using this, the prevalence of infection among unvaccinated, vaccinated children and children irrespective of BCG scar, is estimated to be 10.5% (95% C.I.: 7.4, 13.6), 9.2% (95% C.I.: 7.1, 11.2) and 9.5% (95% C.I.: 7.4, 11.6) respectively. The difference in the proportions of children infected among unvaccinated and vaccinated was not statistically significant. The ARTI computed from the above infection proportions were 2.0 (95% C.I.: 1.4, 2.6), 1.7 (95% C.I.: 1.3, 2.1) and 1.8% (95% C.I.: 1.4, 2.2) respectively. The proportion infected among children in slum being 11.1% (95% C.I.: 7.7, 14.4) was higher than that among children in non-slum 8.9% (95% C.I.: 6.6, 11.1); but the difference was not statistically significant. The corresponding ARTI were 2.1% (95% C.I.: 1.1, 2.8) and 1.7% (95% C.I.: 1.2, 2.1). The infection was significantly higher among children aged 5-9 years compared to children 1-4 years 13.1% (95% C.I.: 10.1, 16.1) vs 4.2% (95% C.I.: 3.1, 5.4); P<0.001. Similarly, proportion infected was more among girls than boys 10.6 (95% C.I.: 8.3, 12.9) and 8.4% (95% C.I.: 6.0, 10.8) and the difference was not statistically significant.

DISCUSSION

The nation-wide tuberculin survey had shown that the ARTI was higher among urban children. In Delhi, the infection was to the extent of 18.7% as reported in the nation-wide survey[4]. In south zone[5], it was 4.7% (95% C.I.: 2.5, 6.8) in rural and 8.8% (95% C.I.: 5.1, 12.4) in urban population.

Narmada et al[8] had reported the tuberculosis situation in Chennai city. In this prospective study in Choolai, Chennai city conducted during April-June

1968, about 4600 unvaccinated children aged one month - 12 years were tuberculin tested with 5 TU of PPD-S. The prevalence and ARTI among children aged below ten years were estimated to be 15.0% and 3.2% respectively. A study[9] conducted in Trivandrum among children aged 10 years showed an ARTI of 0.9%. A study[10] conducted by NTI in Bangalore city estimated an ARTI of 1.8% similar to our findings in Chennai city.

The present study has given a precise estimate of the risk of infection for the first time in Chennai city. ARTI was found to be higher among slum children (2.1%) compared to non-slum children (1.7%). This showed that the tuberculosis situation is higher among children living in congested areas and in poor socio-economic conditions. However, the difference was not statistically significant.

The reason for not getting a clear anti-mode could be due to high non-specific sensitivity prevalent in the city. The BCG coverage to the extent of more than 75% and the fact that the infection estimated by mirror image technique eliminate the cross reaction due to the BCG induced tuberculin sensitivity justified the inclusion of vaccinated children in our analysis. Our present findings of infection among unvaccinated and vaccinated children were similar to the earlier reports [11, 12].

In conclusion, our findings showed that tuberculosis situation was higher in the city than rural areas in terms of prevalence of infection and ARTI The current infection rate could serve as baseline information to study future trends of TB in the city after an intervening period of five years[13].

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ABSTRACTS

Immunophenotypic Characterization of peripheral T Lymphocytes in Pulmonary Tuberculosis

F.M. Al Majid and A.A. Abba. *J Postgrad Med* 2008; **54(1)**: 7-11.

The cellular immune response plays an important role in determining the outcome of infection and disease in *Mycobacterium tuberculosis*. Many studies of these disease inter-actions yield contradictory results. This study aims at determining the changes that take place in the sub-populations of T Lymphocytes in the blood of patients with pulmonary tuberculosis. This cross-sectional study was done at King Khalid University Hospital, Riyadh, Saudi Arabia. Flow cytometry was used to determine the absolute numbers and percentages of T CD3, T CD4, T CD8, T CD19 and natural killer (NK) T cells in 54 patients with active pulmonary TB before the commencement of treatment and in 25 healthy PPD negative volunteers. Statistical Package for Social Sciences (version 11.5) was used for analysis. There were significant differences in the values of CD3, CD4 and NK T cell among the groups. The numbers of CD3 and CD4 cells were lower in subjects than in controls [1091.9 ± 321.4 vs. 1364.6 ± 251.2; $P < 0..001$ and 639.8 ± 285 vs. 822 ± 189.9; $P < 0.004$ respectively] while numbers of NK T cells were much higher in patients than in controls [410.7 ± 286 vs. 182.3 ± 140m $P < 0.001$). The number of CD8 cells were not significantly changed with disease (609 ± 233.5 in subjects and 613.4 ± 170.3 in controls P = 0.761). There are significant changes in the cellular immune response, particularly affecting the CD3, CD4 and NK T cells with the development of pulmonary TB.

