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**Editorial**

## FIFTY YEARS OF CHRONICLING TUBERCULOSIS

The maiden issue of the *Indian Journal of Tuberculosis (IJT)* was published in December 1953, in fulfilment of the long cherished desire of some senior members of the Tuberculosis Association of India (TAI). They had worked hard for several years on bringing out a technical journal of high standard to chronicle the tuberculosis situation, as it evolved with time, and the progress of the anti-tuberculosis movement in the country. The *IJT* was to be an important instrument for educating tuberculosis workers about tuberculosis as well as other allied diseases, and for updating their knowledge of technical advances made and operational successes achieved in the fight against tuberculosis. The issue in your hands marks the golden jubilee of that endeavour.

Dr. P.V. Benjamin, then Tuberculosis Adviser to the Government of India, and Technical Adviser to the TAI, was the first Editor. And Prof. P.K. Sen as well as Dr. T.J. Joseph, Medical Superintendent, Lady Linlithgow Sanatorium, Kasauli (Simla Hills) were the co-editors. The TAI itself had come into existence in February 1939, on account of some highly placed persons in the government, including the vicereine, the Marchioness of Linlithgow, and many more in public life. The Association had been conceived as the national level non-official organisation to become the motor for the fledgling anti-tuberculosis movement in India, considered to have been set motion with the establishment of the Bengal Tuberculosis Association, in 1929. The coming up of affiliated associations in the states and the starting of a large scale public awareness campaign followed thereafter.

The background as well as anticipated contours of the anti-tuberculosis movement in the country were clearly spelled out by Dr. Benjamin[1]. Dr. A. Lankaster had strongly advocated in 1921 the starting of a countrywide anti-tuberculosis movement following the startling findings of his survey in the Calcutta area, and Rogers had already reported the spread of tuberculosis from the cities to rural areas[2]. It was suggested that the movement could be on the lines of the National Association for Prevention of Tuberculosis, established in U.K. in 1908. However, the establishment of TAI and the manner of its funding had been largely by official blessings. The *IJT* recorded that Lady Linlithgow collected in 1937 a fund of over Rs. ten million, which along with the King George V Thanks - giving Fund provided the TAI its corpus. State governments along with voluntary organisations in the country were expected to play different but complementary roles in the fight against tuberculosis[1]. Until then, the many voluntary organisations started with private philanthophy and a few government institutions had been providing sanatorium treatment or TB Clinic care to a limited number of tuberculosis patients on the lines practised in the West because these institutions had been put up by British physicians, or the Christian missioneries or the Indians who had studied abroad. This period, which could be termed as 'catching up with the Western practices' had already started giving way to the study of the local tuberculosis situation and public health approaches for dealing with the very large numbers of tuberculosis patients in need[3]. The pages of the *IJT* during the 1950s are interspersed with an occasional article or two on limited tuberculin surveys in selected population groups, laboratory studies on microscopy and or culture; clinical studies of treatment with Streptomycin and Isoniazid and home treatment as well as Organised Home Treatment, along with a plethora of articles on sanatorium treatment, cavity closure, clinical presentations etc. Like straws in the wind, these few articles presaged the decline in the then prevalent care of individual tuberculosis patients in institutions to the control of the disease in the community, according to local conditions.

The fountainhead of public health approaches to control tuberculosis was the Health Survey and Development Committee (Bhore Committee) Report[4]. To make progress in the new direction, a body of information relating to the various aspects of tuberculosis relevant to the Indian conditions was needed. Thus, the golden era of tuberculosis research in India was ushered in from the 1960s onwards preceded by the landmark National Tuberculosis Survey of 1955-58. The Tuberculosis Research Centre (TRC) in Chennai and the National Tuberculosis Institute (NTI), Bangalore did outstanding research, which changed the entire approach to dealing with tuberculosis not only in India but even worldwide[3]. Several of the studies were published in the *IJT*, and the published studies reflect the changes that were occurring with time even though overly clinical articles, considerably reduced in number, continued to be published.

In the 1960s, the focus of research was on epidemiological surveys[5], case-finding technology[6], and treating rural tuberculosis patients near to their homes[7]. NTI, Bangalore devoted a lot of attention to standardizing the technology of tuberculin survyes[8] and formulating the organised and integrated National Tuberculosis Programme (NIP)[9] which the government adopted for countrywide implementation in 1962. That was a giant step forward compared to the erstwhile approach of caring of a limited number of tuberculosis patients in sanatoria, hospitals and TB Clinics. In a sense, the anti-tuberculosis movement had by then achieved its logical end, although the tuberculosis situation remained unchanged.

The newly organised NTP was bound to throw up problems which continued to receive research attention throughout the 1970s[10-13]. Besides, there was the question of monitoring and assessment of NTP to judge if the programme activities were proceeding on the right lines[14]. Around this time, the problem of collection and consumption of drugs and default in taking regular treatment became an important issue, and received attention from several quarters[15-20]. The NTI, Bangalore also continued with its epidemiological, bacteriological, sociological and operational studies, connected with NTP, throughout the 1970s[21-24].

After two decades of NTP, came up the consideration of its impact on the tuberculosis siutuation. And this remained the main theme of research during the 1980s[25-30]. It was evident by this time that NTP had not performed as per the expectations[34,35]. While some researchers focused on its better performance by fine tuning the case-finding and treatment activities[36,37], others recommended the setting up of a National Task Force, which met at Surajkund in 1992, for reviewing the shortcomings of NTP as well as doing more operational research to remove the lacunae[38-42].

The additional concern introduced by the HIV epidemic, reported in 1986, and its impact on the tuberculosis situation became prominent in the 1990[43-45]. Some workers thought that the training aspect[46-47] and handling of multi-drug resistance[48,49] as well as sero-diagnosis of tuberculosis had not received due attention[50-51].

The multi-direction multi-focus situation prevailing around the mid-1990s was resolved by the publication of an epidemiological perspective presentation by Grzybowski[52] and the adoption of the Revised National Tuberculosis Control Programme(RNTCP) with technical assistance of WHO and financial support of the World Bank[53]. The basis of RNTCP was the erstwhile NTP with empirical modifications introduced to remove the observed lacunae. Therefore, many workers felt that pointed operational research should continue in order to keep scientific information available for use by RNTCP, as it progressed and replaced the NTP[54-60]. The first performance report on RNTCP was quite reassuring[61] but research on technical aspects of the programme continued, with the addition of the genetic dimension[62-64] as well as Annual Risk of Tuberculosis Infection studies so that the impact of RNTCP could be assessed with time[65-70].

For 50 long years, the *IJT* has chronicled the extraordinary Indian contributions in the field of

tuberculosis research. From that early period of 'catching up with the Western practices' to a leadership role in tuberculosis control strategy is certainly remarkable, especially for a developing country. With a countrywide tuberculosis programme in place, there is no more need for the *IJT* to keep a watch over the anti-tuberculosis movement. But, tuberculosis is not yet vanquished, probably because of inadequate implementation, and the *IJT* has still a lot of chronicling to do, hopefully not for too long.

**D.R. NAGPAUL**

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# ASSOCIATION BETWEEN SMOKING AND TUBERCULOSIS

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## INTRODUCTION

Smoking is prevalent worldwide. In USA, 20% of adults are smokers and a majority of them start smoking before the age of 21. The USA exports 194 billion cigarettes yearly, mainly to the developing world, where the level of smoking habit is largely unrecorded. However, the annual rise in the number of smokers is estimated to be 2.1%[1].

The problem of tuberculosis is now universal, after the epidemic of AIDS. Nearly one third of world's population is infected with *Mycobacterium tuberculosis* (MTB) and 3 million people die due to tuberculosis every year[2]. In 1993, WHO declared tuberculosis (TB) as a global emergency. India is included in the list of high TB burden countries. It is estimated that between the years 2000 and 2020, nearly one billion people will be newly infected, 200 million people will get sick and 35 million will die from TB world wide, if control of the disease is not further strenghthened[3].

Smoking and tuberculosis primarily affect the lungs as both enter the lung through the inhalation route. Although smoking has no etiological role in TB, yet higher prevalence of TB has been observed in smokers[4-8]. Alcohol intake may act as a contributing factor as most chronic alcoholics are smokers too[9]. It has been observed that prevalence of TB increases with increasing number of cigarettes smoked, after adjustment for age, sex, type of work, history of contact and how spacious is housing[1,10]. So much so that in young adults, cigarette smoking has become a risk factor for development of active disease in family contacts of pulmonary tuberculosis cases (PTB), with a close relationship to the number of cigarettes smoked daily[5].

## CLINICAL PROFILE

In a study of 485 patients with PTB, 87.7% were males and 12.2% females, the proportion of smokers was more than that in the general population[6]. In another study, among tuberculosis patients of both sexes aged more than 30 years, as compared with the same age and sex sufferers from other diseases, there were more high to moderate smokers and fewer light to non-smokers among the tuberculous[7].

Shprykov et al[11] found, in 297 patients, strong relationships between smoking, disease, clinical course and treatment results. In smokers, the disease was of a more severe and disseminated type with more pulmonary tissue destruction and bacterial discharge. The healing process in smokers progressed more slowly, often requiring a hospital stay. Sputum conversion was also delayed, and cavities got closed in fewer patients. Various drugs like cocaine, marijuana, heroin etc. are also smoked, with or without tobacco. A group of 89 persons with tuberculosis was identified in California who either resided in or visited two houses frequented by persons for smoking cocaine[12]. In them, thirteen persons (15%) including 11 children were diagnosed with active pulmonary TB.

## PASSIVE SMOKING

Among children, exposure to tobacco smoke has been found to be associated with an increased risk of pulmonary tuberculosis. Contacts, 0-4 and 5-9 years old, showed a significantly higher risk of developing TB than those aged > 10 years. There was even a dose-response relationship between the risk of developing active PTB immediately following

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infection and the number of cigarettes smoked by the household adults[13]. In illicit drug smoking "Shot gunning" of drugs refers to the practice of a drug smoker exhaling the smoke into another individual's mouth. This has been found to have the potential of transmission of respiratory pathogens, including TB, to others passively[14].

## SMOKING AND AIRWAYS

Airways of smokers are often compromised. Smoke induced oxidative cellular damage along with inflammation leads to recruitment of inflammatory mediators from serum, resulting in damage to the respiratory passages. Alveoli and airways secretions are increased through goblet cell metaplasia. Peribronchial fibrosis leads to air flow obstruction causing irreversible anatomical changes in the lungs. There can be heterogenic response due to varied host response to tobacco (drug) smoke. Lung defence mechanism is further affected by impairment of mucociliary clearance of MTB and other potential pathogens[15].

## MOLECULAR BIOLOGY

It has been seen that leucocyte count in peripheral blood goes up in smokers. The chemotactic, microbicidal and secretory functions of leucocytes appear to be normal but monocytes may partially lack the ability to kill an intracellular organism. Total number of T-lymphocytes also goes up but there is variability in their further subdivisions. In light to moderate smokers, an increase in $OKT3^+$ (Total T-cells) and in $OKT4^+$ (T-helper cells) is seen, whereas in heavy smokers there is a fall in $OKT4^+$ count but increase in $OKT8^+$(T-suppression cells)[16]. Antigen-specific cell-mediated immunity(CMI) is compromised in newly diagnosed cases of PTB. Any further burden may accelerate progression of the disease[17].

## PATHOGENESIS

Pulmonary tuberculosis is more prevalent in populations living in a congested close environment where on account of population density the chances of transmission of MTB are high[18,19]. Smoking worsens the environment. Similarly, smokers usually suffer from chronic bronchitis with constant coughing which leads to increased chances of droplet infection[4]. Besides smoke itself may act as carrier[20]. Tuberculosis patients who smoked were more often sputum smear positive for AFB compared to non-smoker tuberculosis patients[21], probably because smoking acted as an expectorant and produced better sputum specimens[4].

In the pathogenesis of extra-pulmonary tuberculosis too, smoking has been shown to be a likely risk factor: More than 50% of the extra-pulmonary tuberculosis patients in a study were smokers[22]- tuberculous pleural effusion (29%), genitourinary cases (22%) and lymphadenopathy (20.5%). In another study, all the patients with laryngeal tuberculosis were smokers, with most common involvement of unilateral vocal cord, and 29% were without any pulmonary involvement[23]. These observations call for a deeper study of the association between smoking and PTB.

## SOCIAL ASPECTS

People generally believe that smoking precipitates the break down to tuberculosis[24-25]. Among various community groups, mortality from pulmonary tuberculsosis has been shown to increase significantly with the number of cigarettes smoked, among doctors[26] as well as US veterans[27]. In sanitation workers who smoked, the relative risk for tuberculosis was 2.17, independent of age, sex contact history, place or type of work[28]. In rural areas of Kishtwar (Jammu and Kashmir), the prevalence of tuberculosis was attributed to excessive smoking (both active and passive) along with other factors[29]. However, among elderly Chinese no association was found between tuberculosis prevalence and smoking[30].

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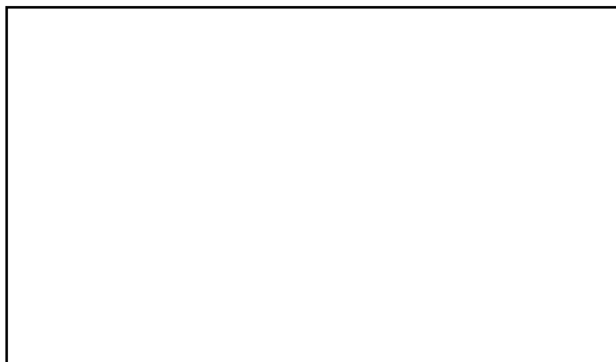
## LEAVES FROM HISTORY - 14

## THE FIRST ANTI-TB ASSOCIATION IN INDIA



The era that celebrated the cliched saying ‘What Bengal thinks today, India thinks tomorrow’ also saw the dawn of the Anti-TB movement in India in Bengal. As early as June 1929, the Bengal Tuberculosis Association, with headquarters in Calcutta, was formed marking the dawn of organised anti-tuberculosis movement in the country. The sagacity of its founding fathers can be appreciated better if it is recalled that the first organisation of its kind in the world was established in 1908, in U.K., under the patronage of King Edward VII.

The *raison d’etre* of starting such an organisation in Calcutta, then, was to provide some care to the large numbers dying from tuberculosis, especially in the congested ‘bustees’. Later, a 40 bed sanatorium, first ever in Bengal, was established in Jadavpur, in 1930, but only the rich could afford treatment there. It was believed in those days that tuberculosis was largely a social problem with a relatively small medical aspect. So, social work in patients’ homes was adopted as the approach to provide them relief. Tuberculosis workers of the Association visited and guided the poor wage earners on how to rest while they worked, how meagre resources could be used for better food and nutrients and the other do’s and dont’s of TB.

Taking a cue from Sir Robert Philip’s Tuberculosis Dispensary in Edinburgh (1887) and Ramakrishna Mission Free Dispensary in Delhi (1933), the Central Dispensary in Calcutta soon got the social workers trained as Tuberculosis Health Visitors (THV) at the Medical College, Calcutta to work under medical doctors who offered honorary services. The THVs helped to disinfect the affected houses and isolated patients from healthy family members, spread awareness about the disease and also brought the household contacts to the Central Dispensary for examination and advice. Thus, awareness among the people, advice to patients and examination of contacts became the hallmark of Anti-TB movement, as launched in Bengal.

So popular did the socially oriented approach become that similar dispensaries were established in Howrah,Hooghly, Jalpaiguri, Pabna, Mymensingh and Noakhali (now in Bangladesh). Among the pioneers who guided and steered the Anti-TB movement in Bengal were Mrs. Florence Becker - the first General Secretary of the Association - and Dr. (Mrs.) Mary Remfry, from England, Dr. A.C. Ukil, Dr.C.A. Bentley, Dr. E. Muir, Dr. D.N. Mitra, Dr. B.C. Ghosh and Dr.(Mrs.) Edith Ghosh, Dr. B.C. Roy and Dr. T.N. Majumdar.

It was on the advice of the Bengal Tuberculosis Association that tuberculosis was first made a notifiable disease by the Government in 1936.

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# FEMALE GENITAL TUBERCULOSIS - NEED FOR MORE RESEARCH

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## INTRODUCTION

Genital tuberculosis (TB) in females is found in 0.75 to 1% of gynaecological admissions in India[1] with considerable variation from place to place.[2] The disease is responsible for 5% of all female pelvic infections and occurs in 10% cases of pulmonary tuberculosis[3]. Although most of the affected belong to reproductive age-group, the disease has been reported in postmenopausal females as well.[1,4]

Lately, an increase in the trend of the disease has been reported[5] which may be partly due to increase in the population with overall rise in tuberculosis cases. The other contributory factor may be HIV infection with increased incidence of pulmonary and extra-pulmonary forms of tuberculosis including the drug resistant forms[6]. A rare case of vaginal tuberculosis in an HIV seropositive female had been earlier reported by the author[7]. The immunocompromised state due to HIV infection causes reactivation of endogenous tuberculosis infection to development of tuberculosis disease. In the case of vaginal tuberculosis, the changed vaginal pH may also play a part in the causation of disease[7].

Genital TB occurs mostly secondary to pulmonary tuberculosis, commonly by the haematogenous route in a manner similar to spread to other extra-pulmonary sites like urinary tract, bones and joints etc. The fallopian tubes are affected in almost 100% of the cases followed by the endometrium in 50%, ovaries in 20%, cervix in 5% and vagina and vulva in <1%.[3,7] However, a few reports have found endometrium to be the most commonly involved site.[1,5] Direct inoculation of tubercle bacilli can also take place over vulva or vagina during sexual intercourse with a partner suffering from tuberculous lesions of genitalia.

## CLINICAL PROFILE

Clinical symptoms and of their development can be variable. Whereas infertility (in 60% of cases), pelvic pain and menstrual disorders like scanty menstruation and amenorrhoea are the usual presentation, some patients may be asymptomatic[3]. Dysfunction of menstruation is largely attributed to endometrial caseation[8], infertility is considered due to pathology in endometrium and fallopian tubes and a blockage of ovum transport[8,9]. The anti-gonadotrophic effect of *Mycobacterium tuberculosis* may be responsible for menstrual irregularities that take place in cases of active pulmonary tuberculosis having no demonstrable lesions in genital tract[9].

The diagnosis of the disease is difficult. Apart from varied clinical presentation, a past history of tuberculosis or a history of contact may not be forthcoming and an evidence of tuberculous lesion elsewhere may be lacking. The abdomenal and vaginal examinations may be normal. A high erythrocyte sedimentation rate and a positive Mantoux test are non-specific. The chest skiagram is normal in most cases. A pelvic ultrasound and hystero-salpingography examinations may be of some help. Histopathological evidence in biopsy of premenstrual endometrial tissue or demonstration of tubercle bacilli in culture of menstrual blood or endometrial currettings only can provide the certain diagnosis of disease[1]. Laparoscopy should be done carefully to

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avoid injury to an adherent bowel loop. A laparotomy, of course, shows the presence of tubercles and can provide adequate histological and bacteriological evidence. Certain conditions like tubo-ovarian mass (T-O mass) of gonococcal / pyogenic origin, pelvic endometriosis, small ovarian cyst and old pelvic haematocoele may closely mimic a T-O mass[3]. Therefore, all the available diagnostic techniques should be combined judiciously and correlated with the clinical profile prior to instituting the anti-tuberculosis treatment (ATT).

**WHY MORE RESEARCH?**

In view of the probems of making a definitive diagnosis of genital TB in females,many physicians tend to adopt the therapetietest for elimination of any type of TB including the genital type by prompt execution of ATT for the requisited period of time. But, a prescription error or poor compliance can delay the response to treatment leading to failure, thereby resulting in continued morbidity despite the fact that good quality ATT is available under RNTCP and the results are quite encouraging[10].

However, Rifampicin has been known to induce menstrual disturbances in a few cases which got normalised on further continuation of their anti-tuberculosis therapy[11]. Rifampicin induced increased enzymatic catabolism of oestrogens is believed to affect the leutinizing hormone surge resulting in anovulatory cycles and causing minimal peeling of the functionalis layer in proliferative endometrium, which manifests in the form of oligomenorrhoea or amenorrhoea. Reversal of these disturbances is thought to take place due to the transitory nature of the effect or lowered threshold for the pituitary stimulus. Case reports have mentioned amenorrhoea and infertility to be frequently present following ATT[1,12]. Persistence of these symptoms may occur as a result of the disease process or due to healing caused by the chemotherapy[1]. Continuing search is needed for finding simpler and practicable methods for making definitive diagnosis in respect of female genital TB and the use of therapeutic test should be avoided.

Prompt ATT and appropriate surgical intervention has improved the results in terms of cure from disease, restoration of female reproductive function and reduction of procedural and post-operative complications. The chances of pregnancy in females suffering from genital TB have so far been poor (5%) even after the completion of treatment[3]. But, results have been reported in difficult cases managed timely with combined medical treatment and a surgical intervention[5,13]. In vitro fertilization has also provided a ray of hope to the desperate infertile women in recent times [14]. Further research may help further improve the fertility rate after cure of genital TB.

It may be mentioned that research is considerably hampered due to a non-availability of clear criteria for monitoring the treatment efficacy, unlike in pulmonary TB[1]. Therefore, more research is needed, so that delivery of therapy can become more certain and therapeutic effects get better defined in terms of the normalisation of the pathologic process and the desirable reproductive function.

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**53rd TB Seal Campaign**

His Excellency Dr. A.P.J. Abdul Kalam, the President of India and Patron of the Tuberculosis Association of India inaugurated the 53rd TB Seal Campaign on 2nd October, 2002 at Rashtrapati Bhawan, New Delhi. TB seals depicting paintings of two parrots and two lotus flowers were presented to the President of India by Hon'ble Shri Shatrughan Sinha, Minister of Health and Family Welfare, Government of India. Shri S.K. Naik, Health Secretary, Ministry of Health and Family Welfare, presented the special souvenir while Dr. S.P. Agarwal, Chairman, Tuberculosis Association of India and Director General of Health Services presented a film on TB and a flip chart to the Hon'ble Rashtrapatiji.

**57th National Conference on Tuberculosis and Chest Diseases**

The 57th National Conference on Tuberculosis and Chest Diseases was held in Panaji (Goa) from 26th to 29th September, 2002 under the joint auspices of the Tuberculosis Association of India and the Anti-TB Association of Goa. In all, 49 scientific papers were presented, in addition to 3 orations, a panel discussion and a guest lecture.

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# TUBERCULOSIS AND PREGNANCY

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## INTRODUCTION

Tuberculosis (TB) and pregnancy are two different types of stresses experienced by women. Their simultaneous presence affects them both physically and mentally. To the concerned physicians, genital tuberculosis presents a diagnostic challenge and management of the underlying disease in a pregnant woman requires great care. Management of such cases in the context of the Revised National Tuberculosis Programme and the adoption of the Directly Observed Treatment-Short Course (DOTS) needs a strategy.