Chemokine profile among HIV-l infected individuals

Sandeep Ramalingam, Rajesh Kannangai, O.C. Abraham, Swaminathan Subramanian, Priscilla Rupali, S.A. Pulimood, Mary V. Jesudason and Gopalan Sridharan. *Indian J Med Res* 2008; **127**: 133-139.

Individuals infected with HIV-1 have higher levels of chemokine producing cells compared to uninfected individuals. It is important to know the changes in chemokine levels associated with rate of progression of disease. There is paucity of information on the plasma chemokines in HIV-1 infected individuals from India. We, therefore, carried out this study to estimate the levels of three chemokines namely Macrophage Inflammatory Protein alpha (MIP1á), MIPlâ and Regulated on Activation, Normally T Cells Expressed and Secreted (RANTES), in relation to disease status in HIV-1 infected individuals and compared with uninfected individuals. RANTES and MIP1á were estimated using ELISA in 114 HIV-1 infected and 30 controls, whereas MIPlâ was estimated in 101 HIV infected individuals only and 30 controls. The values were compared to the T cell subsets, HIV-1 viral loads and plasma cytokines (interferon gamma and interleukin-10). Compared to controls the mean MIP1á and RANTES level among the HIV-1 infected individuals was higher while MIPlâ level was lower in HIV infected individuals except CDC C groups. There was a significant positive correlation for MIP1á with HIV-1 viral load and IFNã, for MIP1á with viral load and IL10. There was a significant negative correlation between MIP1á with CD4 count and CD4: CD8 ratio and MIPlâ with CD4 count and CD8 count. There was a negative correlation between RANTES values and CD8 per cent.

Clinical Application of a rapid Lung-orientated Immunoassay in individuals with possible Tuberculosis.

R.A.M. Breen, S.M. Barry, C.J. Smith, R.J. Shorten, J.P. Dilworth, I. Cropley, T.D. McHugh, S.H. Gillespie, G. Janossy and M.C.I. Lipman. *Thorax* 2008; **8(2)**: 113-117.

Immunological ex-vivo assays to diagnose tuberculosis (TB) have great potential but have

largely been blood-based and poorly evaluated in active TB. Lung sampling enables combined microbiological and immunological testing and uses higher frequency antigen- specific responses than in blood. A prospective evaluation was undertaken of a flow cytometric assay measuring the percentage of interferon-ã synthetic CD4+ lymphocytes following stimulation with Purified Protein Derivative of *Mycobacterium tuberculosis* (PPD) in bronchoalveolar lavage fluid from 250 sputum smear-negative individuals with possible TB. A positive assay was defined as >1.5%. Of those who underwent lavage and were diagnosed with active TB, 95% (106/111) had a positive immunoassay (95% CI 89% to 98%). In 139 individuals deemed not to have active TB, 105 (76%) were immunoassay negative (95% CI 68% to 82%). Of the remaining 24% (34 cases) with a positive immunoassay, a substantial proportion had evidence of untreated TB; in two of these active TB was subsequently diagnosed. Assay performance was unaffected by HIV status, disease site or BCG vaccination. In culture-positive pulmonary cases, response to PPD was more sensitive than nucleic acid amplification testing (94% vs 73%). The use of Early Secretory Antigen Target-6 (ESAT-6) responses in 71 subjects was no better than PPD and 19% of those with culture-confirmed TB and a positive PPD immunoassay had no detectable response to ESAT-6. These findings suggest that lung-orientated immunological investigation is a potentially powerful tool in diagnosing individuals with sputum smear-negative active TB, regardless of HIV serostatus.

Performance of Quantiferon-TB testing in a tuberculosis outbreak at a primary school.
P. Molicotti, A. Bua, G. Mela, P. Olmen, R. Delogu, S. Ortu, L.A. Sechi and S. Zanetti. *J Pediatr* 228; **152(4)**: 585-586.

This study compared the effectiveness of the Quntiferon- TB Gold (QFT) assay with the Mantoux tuberculin skin test to detect *Mycobacterium tuberculosis* infection in 29 children during a school outbreak of tuberculosis. Of the children with *M. tuberculosis* infection, 11 had a radiograph suggestive of the infection. The QFT assay was positive in all 21 of the children, and the Mantoux test was negative at first testing in two children (1 of whom was the sentinel case). The findings demonstrate that the QFT test is extremely useful in accurately identifying infected and un-infected children permitting rapid intervention.

Adenosine Deaminase in the diagnosis of Tuberculous Pericardial Effusion.
Am J Med Sci 2008; 335(3): 227-229

Pericarditis is a rare finding seen with tuberculosis, but its prognosis is excellent with treatment, so early diagnosis is crucial. Pathogenesis is particularly important, and it must be taken into consideration when interpreting diagnostic tools. Herein we report a female patient who presented with a one month history of febrile illness, malaise, and weakness; more recently, she had resting dyspnea, which was progressively worsening. A positive PPD and an abnormal chest radiograph prompted hospitalization, where she was found to have pulsus paradoxus of 20 mm Hg. The echocardiogram showed diastolic right chamber collapse along with respiratory variation of the mitral inflow, consistent with pericardial tamponade. Pericardiocentesis was performed with resolution of her resting dyspnea; more than 1000 ml of serous fluid drained from the pericardial space over the following 24 hours. Although sputum and pericardial fluid cultures and smear AFB and other organisms were negative, as well as a negative pericardial fluid PCR for *Mycobacterium tuberculosis* DNA; an elevated (44.4 U/L [normal, 0 to 18]) adenosine deaminase level in the pericardial fluid was consistent with the probable diagnosis of tuberculous pericardial effusion. The patient was treated with resolution of the clinical syndrome and no recurrence of the effusion thereafter. Adenosine deaminase, an enzyme marker of cell-mediated immune response activity to *M tuberculosis* that includes activated T -lymphocytes and macrophages, appears in pericardial fluid. The diagnosis of probable tuberculous effusion can be made without demonstration of mycobacterium.

Predictive value of a whole blood IFN-gamma assay for the development of active tuberculosis disease after recent infection with *Mycobacterium tuberculosis*

R. Diel, R, Loddenkemper, K. Meywald-Walter, S. Niemann and A. Nienhaus. *Am J Respir Crit Care Med* 2008; **177(10):** 1055-57

Numerous studies have been published on the new *Mycobacterium tuberculosis* (MTB)-specific II gamma release assays. However, their prognostic value for progression from latent tuberculosis infection (LTBI) to active TB has yet to be established.. The objective was to compare the Quantiferon-TB Gold In-Tube assay (QFT) with the tuberculin skin test (TST) in recently exposed close contacts of active TB cases with respect to their development of TB disease within two years. Close contacts (n = 601) of MTB-positive source cases underwent both TST and QFT testing and were subsequently observed for 103 (+/-13.5) weeks. Risk factors for *M.* infection were evaluated by multivariate analysis. For the TST, 40% (243/601) of contacts were positive at a 5-mm cut-off, whereas only 66 (11%) were QFT positive. QFT positivity, not TST, was associated with exposure time ($P < 0.0001$). Six contacts progressed to TB disease within the two years follow-up. All were QFT positive and had declined preventive treatment, equating to a progression rate of 14.6% (6/41) among those who were QFT positive. The progression rate for untreated TST-positive subjects was significantly lower ($P < 0.003$), at 2.3% (5 of 219), and one subject who progressed was TST negative. Results suggest that QFT is a more accurate indicator of the presence of LTBI than the TST and provides at least the same sensitivity for detecting those who will progress to active TB. The high rate of progression to active TB of those who are QFT positive (14.6%), which is far greater than the 2.3% found for those who are tuberculin positive, has health and economic implications for enhanced TB control, particularly if this higher progression rate is seen in studies of other at-risk populations.

A nationally representative case-control study of Smoking and Death in India.

P. Jha, B. Jacob, Y. Gajalakshmi, P.C. Gupta, N. Dhingra, R. Kumar, D.N. Sinha, R.P. Dikshit, D.K. Parida, J. Borcham, and R. Peto. *N Engl J Med* 2008; **358(11):** 1137-1147.