## Magnitude of problem in India

India accounts for 30% of the burden of all TB cases in the world[1]. More than 80% of the patients are in the economically productive age-group of 15 – 54 years.[2] The disease is responsible for killing more women of reproductive age than all the combined causes of maternal mortality[3] and gives rise to nearly one-third of the female infertility in the country[4]. Exact data in respect of the proportion of pregnant women harbouring TB are unavailable in the Indian context because of the variance in the observed maternal outcomes in pregnancies complicated by TB. However, an increased obstetric morbidity has been reported in such women[5]. The weight gain as well as the height of uterus vs the period of gestation in tuberculous pregnant women has been found to be significantly less in comparison with healthy pregnant women[6]. An adverse pregnancy outcome was also observed in 20% cases (abortion in 6, premature delivery in 2 and intra-uterine death in 2 cases). Studies have also suggested no unusual increase in pre-term labour or other adverse pregnancy outcomes in treated cases of TB[7,8].

## How Does TB Effect Pregnancy?

The effects of TB on pregnancy depend upon various factors such as type, site and extent of the disease, stage of pregnancy when management gets instituted, nutritional status of mother, presence of concomitant disease, immune status and co-existence of HIV infection, availability of facilities for early diagnosis and treatment, and so on. The pulmonary and extra-pulmonary forms of TB effect pregnant women in the same way as the non-pregnant ones. A study of 27 pregnancies with culture positive TB detected abnormal radiographs in all the patients[9]. If anti-tuberculosis treatment (ATT) is started early in pregnancy, the outcome is same as that in non-pregnant patients, whereas late diagnosis and care is associated with 4-fold increase in obstetric morbidity and 9-fold increase in pre-term labour[5]. Poor nutritional states, hypo-proteinaemia, anaemia and associated medical conditions add to maternal morbidity and mortality. Co-existing HIV infection is known to augment progression of TB and worsens the immuno-suppression. The two most common opportunistic diseases encountered in HIV-related lung complications during pregnancy are infection with *Pneumocystis carinii* and *Mycobacterium tuberculosis*.[10] Besides, the availability of appropriate diagnostic/therapeutic facilities and/or affordability of their use tend to result in poor management and outcome of pregnancy. The stage of pregnancy at which ATT is begun is the factor of paramount importance that chiefly determines the maternal outcomes in pregnancies associated with TB.

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**How Does Pregnancy Effect TB?**

The belief that the raised diaphragm due to pregnancy helped collapse of pulmonary cavities situated mostly in the lower lung regions, just as artificial pneumo-peritoneum does, was held until 19th century[11]. By early 20th century, induced abortion became the recommendation for pregnant tuberculous women[12].

Now, TB is believed to get flared up by the stress of pregnancy, especially in association with a poor nutritional status, immuno-deficient state, or co-existent diseases. The loss of protective antibodies in mother during lactation too favours the development of post-partal TB. However, more studies are needed to substantiate the hypothesis.

**How Does Maternal TB Affect Foetus and Neonate?**

A foetus can get TB infection either by haematogenous spread through umbilical vein to foetal liver or by ingestion or aspiration of infected amniotic fluid.[13] True congenital TB is believed to be rare. The risk to neonate of getting TB infection shortly after the birth is greater[14]. Cantwell et al criteria for confirming foetal/neonatal TB comprise demonstration of either primary hepatic complex/ caseating hepatic granulomas or per cutaneous liver biopsy at birth or presence of maternal genital tract/ placenta TB or the presence of lesions during first week of life by excluding postnatal transmission by a thorough investigation of all the contacts (including the attendants).[15] A neonate having congenital TB may present with respiratory distress, fever, poor feeding, lethargy, irritability, abdominal distention, lymphadenopathy and hepato-splenomegaly. A failure to obtain favourable response with broad spectrum antibiotics along with negative results for other congenital infections should lead to the suspicion of congenital TB. An abnormal chest radiograph is found in all such cases, half of whom have a miliary pattern.[16] The overall mortality for congenital TB is 38% in the untreated and 22% in the treated[15].

An Indian study found a 2-fold increased occurrence of pre-maturity, smaller than expected size and low-birth weight babies in women treated with ATT for 6-9 months during pregnancy[17]. However, late pre-natal diagnosis of disease, late institution of ATT, incomplete / irregular adherence to therapy, advanced lung lesions and maternal nutrition due to poverty, ignorance, etc. contribute to poor foetal health.

**Diagnosis of TB in Pregnancy**

*Diagnosis under programme conditions*

For diagnosis of TB in pregnancy, programme workers have to keep in mind similarities of symptoms between TB and pregnancy like tachycardia, anaemia, raised ESR and low serum albumin level, as well as dissimilar parameters (like increase in weight during pregnancy and decrease due to TB, hypertension in the former and hypotension in the latter etc.) which may confuse the clinical presentation.

Under RNTCP, sputum examination done as per an algorithim is the preferred method for diagnosis of pulmonary TB[18]. A chest skiagram (performed after shielding the abdomen) is done if all the 3 sputum smears are negative and symptoms persist despite giving antibiotics for 1-2 weeks. The presence of suggestive radiographic abnormalities and a medical officer's decision to treat with ATT labels the patient as a 'smear-negative' TB case. A pregnant woman with extra-pulmonary TB has constitutional and organ-affection symptoms. Routine haematology and Mantoux test ( not commonly advocated in programme) along with investigations specific for the site are carried out for the establishment of specific diagnosis. Co-existence of HIV infection should specially lead to a thorough search for any extra-pulmonary tuberculous focus. A mediastinal or retro-peritoneal adenopathy, pleural effusion or parenchymal infiltrate may be detected in chest skiagram in late course of disease, whereas cavitary lesions could exist in early HIV co-infection.

*Management*

ATT should be started promptly as untreated disease presents a hazard to the mother and foetus.

The same regimens are recommended for use in pregnancy as for the non-pregnant state except for witholding of Streptomycin. Doubts about the use of Pyrazinamide in pregnancy have since been set as rest. Currently, an intermittent regimen (thrice weekly on alternate days) under the DOTS strategy of RNTCP is being increasingly used world-wide for the pregnant women having TB[19].

A retrospective analysis of 12,367 TB patients put on DOTS had 16 pregnant women suffering from the either pulmonary or extra-pulmonary form of disease; 25% of them had become pregnant while receiving ATT. All the 16 were able to complete their treatment. The overall drug tolerance was good and no adverse pregnancy outcome took place[20].

A question-mark exists on the safety of second line drugs in the pregnant state. Therefore, expectant mothers with MDR-TB should be advised to terminate the pregnancy. If a woman insists on its continuation, the possible consequences of the same should be discussed with her in detail. The management of pregnant tuberculous women becomes complicated in the presence of HIV infection due to the involved drug interactions. Hence, the regimens and drug dosages need appropriate adjustments.

Supportive measures during ATT administration include :

a) An intake of Pyridoxine with Isoniazid during the entire period of therapy to prevent peripheral neuropathy (as being practised under the RNTCP).
b) Prophylactic vitamin K administration to baby at birth for preventing haemorrhagic disease of the newborn.
c) Segregation of the mother from neonate if she has active and infectious disease (especially MDR-TB) and is either not likely to receive ATT due to maternal non-compliance or has received it only for less than 2 weeks prior to delivery.
d) Substitution of either protease inhibitors with another class of anti-retroviral drugs or Rifampicin with Rifabutin in case of their co-administration.
e) Cautious addition of drugs in case multiple therapies need to be given during the co-existence of various diseases.
f) Examination of the contacts of the pregnant woman's household.
g) Necessary procedural interventions like pleural, pericardial or ascitic tapping, intercostal chest drainage tube etc.

**Effects of Chemotherapy on Mother and Foetus**

*Maternal effects*

Isoniazid may cause cutaneous hypersensitivity, hepatitis, peripheral neuropathy. The risk of INH-induced hepatitis may be 2.5 times higher in pre-natal patients than the general population[7], although largely unconfirmed[21]. Rifampicin may cause nausea, vomiting and hepatitis. Retrobulbar neuritis occurs in <1% of cases on a daily dose of 15 mg /kg of Ethambutol[22]. Pyrazinamide may produce gastrointestinal upsets, arthralgia, hyperuricemia and hepatitis. Streptomycin may commonly cause vertigo in mother apart from ototoxicity and nephrotoxicity, related to speak serum concentration and total dose of administered drug. Pregnant tuberculous women generally tolerate primary chemotherapy well. If second line drug therapy becomes necessary during pregnancy, gastrointestinal disturbances may be observed with Ethionamide or PAS; nephrotoxicity with Kanamycin; and psychoses, suicidal tendencies or increase in number of seizures following usage of Cycloserine.Pregnancy has been known to result if there was a simultaneous administration of Rifampicin and oral contraceptives. Rifampicin also accelerates the metabolism of protease inhibitors resulting in sub-therapeutic serum levels, whereas the latter increases the serum levels of Rifampicin and enhances the likelihood of drug toxicity[22]. The

ototoxicity and nephrotoxicity of Streptomycin (or aminoglycosides) may get enhanced when used in conjunction with other ototoxic or nephrotoxic drugs.

*Foetal effects*

First line drugs barring Streptomycin are safe. Congenital deafness has been reported in infants with the use of Streptomycin and Kanamycin during pregnancy and various birth defects with the use of Ethionamide and PAS[22].

*Effects on Breast feeding*

Use of Isoniazid, Rifampicin, Ethambutol, Pyrazinamide, Streptomycin, Kanamycin and Cycloserine has been considered safe for breast feeding, but safety of PAS is unproven[22]. The effect of these drugs gets minimized, if the mother breast feeds before taking the drugs and substitutes the next feed with formula preparation. Under RNTCP, breast-feeding of neonates is recommended regardless of the mother's TB status[18].

*Care of neonates*

Neonates born to mothers having infectious TB should be given chemoprophylaxis with INH for 3 months or till the mother becomes non-infectious. BCG vaccination may be postponed or done with INH-resistant BCG vaccine. After 3 months, if mother has a negative sputum smear and the neonate (with a normal chest skiagram) has a negative Mantoux test, then INH chemoprophylaxis may be discontinued. In case, the Mantoux test is positive, a thorough search should be made for locating the presence of pulmonary or extra-pulmonary focus and administration of ATT may be decided accordingly.

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# A COMPARATIVE EVALUATION OF FACTORS AND REASONS FOR DEFAULTING IN TUBERCULOSIS TREATMENT IN THE STATES OF WEST BENGAL, JHARKHAND AND ARUNACHAL PRADESH

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***Summary*:** A comparative evaluation was undertaken to determine the influence of organizational set-up and other factors on the defaulting behaviour of tuberculosis patients. The defaulting pattern was analysed in four centres, one of which was a private hospital (TMH, Jamshedpur), one an NGO (ADMH, Jamshedpur in Jharkhand) and the other two were government institutions (DTC, Purulia, West Bengal and TB Centre, Roing, Arunachal Pradesh).In all, 1258 patients on short course chemotherapy were enrolled. Defaulters were identified by record review and interviewed either at home or in the clinic.

Defaulter rate was least in TMH followed by ADMH and DTC, Purulia in that order and maximum in TB Centre, Roing. Age distribution of the defaulters was similar in ADMH and DTC, the percentage significantly increasing with age, the maximum being in 45-59 years and declining thereafter. In TMH and TB Centre, the percentage of defaulters continued to remain high even in the older age groups. The percentage of defaulters decreased uniformly with increasing income in the DTC and TB Centre with a peak in the middle income group in ADMH and all high income group defaulters in TMH. For all, the proportion of defaulters decreased uniformly with increasing educational status. The time of defaulting was similar in all institutions, starting at the third month, increasing upto the fourth month and declining subsequently. Among the various reasons for defaulting, the important ones were distance from treatment centre, indifference due to improvement in symptoms and lack of motivation.

***Key Words*:** Tuberculosis defaulters, Factors influencing defaulting

## INTRODUCTION

Tuberculosis remains a major public health priority in the world with 8-10 million new cases added every year[1]. In India, 14 million people are affected and 2.2 million cases are added every year[2]. Defaulting in tuberculosis treatment is one of the major barriers to its control[3]. The objective of the present analysis was to determine the factors that influence defaulting behavior and to identify the reasons for defaulting and irregular treatment.