In a nationally reppresentative sample of 1.1 million homes, we compared the prevalence of smoking among 33,000 deceased women and 41,000 deceased men (case subjects) with the prevalence of smoking among 35,000 living women and 43,000 living men (unmatched control subjects). Mortality risk ratios comparing smokers with non-smokers were adjusted for age, educational level, and use of alcohol. About 5% of female control subjects and 37% of male control subjects between the ages of 30 and 69 years were smokers. In this age group, smoking was associated with an increased risk of death from any medical cause among both women (risk ratio, 2.99% confidence interval [CI], 1.8 to 2.3) and men (risk ratio, 1.7; 99% CI, 1.6 to 1.8). Daily smoking of even a small amount of tobacco was associated with increased mortality. Excess deaths among smokers, as compared with non-smokers, were chiefly from tuberculosis among both women (risk ratio, 3.0; 99% CI, 2.4 to 3.9) and men (risk ratio, 2.3; 99% CI, 2.1 to 2.6) and from respiratory, vascular, or neoplastic diseases. Smoking was associated with reduction in median survival of eight years for women (99% CI, 5 to 11) and six years for men (99% CI, 5 to 7). If these associations are mainly causal, smoking in persons between the ages of 30 and 69 years is responsible for about one in 20 deaths of women and one in five deaths of men.

Rapid Molecular Screening for Multi-Drug-Resistant Tuberculosis in a high volume public health laboratory.

M. Bernard, H. Alnbert, G. Coetszee, R. O'Brien and M.E. Bosman. *Am J Respir Crit Care Med* 2008; **177(7):** 676-677.

The dual challenges to tuberculosis control of HIV infection and multi-drug resistance are particularly pressing in South Africa. Conventional methods for detecting *Mycobacterium tuberculosis*

drug resistance take weeks to months to produce results. Rapid molecular testing for drug resistance is available but has not been implemented in high-TB-burden settings. The objective was to assess the performance and feasibility of implementation of a commercially available molecular line-probe assay for rapid detection of rifampicin and isoniazid resistance. We performed the assay directly on 536 consecutive smear-positive sputum specimens from patients with increased risk of multi-drug-resistant (MDR) TB in a busy routine diagnostic laboratory in Cape Town, South Africa. Results were compared with conventional liquid culture and drug susceptibility testing on solid medium. Overall, 97% of smear-positive specimens gave interpretable results within one to two days using the molecular assay. Sensitivity, specificity, and positive and negative predictive values were 98.9, 99.4, 97.9 and 99.7%, respectively, for detection of rifampicin resistance; 94.2, 99.7,99.1, and 97.9%, respectively, for detection of isoniazid resistance; and 98.8, 100, 100, and 99.7%, respectively, for detection of multi-drug resistance compared with conventional results. The assay also performed well on specimens that were contaminated on conventional culture and on smear-negative, culture-positive specimens. This molecular assay is a highly accurate screening tool for MDR-TB, which achieves a substantial reduction in diagnostic delay.

Indian J Tuberc 2008; 55: 166-169

FORUM

TUBERCULOSIS AND HEALTH CARE WORKERS*

India accounts for 1/5th of the global burden of tuberculosis. Incidence of tuberculosis in India is 1.8 million and out of which 0.8 million are sputum positive. Since health care workers in our country attend a large number of TB patients and many of them require hospitalization, the risk to health care workers is substantially higher. It is of even greater concern if the patients suffer from drug resistant, MDR/XDR-TB.

Evaluation of risk of TB to health care workers needs consideration of following points:-

Infection and pathogenesis : Tuberculosis is an air-borne infectious disease caused by droplet infection. The risk of an individual becoming infected depends on the exposure to droplet infection and duration of contact with a source case. Usually a prolonged and intimate contact is required for infection[1]. The TB bacilli slender straight or slightly curved rods with rounded ends of the size of 2-4µ x 0.3-0.5µ carried by these droplets reach the alveoli of the healthy uninfected individual, get a foothold, multiply and initiate infection – primary infection. About 95% of the primary infections heal and the person may not develop any symptoms but in 5% cases the patient may suffer from symptoms – primary disease. Bacilli may be carried from lymphnodes via lymphatics to the blood and may result in haematogenous spread and cause early post primary disease; when miliary and meningeal tuberculosis may occur depending upon the number and virulence of the organisms and the body immunity. The bacilli may be carried to different organs; these bacilli in due course become dormant and are responsible for development of extra-pulmonary tuberculosis. The late post primary disease or adult type of disease is either due to endogenous re-activation when the body immunity gets lowered due to any risk factor or it may be due to exogenous re-infection.