## MATERIAL AND METHODS

Tuberculosis patients attending four different kinds of health institutions were observed. The selected institutions were Ardeshir Dalal Memorial Tuberculosis Hospital (ADMH), Jamshedpur, Bihar run by a non-governmental organisation, Tata Main Hospital (TMH), Jamshedpur, Bihar, a private hospital, District Tuberculosis Centre (DTC), Purulia, West Bengal, and Tuberculosis Centre, Roing, Arunachal Pradesh, being governmental institutions. The total number of patients studied was 1258, ADMH accounting for 215, TMH 102, DTC 802 and TB Centre, Roing 139 patients.

Four different kinds of centres were chosen purposely to observe if the organisational set up of an institution was also a determinant for defaulting

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behaviour. All the patients were receiving short course chemotherapy as outpatients except in TMH where patients were hospitalized. The defaulters were identified by record review and were then interviewed at home or in the clinic. Data were collected using a pre-designed proforma.

The study being multicentric took into consideration the variations prevailing in three states of India, namely Jharkhand, West Bengal and Arunchal Pradesh.

**FINDINGS**

The average default rate in 4 institutions was 27.19 percent. The institutional rates were : ADMH, Jamshedpur 20.00 percent, TMH, Jamshedpur10.78 percent, DTC, Purulia 29.30 percent and TB Centre, Roing (AP) 38.13 percent. The rates were higher in the two government institutions, highest being in TB Centre, Roing and lowest in the private hospital at Jamshedpur.

The age distribution of defaulters was similar in ADMH and DTC, Purulia (Table 1), their percentage significantly increased ($p<0.05$) with age upto a maximum of 45.5 percent (ADMH) and 36 percent (DTC) in the 45-59 years of age and declined thereafter. For TMH and TB Centre, Roing, the percentage of defaulters continued to remain high even in the older age groups.

Table 2 shows the educational status of defaulters. For all the centres the proportion of defaulters decreased uniformly with increasing educational status, the difference being significant ($p<0.05$). With increasing family monthly income, the percentage of defaulters decreased uniformly in the DTC and TB Centre, Roing ($p<0.01$) compared

**Table 1.** Age distribution of defaulters according to treating institutions

| Age (in years) | ADMH n=215 | TMH n=102 | DTC n=802 | TB Centre n=139 |
|---|---|---|---|---|
| <24 | 6.0 | 0.0 | 12.0 | 21.9 |
| 25 – 34 | 13.5 | 19.0 | 24.5 | 9.3 |
| 35 – 44 | 29.0 | 27.0 | 24.5 | 15.6 |
| 45 – 59 | 45.5 | 27.0 | 36.0 | 21.9 |
| >60 | 6.0 | 27.0 | 3.0 | 31.3 |
| All ages | 100.0 | 100.0 | 100.0 | 100.0 |
| | 20.0 | 10.78 | 29.30 | 38.13 |

Figures in percentages

**Table 2.** Distribution of defaulters in percentage according to educational status and kind of treating institution

| Education | ADMH n=215 | TMH n=102 | DTC n=802 | TB Centre n=139 |
|---|---|---|---|---|
| Illiterate or just literate | 48.0 | 0.0 | 59.4 | 64.9 |
| Primary school | 24.0 | 40.0 | 19.1 | 22.5 |
| High school | 21.5 | 40.0 | 15.9 | 12.6 (High school and College combined) |
| College | 6.5 | 20.0 | 5.6 | |
| All categories | 100.0 | 100.0 | 100.0 | 100.0 |

Figures in percentages

to a peak in the defaulters in the middle-income group in ADMH. All the defaulters in TMH belonged to high-income group (Table 3) because of an unusual reason (see Discussion).

Sputum status of defaulters showed about 80 percent to be sputum positive in ADMH and TMH, Jamshedpur, whereas in TB Centre, Roing, 42 per cent of the defaulters were sputum positive.

Time of defaulting (Table 4) was similar in all the institutions starting at the third month, increasing upto the fourth month and declining subsequently.

Reasons for default (Table 5) were categorized according to the actual stated responses of the defaulters. Multiple responses were included important factor in both TMH (36.5 per cent) and DTC (36.1 per cent), followed closely by indifference due to amelioration of symptoms and lack of motivation whereas TMH and TB Centre, Roing, indifference due to the improvement was the major factor responsible for default in 40 percent and 56 percent respectively.

## DISCUSSION

Under India's National Tuberculosis Programme (NTP), treatment completion rate of only 30 percent could be achieved, and the programme did not make a significant dent into the problem[4]. This was mainly due to treatment default which remains a serious problem in therapy. It is estimated that 70 to 90 per cent of patients fail to take the drugs regularly[5]. In the present study, defaulter rate was much lower, ranging between 10.78 percent (TMH) and 38.13 percent (TB Centre, Roing) under different set ups. Of the different types of organizations, government organizations, showed higher rates of default (TB Centre, Roing, 38.1 per cent and DTC, Purulia, 29.3 percent) compared to the NGO (ADMH 20 percent) and private hospital (TMH 10.78 percent).

Age distribution pattern in the present study was similar to other studies, which have shown peak levels of defaulting at ages 40-49 years[6]. Singh et al found highest defaulting in the 21-30 years old[7]. The high percentage of elderly defaulters in TMH (27 per cent in the above 60 year age group) was on

**Table 3.** Distribution of defaulters in percentage according to monthly family income and kind of treating institution

| Monthly income (Rupees) | ADMH | TMH | DTC | TB Centre* |
|---|---|---|---|---|
| 501-1000 | 24.5 | 0.0 | 54.0 | 63.0 |
| 1001-2000 | 45.5 | 0.0 | 33.0 | 24.5 |
| >2001 | 30.0 | 100.0 | 13.0 | 12.5 |
| All categories | 100.0 | 100.0 | 100.0 | 100.0 |

Figures in percentages *p<0.01.

**Table 4.** Distribution of defaulters according to time when default occurred and type of treating institution

| Month | ADMH | TMH* | DTC | TB Centre |
|---|---|---|---|---|
| 3 months | 27.0 | 40.0 | 29.5 | 33.0 |
| 4 months | 32.0 | 40.0 | 33.5 | { 67.0 |
| 5 months | 23.0 | 20.0 | 13.5 | |
| 6+ months | 18.0 | 0.0 | 23.5 | |

Figures in percentages *p<0.01

**Table 5**. Distribution of defaulters in percentage according to reason for default and type of treating institution

| Reason for default | ADMH | TMH | DTC | TB Centre |
|---|---|---|---|---|
| Distance from treatment centre | 36.5 | Nil | 36.1 | 17.4 |
| Indifference due to improvement | 24.5 | 40.0 | 19.0 | 56.0 |
| Lack of motivation | 15.0 | Nil | 20.0 | 7.0 |
| Intolerance to drugs | 9.0 | 20.0 | 5.6 | 9.0 |
| Temporary illness | 9.0 | Nil | 3.7 | Nil |
| Others | 6.0 | 40.0* | 15.0 | 20.0 |

*40% in TMH defaulted due to retirement from service Figures in percentages

account of railway employees treated at this hospital in reserved beds who left after retirement and moving away from the area. This peculiar factor was not taken into consideration at the time of selection of centres and, apparently, became responsible for all the enrolled cases being in the high income group, of whom 40% left the hospital after their retirement from service.

Socio-economic factors like literacy and income showed significant inverse association with drug default. This was also reported by Singh et al[7] but Mankodi found no difference among the poor and not poor when it comes to defaulting or incomplete treatment[8]. About 80 per cent of defaulters were found to be sputum positive which is in concordance with the findings of Sivaraman et al[6]

Many patients, who do not receive directly observed treatment, stop taking drugs from the 4th months onwards[9]. In the present study, defaulting was found to start at the 3$^{rd}$ month, rise upto 4$^{th}$ month and then decline subsequently. The pattern was similar in all the institutions. Similar findings have been reported by Chatterjee et al,[10] wherein a modified life table analysis of defaulters showed default starting from the 3$^{rd}$ month, continuing upto the 7$^{th}$ month and then levelling off.

Among the various reasons for defaulting, the important ones were: indifference after improvement in symptoms, distance from treatment centre and lack of motivation. Intolerance to drugs and temporary illness caused defaulting in some patients. A variety of other reasons have been stated by other workers, such as family events, financial difficulty, carelessness and forgetfulness, lack of time etc[7-11]. **Thus the study emphasises the need for situation specific measures for reducing default in treatment as well as proper and repeated motivation of patients during treatment. Nevertheless, the purposeful selection of institutions of different kinds (organisational set up, character of administrative control, etc.) to study the effect of organisational factor on treatment default introduced certain variables, such as default due to retirement from service, etc, which could not be foreseen at the stage of planning of the study. Therefore, known and unknown confounders in the study would suggest that the conclusions from this study should be verified by different workers working under different conditions.**

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**Essay Competition For Medical Students-2003**

The Tuberculosis Association of India awards every year a cash prize of Rs. 500/- to a final year medical student in India for an original essay on tuberculosis. The subject selected for the year 2003 competition is 'TB and HIV' The essay should be written in English, typed double spaced, on foolscap size paper and should not exceed 15 pages (approximately 3,000 words, including tables, diagrams, etc.). Four copies of the typescript should be forwarded through the Dean or Principal of a College/University to reach the Vice-Chairman, Tuberculosis Association of India, 3 Red Cross Road, New Delhi-110 001, before 31st August 2003 along with a certificate that the author is a final year medical student.

**Chanchal Singh Memorial Award - 2003**

The Tuberculosis Association of India awards every year a cash prize of Rs. 1000/- to a medical graduate (non-medical scientists working as bacteriologists, biochemists, etc, in the field of tuberculosis included) who is below 45 years of age and is working in tuberculosis, for an original article not exceeding 30 double spaced foolscap size pages (approximately 6,000 words, excluding charts and diagrams) on tuberculosis. Articles already published or based on work of more than one author will not be considered. Papers may be sent, in quadruplicate, to reach the Vice-Chairman, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110001, before 31st August 2003.

# EVALUATION OF PLASMA-PLEURAL EFFUSION ALBUMIN GRADIENT FOR DIFFERENTIATING BETWEEN PLEURAL TRANSUDATE AND EXUDATE

**K.B. Gupta, S.K. Aggarwal*, Sanjay Kumar and Manav Manchanda**

*(Received on 5.3.02; Accepted on17.10.02)*

***Summary:*** A total of 60 patients of pleural effusion of diverse etiology were evaluated for plasma-pleural effusion albumin gradient and results were compared with Light's criteria to distinguish between transudate and exudate. The cut off value of 1.2 g/dL albumin gradient was able to differentiate between transudates and exudates with sensitivity and specificity of 97.9% and 100% respectively.

Thus, this parameter was found to be better than Light's criteria to differentiate between transudate and exudate, especially in respect of misclassified pleural effusions.

***Key words:*** Pleural effusion, Transudates, Exudates, Plasma-pleural effusion albumin gradient

## INTRODUCTION

Pleural effusion is a common clinical entity where differentiation between transudate and exudate is necessary to assist in differential diagnosis[1-10].

Presently, Light's criteria[2] are used to distinguish between transudates and exudates (pleural fluid/serum protein ratio >0.5, pleural fluid/serum LDH ratio >0.6 and absolute pleural fluid LDH >200U denote an exudate). But many pleural effusions, misclassified as transudates or as exudates have been reported using these criteria[11-12].

Recently, many new parameters have been reported to distinguish transudates from exudates, like pleural fluid cholesterol[11-12], pleural fluid to serum bilirubin ratio[13], pleural fluid cholinesterase[14],alkaline phosphatase[15], creatinine kinase, uric acid [16] and pleural fluid malondialdehyde(MDA)[17]. But, none have better sensitivity and specificity than Light's criteria.

Recently, plasma-pleural effusion albumin gradient(PPEAG) has been reported as a good parameter with sensitivity and specificity of 95% and 100% respectively[18]. The present study was planned to evaluate (PPEAG) for differentiating pleural transudates from exudates.

## MATERIAL AND METHODS

A total of 60 patients having pleural effusion of diverse etiology were divided into 2 groups:

*Group I (transudates):* Comprising 12 patients of congestive heart failure (n=7) and nephrotic syndrome (n=5).

*Group II (exudates):* Comprising 48 cases of tuberculous (n=24), malignant (n=12) and parapneumonic effusions (n=12).

Cases, in which either no cause was definitely diagnosed or more than one cause was present, were excluded from the study.

After detailed history taking, thorough clinical examination and investigation, each patient was evaluated for the following:

*Blood:* Serum LDH, total plasma protein and

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plasma albumin levels

*Pleural fluid:* Total proteins, LDH and albumin levels

**Estimations**

A. Protein estimation: Plasma and pleural fluid total protein levels were estimated by the method described by Reinhold[19].

B. LDH estimation: LDH level was estimated by UV kinetic method recommended by the Scandinavian Society for Clinical Chemistry and was expressed as IU/L[20].

C. Albumin estimation: Determination of plasma and pleural fluid albumin was done using manual method of Doumas et al[21] and modified Spencer and Price method[22] .

**Statistical analysis**

The mean and S.D. were calculated for each parameter both for exudates and transudates, and unpaired 't' test was used to compare them with respect to various parameters.

**RESULTS**

The mean age of the 60 patients was 45 years. Male to female ratio was approximately 3:2, the ratio of smokers to non-smokers was 1:1, the ratio of vegetarian and non-vegetarian was 2:1 and the ratio of alcoholic to non-alcoholic was 2:1. Pleural fluid examination results were analysed on the basis of Light's criteria and compared with PPEAG parameter.

Table 1 shows the average values of various parameters studied which were significantly higher for exudates than transudates.

As shown in Table 2, the sensitivity, specificity, PPV and NPV of plasma-pleural effusion albumin gradient(PPEAG) were 97.9%, 100%, 100% and 92.3% respectively. These were significantly higher than various Light's criteria.

As shown in Table 3, on the basis of plasma-pleural albumin gradient, none of the transudates and 2% of exudates were misclassified as compared to the Light's criteria misclassifications.

**DISCUSSION**

Pleural effusion is a common clinical entity: approximately 4% of all attendances at chest clinics. The initial step in diagnosis is to distinguish between transudates and exudates[1-10]. The criteria used for the

**Table 1:** Comparison of transudates and exudates with respect to different parameters

| Parameters | Transudates | | Exudates | | Level of p |
|---|---|---|---|---|---|
| | Range | Mean±SD | Range | Mean±SD | |
| Pleural fluid to plasma protein ratio | 0.15-1.66 | 0.46±0.26 | 0.29-1.00 | 0.69±0.02 | <0.01(S) |
| Pleural fluid to serum LDH ratio | 0.29-0.81 | 0.43±0.12 | 0.42-1.78 | 0.86±0.06 | <0.001(HS) |
| Pleural fluid LDH level (IU/L) | 70-346 | 147.8±58.26 | 95-554 | 324.52±29.33 | 0.001(HS) |
| Plasma-pleural effusion albumin gradient(g/dl) | 1.2-2.7 | 1.93±0.21 | 0.3-1.9 | 0.82±0.03 | <0.001(HS) |

S=Significant HS= Highly Significant

**Table 2**. Sensitivity, specificity, positive predictive value and negative predictive values of various parameters studied

| Parameters | Percent | | | |
|---|---|---|---|---|
| | Sensitivity | Specificity | PPV | NPV |
| Pleural fluid proteins | 83.3 | 75.0 | 93.0 | 52.9 |
| Pleural fluid to plasma protein ratio | 85.4 | 66.6 | 91.1 | 53.3 |
| Pleural fluid LDH level (IU/L) | 79.1 | 75.0 | 92.6 | 47.3 |
| Pleural fluid to serum LDH ratio | 85.4 | 75.0 | 93.1 | 56.2 |
| Plasma-pleural effusion albumin gradient | 97.9 | 100 | 100 | 92.3 |

purpose were proposed by Light et al[2], with misclassifications varying from 2% to 40%[23-25]. Later, many more parameters like pleural fluid cholesterol, pleural fluid to serum cholesterol ratio, pleural fluid MDA and pleural fluid to serum MDA ratio, pleural fluid to serum bilirubin ratio, pleural fluid to serum cholinesterase ratio, plasma-pleural effusion albumin gradient were suggested, but no parameter has yet been proved to be satisfactory. Thus, the search for an improved method is kept alive.

Light's criteria are being used widely for differentiating between transudates and exudates in clinical practice. However, many workers have found low specificity and misclassification in about 20-30% of patients. In the present study too, we found 33.3% misclassification in transudates and 14.5% in

**Table 3.** Number of cases misclassified in transudative and e xudative pleural effusions for every parameter studied

| Parameters | Transudates (n=12) | % | Exudates (n=48) | % |
|---|---|---|---|---|
| Pleural fluid protein | 3 | 25.0 | 9 | 18.7 |
| Pleural fluid to plasma protein ratio | 4 | 33.3 | 7 | 14.5 |
| Pleural fluid LDH level (IU/L) | 3 | 25.0 | 10 | 20.8 |
| Pleural fluid to serum LDH ratio | 3 | 25.0 | 7 | 14.5 |
| Plasma-pleural effusion | 0 | 0.0 | 1 | 2.0 |

**Table 4.** Number of misclassified effusions in pleural fluid protein range of 2.0-3.0 gm/dL by different parameters.

| Parameters | Number | Percentage |
|---|---|---|
| Pleural fluid protein | 9 | 15.0 |
| Pleural fluid to plasma protein ratio | 8 | 13.3 |
| Pleural fluid LDH level (IU/L) | 7 | 16.6 |
| Pleural fluid to serum LDH ratio | 7 | 11.6 |
| Plasma-pleural effusion albumin gradient | 1 | 1.6 |

exudates by using pleural fluid/serum protein parameter. Pleural fluid LDH misclassified 25% transudates and 20.8% exudates, while pleural fluid/ serum LDH misclassified 25% transudates and 14.5% exudates.

Recently, PPEAG has been reported as a useful parameter to differentiate transudates from exudates. Possibly, the total fluid protein level is greatly increased after diuresis due to a greater percentage of non-albumin protein that originates in the pleural space. Alternatively, the mathematics of the gradient may be more representative of protein diffusion than a ratio.

In the present study, the mean albumin gradients were signficantly raised in transudates (1.93± 0.21 gm/dL) as compared to exudates (0.82± 0.03 gm/dL) with p value of <0.001. Thus, confirming the findings of the previous studies.

By using a cut off value of 1.2 g/dL of plasma-pleural effusion albumin gradient, none of transudates and 2% exudates were misclassified with the sensitivity, specificity, PPV and NPV of 97.9%,100%,100% and 92.3% respectively (Table 2).

In the present study too, the exudative effusions based on pleural fluid protein in the range of 2.0 to 3.0 g/dL, 9 (18.7%) cases were misclassified. These cases, except one , were rightly classified by plasma-pleural effusion albumin gradient. Out of 9 misclassified cases, 5 pertained to tuberculous effusion, 1 to parapneumonic effusion and 3 to malignant effusion, whereas 1 misclassified on the basis of albumin gradient was tuberculous effusion. In transudative effusions, 3 cases of congestive heart failure classified as exudate as per pleural fluid protein >3.02% were also rightly classified by plasma-pleural effusion albumin gradient. **Hence, plasma-pleural effusion albumin gradient has been found to be a better criterion for rightly classifying transudate and exudate in misclassified effusions.**

**Thus, the present study demonstrates the usefulness of plasma-pleural effusion albumin gradient (PPEAG) parameter to differentiate between exudates and transudates, especially in cases misclassified by Light's criteria.This parameter can also be used as complementary parameter.**

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**Global Drug Facility (GDF)**

GDF, launched by WHO in 2001, is expected to increase access to essential high-quality anti-tuberculosis drugs so that DOTS expansion can reach the global TB control targets by the year 2005. So far, applications from more than 20 countries covering the treatment of over one million patients have been approved. Besides, the Global Fund to Fight AIDS, TB & Malaria (GFATM) proposed by Kofi Anan, the UN Secretary General in 2001, is intended to raise additional resources through a new public-private partnership to reduce the impact of HIV/AIDS, TB and malaria in countries in need.

**Tuberculosis Health Visitors' Course**

The 2003-2004 Tuberculosis Health Visitors' Course of 12 months' duration will be conducted at the New Delhi Tuberculosis Centre. The minimum qualification for admission to this course is 10+2 with science and/or hygiene. Science education upto class 10 is essential. Application forms for admission to the course can be had from the Vice-Chairman, Tuberculosis Association of India, 3 Red Cross Road, New Delhi 110 001. The last date for receipt of application is 30th April 2003.

# MYCOBACTEREMIA IN TUBERCULOSIS PATIENTS WITH HIV INFECTION*

**Ranjani Ramachandran[1], Soumya Swaminathan[2], Sulochana Somasundaram[3], V.N. Asgar, P Paramesh[5] and CN Paramasivan[6]**

***Summary:***

***Background:*** Mycobacteremia in HIV positive tuberculosis patients is associated with extra-pulmonary tuberculosis and disseminated tuberculosis.

***Objective:*** To study the occurrence of mycobacteremia among HIV-infected patients with tuberculosis (both pulmonary and extra-pulmonary forms) using radiometric BACTEC method.

***Methods:*** HIV positive patients admitted to the Government Hospital of Thoracic Medicine with a clinical diagnosis of tuberculosis were screened. HIV serology was reconfirmed using ELISA (two different tests) at Tuberculosis Research Centre. Five ml of venous blood was collected on the day of admission to the ward before start of anti-tuberculosis therapy.

***Results:*** Of the 105 patients screened, 85 were were found to be eligible for analysis. Patients were aged between 20-40 years, with a male preponderance (5:1). Pulmonary tuberculosis was the predominant form of tuberculosis (85%), while 15 % had associated extra-pulmonary involvement. Eight-four percent of the patients had CD4 counts of less than 200 cells/mm$^3$, with 42% being below 50 cells/mm$^3$. Four of the 85 patients were blood culture positive; three were identified as *M.tuberculosis* and one as *Mycobacterium phlei*.

***Conclusions:*** Mycobacteremia was detected in 4% of HIV positive patients with tuberculosis. All of them were immunosuppressed with CD4 counts of <50 cells/m$^3$. More work needs to be done in India to understand the risk factors and outcome of patients with mycobacteremia.

***Key Words***: Mycobacteremia; Tuberculosis; TB/HIV

## INTRODUCTION

Mycobacteremia has been described in febrile HIV-positive individuals with all forms of tuberculosis as varying from 10-64%, depending on the clinical presentation. Both tuberculosis and HIV pose major public health problems in India. Estimated 2 million new cases of tuberculosis and 5,00,000 deaths occur every year in this country. About 40% of the adult population is infected with *M.tuberculosis* and the incidence of smear positive disease is 2-4/100,000[1]. The first HIV positive person in India was located in Chennai in 1986 and since then the epidemic has grown rapidly. It is estimated that there were 3.86 million HIV-positive persons in India at the end of 2001 and that the prevalence in the adult population was about 0.6%. The six high prevalence states where the prevalence in ante-natal women is over 1% include Tamil Nadu, Karnataka, Andhra Pradesh, Maharashtra, Nagaland and Manipur[2].