Risk Factors

Development of tuberculosis is basically a seed and soil phenomenon and all those infected do not develop the disease as all the seeds put in soil do not develop into plants. For the development of disease, certain risk factors are required which could be constitutional, nutritional, hormonal, socio-economical, environmental, psychological, associated intercurrent infections i.e. measles, whooping cough, typhoid, occupational i.e. silicosis or health-care workers. The likelihood of developing disease is almost 1.5% in first year. Within first five years, cumulative risk is between 5-10% and reminder life time risk is 5%. Thus the total life time risk of developing disease after infection by contact with an infectious case is perhaps 15% i.e. about one in six persons[2].

Endogenous re-activation vs Exogenous re-infection

The development of late post primary disease can either be due to engodenous re-activation or exogenous re-infection. Medlar[3] called attention to these two schools of thought regarding pathogenesis. Stead[4] favoured endogenous route while Canetti[5] by and large favoured concept of exogenous re-infection as a cause for late post-primary disease. It was generally believed earlier that the disease was due to endogenous reactivation and the exogenous re-infection was relatively less important. Lately, however, it has been conclusively proved by molecular and genetic techniques e.g. – PCR, DNA fingerprinting and RFPL that exogenous re-infection

* Part of O.A. Sarma Guest Lecture delivered by Dr. V.K. Dhingra, Director, New Delhi TB Centre, New Delhi, at the 62nd National Conference on Tuberculosis & Chest Diseases held in New Delhi from 14-16 December, 2007.

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Health care workers more prone to infection and disease

The health care workers during the course of patient care have much higher chances of exposure to droplet infections and therefore are more at risk of developing disease. The various categories of health care workers who have a particularly higher exposure and thus at higher risk are; (a) Physicians and bronchoscopists, (b) Residents and medical students, (c) Nurses and nursing students, (d) Ward staff and orderlies, (e) Laboratory technician and laboratory attendants. More the possibility of exposure – higher is the risk. The factors responsible may be : (a) Repeated exposure to sputum positive patient, (b) Delay in establishing diagnosis of tuberculosis (c) Delay in initiation of anti-tuberculosis treatment (d) Non-adherence to treatment regimen (e) Prolonged hospital stay (f) Lack of proper isolation.

Studies to substantiate high risk of disease to health care workers

ARI in health care workers has been estimated at 5%[8] in comparison to 1.5% in general population i.e. extra risk of 3.5% is attributable to nosocomical infection. It has been hypothesized that

in a hospital with 1000 workers, about 500 i.e. 50% will have latent infection and 5% of the uninfected i.e. 25 will be infected each year in Indian scenario[9]. Not only the risk of infection is high, incidence of disease is also higher. This was confirmed by a review of 51 studies published by PLOS medicine in 2007[10]. Indian studies from Chandigarh[11], Vellore[12,13] and Sevagram[14,15] between 2004-2006 also substianted these findings. The incidence of extra-pulmonary tuberculosis is higher among health care workers and is mostly pleural involvement. Gopinath et al also observed that health care workers had a higher chance of developing extra-pulmonary tuberculosis as compared to general population[12].

Risk of infection from drug resistant TB – MDR- TB & XDR TB

In view of rising prevalence of MDR TB and the appearance of virtually untreatable form XDR-TB, health workers are prone to being infected with resistant organisms and may develop drug resistant TB. This is, therefore, of great importance that the health workers be protected against the exogenous re-infection and this requires extreme care. Health care workers are essential in the battle against TB; their health needs to be protected as well[16].

Measures to protect health care workers

Infection control measures include isolation rooms, negative pressure ventilation maintenance wards, HEPA filters, germicidal ultra violet radiation. Global Task Force on XDR-TB has suggested series of measures to control the emergence of XDR-TB[17]. CDC guidelines state that the health care workers entering the isolation rooms must wear a NIOSH (National Institute for Occupational Safety and Health) certified respirator. Most of these measures are very costly. WHO has, therefore, recommended low cost interventions which include early diagnosis and treatment and implementation of DOTS strategy. In addition to pre-employment screening of health care workers, high index of suspicion in those developing suggestive symptoms at work is important to diagnose tuberculosis at an early stage.