Pulmonary tuberculosis is still the most common form of tuberculosis, even among HIV positive persons, though extra-pulmonary tuberculosis and disseminated tuberculosis have become more common than before. Mycobacteremia is a key event in the pathogenesis of tuberculosis but is usually not detected in immunocompetent individuals[3]. The reported prevalence of mycobacteremia in HIV+ persons with tuberculosis ranges from 10 to 64%[4]. It has been recognized as an important cause of pyrexia of unknown origin (PUO) in HIV-infected patients[5]. The frequency of mycobacteremia has not been studied well in India. This study was designed to look for mycobacteremia in patients with HIV and tuberculosis admitted to a tertiary care centre.

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## MATERIAL AND METHODS

This prospective study was conducted between June and November 2001 at the Government Hospital for Thoracic Medicine Tambaram. One hundred and five consecutive patients admitted with a clinical diagnosis of tuberculosis were recruited; a detailed history was taken and physical examination was done. Blood was examined by culture and for CD4 counts. Five ml of blood was inoculated into a BACTEC bottle (BACTEC 13A, Becton Dickinson) and processed for isolation of mycobacteria using BACTEC 460 TB system. Positive BACTEC cultures were confirmed for the presence of acid-fast bacilli by fluorescence microscopy and sub-cultured further on conventional (LJ) medium. The CD4 lymphocyte count was measured by flow cytometry by standard techniques using Becton Dickinson FACScan.

## RESULTS

Patients were aged between 20-40 years, with a male preponderance (5:1). In all, 85 tuberculosis patients were confirmed to have HIV infection by positive results on 3 ELISA tests. Of the HIV positive patients, 85% had presented with symptoms suggestive of pulmonary tuberculosis, while 15% had associated extra-pulmonary involvement along with pulmonary disease. The predominant clinical features were fever (75%), cough (69%) and weight loss (50%). Almost 95% had a history of high-risk sexual behavior and 44% of these patients were being simultaneously treated for some type of sexually transmitted disease or HIV associated symptoms like chronic diarrhoea (31%), oral thrush (21%) and lymphadenopathy (19%). The radiographic features included extensive bilateral parenchymal infiltrates (in 80%), the rest showing atypical features like lower lobe infiltrates, pleural involvement and hilar adenopathy.

The CD4 counts of the HIV positive patients ranged between 32 and 750 cells/mm$^3$ (mean 125 cells/mm$^3$); 84% of the patients had CD4 counts of <200 cells/ mm$^3$ and 42% had a CD4 count of <50 cells/ mm$^3$, indicating that most patients had profound immunosuppression at the time of investigation for symptomatic HIV/TB disease. CD4 counts were available for 10 of 20 HIV seronegative pulmonary tuberculosis patients and the mean was 932 cells/mm$^3$ (range 770 to 1100 cells/mm$^3$).

*Mycobacterium tuberculosis* was isolated from the blood of three patients (3.5%) and *Mycobacterium phlei* from one (Table 1). The time taken for identification of mycobacteremia ranged from 22-43 days. All the three patients with *M. tuberculosis* bacteremia had CD4 counts of less than 50 cells/mm$^3$. One of the *M. tuberculosis* isolates was observed to be multi-drug resistant. Considering only those patients who had CD4 counts <100/ mm$^3$, 3(10%) out of 30 had *M. tuberculosis* bacteremia.

**Table 1:** Prevalence of mycobacteremia in patients with tuberculosis with/without HIV sero-positivity

| Category | CD4 Count (cells/mm$^3$) >500 | 200-500 | 100-200 | <100 | NA | Mycobacteremia found |
|---|---|---|---|---|---|---|
| HIV Negative (N=20) | 10 | - | - | - | 10 | 0/20 |
| HIV Positive (N=85) | 2 | 6 | 10 | 30 | 37 | 4/85* |

NA = Not available * 3 patients with *M. tuberculosis* and 1 with *M. phlei*

## DISCUSSION

This study found the proportion of disseminated tuberculosis in Indian tuberculosis patients with HIV and tuberculosis to be 3.5%, with different levels of immunodeficiency. The proportion was somewhat lower than that reported by others[1-3] which could be because patients were not selected on the basis of CD4 counts or for investigation of PUO. Bacteremia due to mycobacteria has been reported in HIV/AIDS patients from developed as well as developing countries; *M. avium* is the most common agent found in studies from developed countries while *M. tuberculosis* is more common in patients from developing countries[6]. Further, the frequency of disseminated tuberculosis as evidenced by mycobacteremia increases as CD4 counts fall[7]. In our study, if only patients with CD4 counts of <100/ml are considered, the occurrence of mycobacteremia due to *M.tuberculosis* increases to 10 %. Occurrence of mycobacteremia is usually related to the form of tuberculosis, being 17% in extra-pulmonary tuberculosis and 43-83% in disseminated tuberculosis[8]. Usually, the diagnosis of disseminated tuberculosis is difficult but blood culture could help in diagnosing mycobacteremia in patients with low CD4 counts. In this study, 3 of the pulmonary tuberculosis patients were found to have disseminated tuberculosis based on mycobacteremia detected, *M. phlei*, which is a saprophyte, having never been reported to cause disease/infection, even in the HIV setting. More work needs to be done in India to determine the prevalence of non-tuberculous mycobacteremia in HIV positive patients. Research is also required to investigate their clinical course and outcome to determine if these patients need more aggressive therapy.

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# GENERAL COUNSELLING FOR HIV

With the uprising HIV epidemic in the country, it has become imperative for every physician to acquire knowledge and skills for HIV counselling, comprising general, post-test and HIV-positive patient counselling.

- General counselling involves several aspects, namely, personal, phycho-social, professional and financial.
- For personal and psycho-social counselling, the physician must educate as well as assist a person to understand and accept the changes, if any, which are required to gain self-assurance, maintain quality of life, review future goals and plans, forge family acceptance/adjustments and decide on social/community relationships.
- For professional and financial counselling, the physician must practise how to educate in order to convince and assure, yet stop short of creating confusion and scare. If the information conveyed regarding the disease, its prevention as well as treatment, is adequate it will help in making a person take control of his situation and make his own decision instead of feeling helpless and dependent on others.
- Try to focus on what can be done and how, instead of what might inevitably happen. Discuss how much can be achieved with the financial and other resources available instead of technology that is available but is out of reach.
- Join hands in equipping the person to cope with the situation, convincing him/her that HIV infection does not always progress to AIDS, that AIDS is not necessarily fatal and that means for long term survival are available.
- Kindle hope that the system will support his efforts for long-term survival and that there is no need to feel lonely and let down.

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# EFFECT OF INTENSIVE HEALTH EDUCATION ON ADHERENCE TO TREATMENT IN SPUTUM POSITIVE PULMONARY TUBERCULOSIS PATIENTS

**Jacintha D'Souza***

*(Received on 1.10.2002; Accepted on 19.12.2002)*

***Summary***: The effect of intensive health education on adherence to treatment was studied in 60 newly diagnosed pulmonary tuberculosis (TB) patients. Also, their knowledge of TB before and after health education was recorded and their health status during the first three months of the treatment was assessed to measure the effect.

The findings of the study revealed a statistically significant difference in the total health status scores of patients, after receiving intensive health education between 1st and 30th day, 30th and 60th day, 60th and 90th day, and 1st and 90th day, higher mean post-test knowledge scores, and a highly significant association between sputum conversion and adherence to treatment. There was no association between adherence to treatment and age, sex, education, income and family support of the patients.

***Key words***: Pulmonary tuberculosis, Intensive health education, Treatment adherence-non-adherence, Treatment outcome, Social factors and family support

## INTRODUCTION

Effective treatment capable of curing almost all tuberculosis(TB) patients in six months has been available for the last 40 years under the National Tuberculosis Programme. However, its impact is yet to be seen and there is a growing tuberculosis mortality curve at the beginning of the 21st century.

The difficulties of winning the battle against TB are that most TB patients are poor, the treatment taken is often non-standardized and follow up of patients started on treatment is inadequate. In both public and private sectors in India, only about a third of patients completed the full course of treatment till the introduction of Revised National Tuberculosis Control Programme in 1993. Low rates of compliance with prescribed medication pose a major challenge to the effective management of most chronic diseases. The high medical and social costs of non-adherence, and the apparent lack of effective methods of dealing with it have evoked considerable interest in this complex issue. Two broad categories of non-compliants have been identified, namely unintentional (or 'accidental') and intentional (or 'deliberate') treatment defaulters. Unintentional non-compliance may result from poor doctor or nurse- patient communication or a lack of ability to follow advice. Intentional non-adherence occurs when the patient knows what is required but decides not to follow advice, to some extent. Improvement in adherence with therapy will require better doctor or nurse-patient communication, improved health education, the tailoring of therapy for each patient and possibly novel strategies, such as providing feedback to the patients on their level of compliance[1].

From the public health perspective, poorly supervised or incomplete treatment of TB can be worse than no treatment at all. When patients remain infectious much longer,they may spread drug resistant strains. While drug-resistant TB is treatable, it requires extensive chemotherapy (up to two years of treatment) which is often prohibitively expensive and is also more toxic.

## OBJECTIVES

1) To determine the health status of

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tuberculosis patients as measured by (a) modified PGI Health Questionnaire[2] N-1, (b) judging knowledge about tuberculosis and (c) sputum examination results

2) To develop and validate an intensive health education programme in terms of:

- Effectiveness as (a) knowledge gained and (b) adherence to treatment measured by

(i) improved health status
(ii) sputum conversion rate, and
(iii) regularity of consumption of prescribed drugs.

- Reasons for adherence/non-adherence as expressed by patients or their family members in the diary maintained by them.

- Association between sputum conversion and adherence to treatment.

- Association between adherence/non-adherence to treatment and (i) age (ii) sex (iii) educational status (iv) economic status of family and (v) family support provided.

The conceptual framework of the study was based on the behavioural systems theory of Dorothea E Johnson[1], which embodies her belief that nursing is an external force which preserves the organisation of a patient's behaviour while under stress by means of putting in place a regulatory mechanism or by providing resources for the purpose. If the patient is given a goal to achieve, he will adhere to the treatment as he will have improved knowledge of TB.

## MATERIAL AND METHODS

An evaluative approach with quasi-experimental pre-test, post-test, control group design was used for the study which was conducted at the District Tuberculosis Centre (DTC) and a private hospital in Mangalore, Karnataka. A sample of 60 new sputum positive pulmonary TB patients who fulfilled the sampling criteria decided by both physicians of the participating health institutions was taken. Thirty patients from the private hospital formed the Experimental group and the rest from DTC were the Control group. Since one patient from the Experimental group died, the study group comprised 59 patients in all.

Written permission to carry out the study was obtained and an oral informed consent was obtained from each tuberculosis patient. A pilot study was conducted on 10 patients before starting the study. The actual data were collected in four stages, with a gap of 30 days. After establishing rapport, a formal interview was conducted. Health status assessment was done first by using the modified PGI H.Q N-I questionnaire. After assessing their knowledge about TB, each patient in the experimental group was given a comprehensive planned health education using 25 Flip Cards. All patients were given a diary and a pencil each, and were requested to place a tick mark in the appropriate column after he/she had taken or not taken the treatment dose, as prescribed. A non-sterile plastic bottle was given to all the patients and they were requested to bring their morning sputum and get the remaining drugs when they came for revisit. All these activities, except for health education , were carried out equally for the control group. Defaulter action was taken if patients failed to return to receive drugs. During the particular revisits (30th day, 60th day, and 90th day), health status assessment was repeated and weight was checked again. Experimental group patients were given reinforcement of health education and sputum results as well as adherence to treatment were recorded. The diary with each patient was examined and they were motivated to continue marking it every day. Each member of the Experimental group was also individually visited at home once to verify if he was taking drugs regularly. On the 90th day, family support provided during the treatment period was verified.

## FINDINGS

In all, 52 out of 60 patients, belonged to the age group of 25-60 yrs, 47 (78.3%) were males, and 26.7% were illiterate, 38.3% had the habit of

**Table 1.** Distribution of Experimental and Control group patients according to health status report

| Health status | 1st day No. | 1st day % | 30th day No. | 30th day % | 60th day No. | 60th day % | 90th day No | 90th day .% |
|---|---|---|---|---|---|---|---|---|
| **Exp.Group** | | | | | | | | |
| Good | 5 | 17.24 | 15 | 51.72 | 22 | 75.86 | 22 | 75.86 |
| Satisfactory | 18 | 62.07 | 12 | 41.38 | 5 | 17.24 | 5 | 17.24 |
| Poor | 6 | 20.69 | 2 | 6.90 | 2 | 6.90 | 2 | 6.90 |
| **Control group** | | | | | | | | |
| Good | 2 | 6.67 | 11 | 36.37 | 17 | 56.67 | 17 | 56.67 |
| Satisfactory | 18 | 60.00 | 15 | 50.00 | 8 | 26.67 | 9 | 30.00 |
| Poor | 10 | 3.33 | 4 | 13.33 | 5 | 16.66 | 4 | 13.33 |
| **All** | | | | | | | | |
| Good | 7 | 11.86 | 26 | 44.07 | 39 | 66.10 | 39 | 66.10 |
| Satisfactory | 36 | 61.02 | 27 | 45.76 | 13 | 22.03 | 14 | 23.73 |
| Poor | 16 | 27.12 | 6 | 10.17 | 7 | 11.87 | 6 | 10.17 |

**Table 2.** Mean differences, Standard error of means, and 't' values of total health status scores of patients in Experimental Group

| Visits | Mean | Mean Diff. | SEM | 't' |
|---|---|---|---|---|
| 1st day | 62.33 | | | |
| | | 12.88 | 2.11 | 5.919*** |
| 30th day | 49.45 | | | |
| | | 4.42 | 2.38 | 4.074*** |
| 60th day | 45.03 | | | |
| | | 1.65 | 2.59 | 2.196* |
| 90th day | 43.38 | | | |
| | | -18.95 | 2.86 | 6.627*** |
| 1st day | 62.33 | | | |

Note: Higher the score, lower the health status
***=P<0.001(28df)
SEM= Standard Error of Means
*=P<0.05(28df)

drinking alcohol and taking tobacco : 63.3% had consumed tobacco or alcohol for more than five years.

At the first visit, only 5 patients (17.24%) in the Experimental group were assessed to have good health status. The number of such patients increased to 22(75.86%) on the 90th day. In the Control group, the number of patients with good health status increased from 2(6.67%) on 1st day to 17(56.67%) on 90th day (Table 1).

The differences in the health status scores on 1st day and 30th day, 30th and 60th days, 60th and 90th days and 1st and 90th days in the Experimental group were tested and it was found that there was a significant difference in the health status - 't'=5.919, 4.074, 2.196 and 6.627, $P<0.05$ respectively (Table 2). However, a highly significant difference was found in the physical health ('t' = 5.102, 3.842, 6.289, $P<0.05$) and mental health status

**Table 3**. Standard Error of Means,SD and't' value of health status scores of Experimental (Group 1) and Control group(Group 2)

| Visit | Mean | Mean Diff. | SEM | SD | 't' |
|---|---|---|---|---|---|
| **1st day** | | | | | |
| Group 1 | 62.33 | | 2.07 | 11.32 | |
| | | 4.14 | | | 1.470(df 58) |
| Group2 | 66.47 | | 1.91 | 10.44 | |
| **30th day** | | | | | |
| Group1 | 49.45 | | 2.38 | 12.80 | |
| | | 6.35 | | | 1.944(df57)[b] |
| Group2 | 55.80 | | 2.25 | 12.30 | |
| **60th day** | | | | | |
| Group1 | 45.03 | | 2.59 | 13.95 | |
| | | 7.20 | | | 1.985(df57)[b] |
| Group2 | 52.23 | | 2.54 | 13.91 | |
| **90th day** | | | | | |
| Group1 | 43.38 | | 2.86 | 15.41 | |
| | | 8.39 | | | 2.174(df57)** |
| Group2 | 51.77 | | 2.60 | 14.21 | |

**P<0.01, [b]P<.10

of patients ('t = 5.095, 5.031, P<0.001) in the experimental group. The physical measure score also was reduced in the Experimental group between 1st and 30th days and 1st and 90th days ('t'=3.057, 4.213, P0.05).

The Experimental group when compared with the control group had better health status during all the four visits but statistically significant difference was found only on the 90th day ('t'=2.174, P<0.05)(Table 3).

There was a highly significant difference between the post test mean knowledge score of Experimental group and Control group ('t'=4.665, P<0.001)(Fig.1).

On the 90th day, 15 patients in the Experimental group were found to be sputum negative compared with 9 patients in the Control group. In the Experimental group, 20 out of 29(69.2%) had completed treatment on the 90th day compared with only 16(53.3%) in the Control group.(Fig.2).

There was no significant association between intensive health education and adherence to treatment ($\chi^2$=0.499,for 1df, P>0.005) a highly significant association was observed between adherence to treatment and sputum conversion ($\chi^2$=11.748, P<0.01) (Table 4).

There was no significant association between adherence to treatment and age, sex, education, economic status of the patient and family support received.

## DISCUSSION

The present study showed that the total health status of patients improved significantly after receiving intensive health education and medication. Balasangameshwara et al had found that persistence

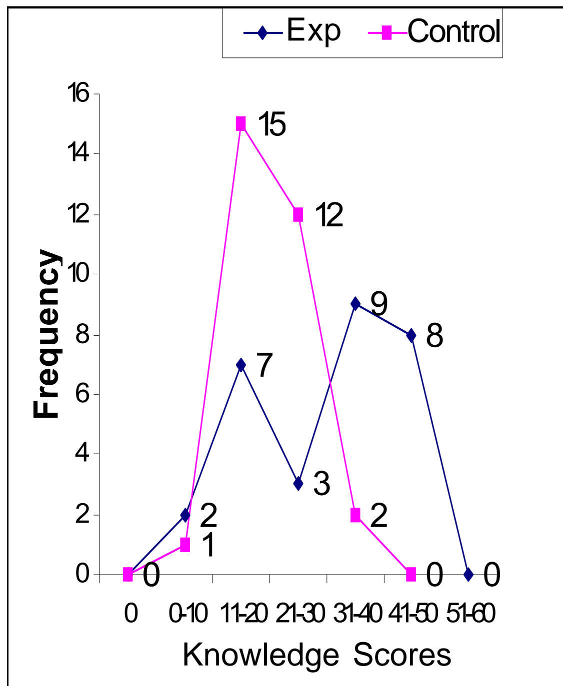


**Figure 1.** Frequency Polygon showing the post-test knowledge scores of Experimental group and Control group

**Table 4.** Chi-square test showing the association between adherence to treatment and sputum results on the 90th day

| Sputum Status | Adherence | Non-adherence | Total |
|---|---|---|---|
| Negative | 21 | 3 | 24 |
| Positive | 11 | 17 | 28 |
| No sputum | 6 | 1 | 7 |
| Total | 38 | 21 | 59 |

$\chi^2$=11.748 for 1df, P<0.01

of symptoms in patients treated with Short Course Chemotherapy (SCC) was less common than in patients treated with SR (standard regiment)[3]. Subramanian et al found an overall increase of knowledge on various aspects of TB, ranging from 18% to 58%, after health education[4-5]. The present study revealed that there was a highly significant difference in the post-test knowledge scores of patients who received intensive health education compared with those who did not receive intensive health education, at 5% level of significance (t=4.665). However we found that intensive health education had no significant association with

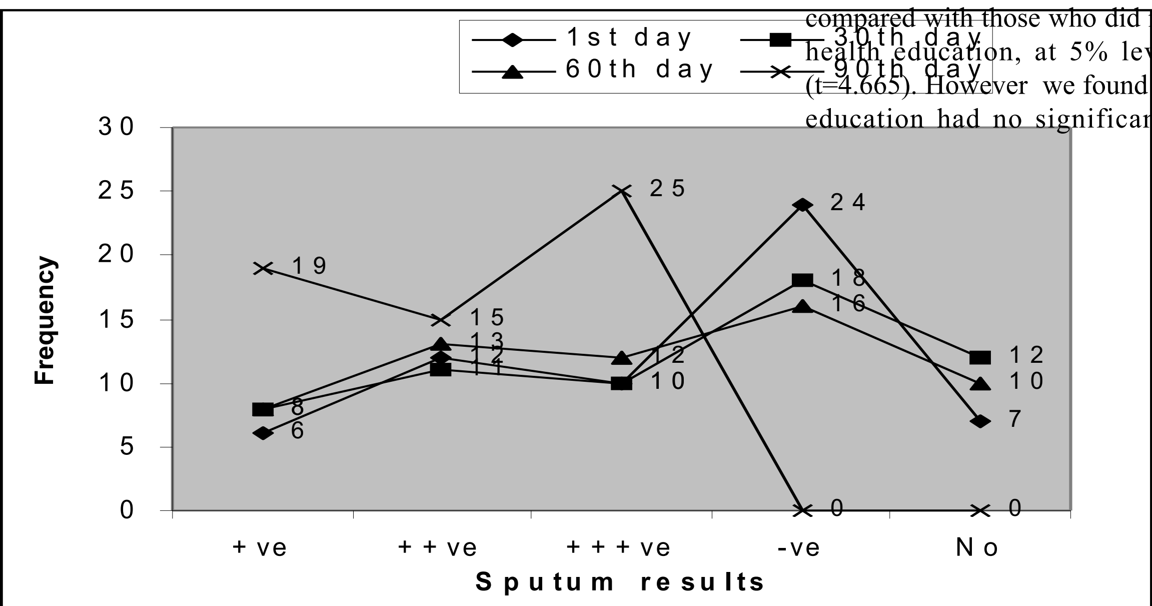


**Figure 2.** Line Graph representing the subjects by severity of disease at four visits

adherence to treatment. This could be because of the routine motivation received by patients in the Control group.

**The results of the present study revealed that there was an increase in treatment completion rate among patients who received intensive health education as reported also by Chadha and Bhagi[6]. About 34.5% patients in the Experimental group and 46.7% patients in the Control group failed to consume drugs regularly[7], non-compliance in the present study was affected mostly by side effects of drugs (43%)[8]. Juvekar et al found that patients who were taking regular treatment during the first two months tended to be adherent throughout, unlike those who defaulted in treatment in the initial period[9]. Our study partially contradicts the findings: While the number of defaults increased with time in the Control group, it decreased in the Experimental group. This could be due to the reinforcement of health education given to them.**

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**Original Article**

*Ind J Tub. 2003,50, 39*

# TREND OF HIV INFECTION IN PATIENTS WITH PULMONARY TUBERCULOSIS IN LUCKNOW AREA

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***Summary***:
***Setting*** : Pulmonary tuberculosis patients attending the Department of TB and Chest Diseases, King George's Medical College, Lucknow.
***Objective*** : To assess the trend of HIV infection in pulmonary tuberculosis patients.
***Design*** : HIV seropositivity was assessed among radiologically and/or bacteriologically confirmed pulmonary tuberculosis patients, selected in randomized manner from those attending the Outpatients Deptt. during 1995-96, 1996-97 and 2000-2001.
***Results*** : HIV seropositivity rate among pulmonary tuberculosis patients was 1.25% in 1995-96, 1.78% in 1996-97 and 4.28% in 2000-2001 (p=0.022).
***Conclusion*** : This study suggests that HIV infection is rising in Lucknow and adjacent districts.