Indian scenario

Revised National Tuberculosis Control Programme (RNTCP) has been implemented throughout the country, total coverage under the programme had been accomplished by March 2006 and RNTCP has entered the second phase. RNTCP has reduced the delay in diagnosis and effective DOTS regimens have also reduced the period of infectiousness. The infectiousness of the patient reduces almost to zero level after about two weeks of the effective DOTS regimen.

Treatment of drug resistant TB is still a challenge for the treating physicians and lack of response of treated patients could be to various factors viz. non-availability of the second line drugs (DOTS Plus Strategy), non-affordability by the patient, non-adherence to the regimen, lack of adequate knowledge among private practitioners, prescription of non-standardised inadequate treatment regimen and sub-standard drugs of unproven bioavailability. These patients keep on transmitting infection to healthy general population – thus worsening the TB situation in the country. Infection control measures also have not been given much priority and there are no isolation facilities for TB patients.

Government of India has now made it mandatory that any infection control plan of the facility should include infection control plan for TB and also of TB/HIV coinfection[18]. The plan includes a) administrative control b) environmental control and c) personal control.

Administrative control includes effective RNTCP implementation i.e. early detection, proper sputum collection procedures and starting treatment without delay, avoiding unnecessary hospitalization, training health care workers and having written protocols with standard operating procedures.

Environmental control includes reducing generation and concentration of droplet nucleii in air in high risk areas. Cough hygiene,

proper ventilation, good cross ventilation with big and open windows and doors so as to have a dilution effect and removal of infectious droplet nucleii. Local exhaust ventilation and controlling direction of air flow to prevent contamination of air in adjacent areas, negative pressure ventilation, use of HEPA filters and ultra violet germicidal irradiation are other methods of environmental control. Such measures, though costly, are entirely justified in view of drug resistance threat of MDR and XDR-TB. One such facility is nearing completion at LRS Institute in Delhi.

Personal control: CDC guidelines make it, a must for HCWS to use NIOSH (National Institute of Occupational Safety) certified respirator when entering respiratory isolation wards, which, however, is not possible in India due to its high cost. Common surgical masks are ineffective for preventing infection for HCWs but the wearing of masks by infectious patients and observing cough hygiene by them does lessen the spread of infection. The HCWs need to be educated and trained initially and also at least once in two years during work[20]. They should also be examined at intervals preferably six months to detect the disease at an early stage. Besides HCWS should also be educated not to neglect universal precautions for sterilization while giving injection streptomycin with a view of TB/HIV prevention. It is also necessary to strictly follow the standard Bio-medical Waste Management Rules' 2000 issued by Government of India under the Environment Protection Act of 1986.

To conclude each one of us has to work together with dedication to achieve millennium development goal by 2015. The guidelines to prevent infection and disease among health care workers need to be strictly observed and followed to preserve their health, since health care workers, who are fit and healthy, can only be expected to contribute efficiently and significantly to fight against TB. There is probably also a need to review the policy of admitting tuberculosis patients in wards of general hospitals which lack infection control measures.

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GUIDELINES FOR CONTRIBUTORS

GENERAL

The *Indian Journal of Tuberculosis (IJT)* is published four times in a year; January, April, July and October. It publishes original articles on tuberculosis, respiratory diseases, case reports, review articles, and abstracts of articles published in other medical journals and book reviews. Every issue contains editorial sections on contemporary subjects, radiology forum and a forum for readers to express their opinions on published articles and raise questions on subjects appearing in the journal.

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An informative summary of not more than 250 words should be provided that can be understood without reference to the text (see Ann Intern Med 1990; 113: 69-76). The summary should be as per Vancouver format as follows: Background, Aims, Methods, Results and Conclusions. Unstructured

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The text should be written as lucidly as possible.

Numerals should be spelt out from one to nine (except measurement) and when beginning a sentence.

l. Research and experimental manuscripts should follow the usual conventions, as fo11ows:

Introduction: Setting forth clearly the aim of the study or the main hypothesis, with reference to previous studies and indicating the method used.
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In case reports, the sections on *"Material and Methods"* and *"Results"* are replaced by the section *"Clinical Record',* and all other sections are appropriately shortened.

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