***Key Words*** : HIV and TB; Trend of HIV infection and Disease; Profile of TB patients with co-infection.

## INTRODUCTION

Prevalence of tuberculosis is increasing in many countries and it is now the leading cause of death from infectious diseases world-wide, being responsible for 3 million deaths annually[1]. Similarly, infection with HIV is increasing and it has emerged as the most important predisposing factor for developing tuberculosis in people co-infected with *Mycobacterium tuberculosis*. WHO has estimated that by December 2001, the number of people worldwide with HIV/AIDS would be 40 million, with 3.5 million in India. It is estimated that there are about 12 million dually infected persons in the world, of which India accounts for over a million[1]. Many reports from India suggest a high prevalence of HIV infection in tuberculosis patients: Most reports are from western[2-6] and southern states[7-9], fewer from northern part of the country[10-13]. We present the trend of HIV infection among pulmonary tuberculosis patients in Lucknow and adjacent districts.

## MATERIAL AND METHODS

In all, 400, 225 and 350 bacteriologically and/or radiologically confirmed patients of pulmonary tuberculosis aged 12 years and above attending the OPD were admitted to Department of TB & Chest Diseases, Kasturba Chest Hospital, King George's Medical College, Lucknow for HIV infection screening during 1995-96, 1996-97 and 2000-2001 respectively. These 975 patients were selected randomly out of 2694 patients of pulmonary tuberculosis. Out of the enrolled 975 cases, 498 were bacteriologically confirmed.

Routine history taking & detailed clinical examination was done in all the patients. They were subjected to Chest X-ray, sputum for AFB on 3 occasions, and Tuberculin test. HIV testing was done in all these patients after the meaning and implication of this test had been explained and written consent obtained. Serum samples were collected and

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**Table 1**. Demographic Profile of Pulmonary Tuberculosis cases studied during 3 periods

| | 1995-96 | 1996-97 | 2000-2001 |
|---|---|---|---|
| **Age Factor** | | | |
| <20 yrs | 51 (12.75%) | 31 (13.78%) | 60 (17.14%) |
| 21-40 yrs. | 229 (57.25%) | 126 (56.00%) | 195 (55.72%) |
| 41-60 yrs. | 99 (57.75%) | 56 (24.89%) | 77 (22.0%) |
| >60 yrs. | 21 (5.25%) | 12 (5.33%) | 18 (5.14%) |
| **Total** | **400** | **225** | **350** |
| Sex | | | |
| Male | 305 (76.25%) | 170 (75.56%) | 226 (64.57%) |
| Female | 95 23.75%) | 55 (24.44%) | 124 35.43%) |
| **Total** | **400** | **225** | **350** |
| Marital Status | | | |
| Married | 348 (87%) | 190 (84.44%) | 295 (84.29%) |
| Unmarried | 52 (13%) | 35 (15.56%) | 55 (15.71%) |
| **Total** | **400** | **225** | **350** |
| Residence | | | |
| Urban | 219 (54.25%) | 122 (54.22%) | 165 (47.14%) |
| Rural | 181 (45.25%) | 103 (45.78%) | 185 (52.86%) |
| **Total** | **400** | **225** | **350** |

assayed for antibodies against HIV at the serosurveillance centre in Department of Microbiology, King George's Medical College, Lucknow. All the ELISA reactive sera were re-tested by a second ELISA. The reactive sera were reconfirmed by Western blot analysis at National Institute of Communicable Diseases (NICD), Delhi in 1995-96 and 1996-97 but not in 2000-2001 (not required as per NACO guidelines). UBI HIV ½ EIA kit (Beijing, China) was used during 1995-96 and 1996-97, and Labsystems EIA kit (Helsinki, Finland), was used during 2000-01.

**RESULTS**

There was no significant difference in the demographic variables like age, sex, marital status and place of residence between the three study populations of 1995-96, 1996-97 and 2000-2001 (Table). Overall (table not put up), HIV infection was detected in 24 (3.07%) patients out of the 975 patients of pulmonary tuberculosis However, a rising trend of HIV infection was observed: from 1.25% in 1995-96 to 1.78% in 1996-97 and 4.28% in 2000-2001. This rising trend was found to be statistically significant (p= 0.022).

Among the 24 HIV positive patients 15 (62.5%), were sputum smear positive for *Mycobacterium tuberculosis* and only 6 (25%) were tuberculin positive; 20-19 (79.16%) males and 5(20.84%) females (83.33%) were in the sexually active age group 21-40 years.

The most common mode of HIV transmission was heterosexual in 21 (87.5%) patients while 1 patient got it through infected blood. Out of the 5 HIV positive female patients, 3 had HIV seropositive spouses and one each had multiple sex partners & HIV infected blood.

The rising trend of HIV infection in patients of pulmonary tuberculosis - from 1.25% in 1996 to 4.28% in 2001 - in Lucknow is in line with the trend Similar rising trend has been reported from Mumbai (2.3% in 1989 to 8.9% in 1993)[2-4], Pune (3.2% in 1991 to 20.0% in 1996)[5] and Chennai (0.59% in 1996 to 8.89% in 1999)[7-8] and from the northern region of India ( 0.5% to 1.42%)[10-13].

This study confirms the rising trend of HIV infection among pulmonary tuberculosis patients in Lucknow[13] and emphasizes the need for screening of tuberculosis patients for HIV infection at regular intervals.

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# PRE-TEST COUNSELLING FOR HIV

With the uprising HIV epidemic in the country, it has become imperative for every physician to acquire knowledge and skills for HIV counselling comprising general post-test and HIV-positive patient counselling. The guidelines for pre-test counselling are:

- Put the person at ease; establish personal rapport.
- Explain in layman's language what HIV is, how it occurs, any wrong perception that may be current, and its consequences (a possibility of progression to AIDS).
- Explain the benefits of HIV testing-medical as well as sociological.
- Detail the steps of HIV testing, the significance of positive or negative result, the margin of error in the test being offered and whether it is for screening or confirmation.
- Stress that a positive result does not mean AIDS or even a prediction that it must occur, sooner or later.
- Discuss at length the confidentiality issue and its implications. Frankly answer doubts and fears; who all shall be informed by the person concerned, if the test is positive. Explain explicitly the meaning and implications of giving written informed consent, the right to refuse the test and the potential consequences of refusal, especially for the spouse and family.
- Assure that medical help will be extended even if the test is refused.
- Allow adequate time for pondering over the situation and making the decision in favour of the test.

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# HEPATIC TUBERCULOMAS ASSOCIATED WITH FATTY METAMORPHOSIS OF LIVER: A CASE REPORT

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*(Received on 20.8.02; Accepted on 18.10.02)*

***Summary***: We report an unusual association of hepatic tuberculomas with fatty metamorphosis of liver secondary to gastrointestinal tuberculosis in a young, immunocompetent patient. The diagnosis was confirmed after the biopsy examination.

## INTRODUCTION

Though hepatic tuberculomas are a known entity in endemic regions like India, it is less commonly seen in immunocompetent hosts. The association of hepatic tuberculomas with fatty metamorphosis of liver has not been reported in literature, to the best of our knowledge.

## CASE REPORT

A 16 year old young female patient attended the medical out-patient department with history of pain in abdomen, recurrent diarrhoea, mild fever, off and on, and loss of appetite for 6 months. On examination, patient was pale with non-specific tenderness in the right iliac fossa and hepatomegaly with liver palpable 4 cm below the right costal margin. There was no ascites but bilateral, non-pitting pedal edema was present. Routine laboratory investigations showed normocytic normochromic anemia with raised erythrocyte sedimentation rate of 72mm at the end of first hour. Chest radiograph was normal. ELISA tests for HbSAg and HIV were non-reactive. Liver function tests showed normal serum bilirubin, alkaline phosphatase, total serum proteins and globulin levels with slightly raised S.G.P.T.-53 IU/L; S.G.O.T.-44 IU/L, and decreased serum albumin levels-2.79 gm/dl.

Ultrasonography of abdomen (Fig.1) showed diffusely increased echogenesity of liver with a well-defined hypoechoic area containing foci of calcification within it, and an adjacent hyperechoic rounded area in the anterior segment of the right lobe of liver. On Doppler study, lesions showed high vascularity. The right branch of portal vein was displaced infero-laterally. There were also multiple small, hypoechoic satellite lesions occupying the right lobe of liver.

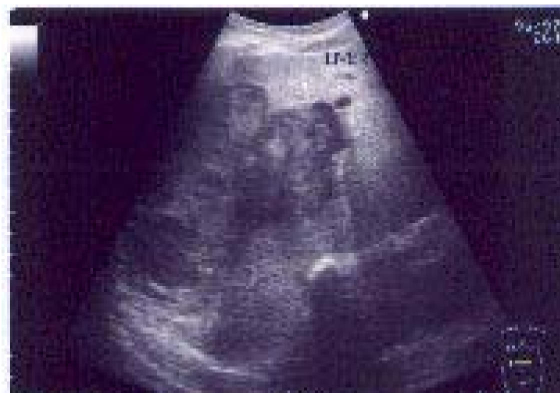

**Fig.1**: Ultrasound examination of abdomen showing fatty metamorphosis of liver with coalescent tuberculomas in the right lobe of liver

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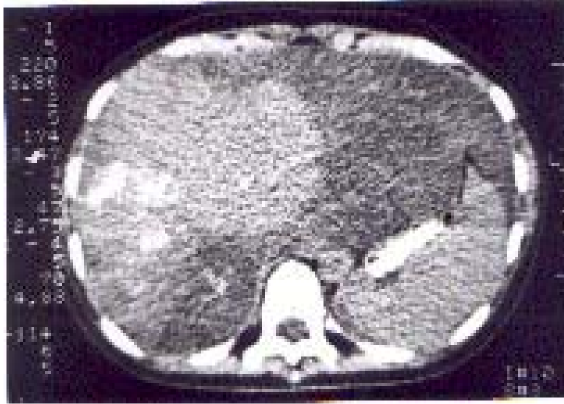

**Fig.2a**: Non-contrast-enhanced tomography of abdomen showing decreased attenuation of liver as compared to normal spleen with lesions in the right lobe of liver showing calcification

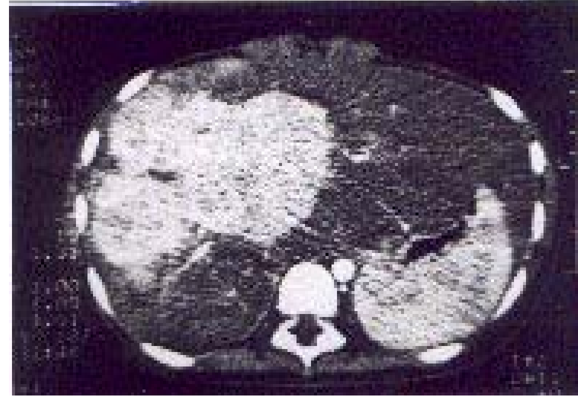

**Fig. 2b**: Contrast-enhanced computed tomography of abdomen showing intense enhancement of hepatic lesions during arterial phase

Plain and dynamic contrast enhanced computed tomography was done for evaluation of hepatic lesions. Non - contrast-enhanced computed tomography (Fig.2a) showed decreased attenuation of liver parenchyma by 10 HU(Housefield Units) compared to normal spleen,with a well-defined isodense area containing foci of calcification in the right lobe of liver. Contrast - enhanced - computed tomography (Fig.2b) showed intense enhancement of the lesion during arterial phase. The enhancement pattern followed the spleen during all phases of dynamic study.

Patient's gastrointestinal tract was evaluated by enteroclysis and barium enema examination for the primary cause of fatty metamorphosis of liver. Enteroclysis showed squaring of the ileal loop walls suggesting mucosal wall edema with features of ileo-caecal tuberculosis. Barium enema examination showed complete loss of haustral pattern with smooth mucosal walls throughout the colon, suggestive of colitis.

Ultrasound guided liver biopsy taken from the lesion revealed granulomatous lesion with acid-fast bacilli. Special stain for acid-fast bacilli was strongly positive suggestive of hepatic tuberculosis. The patient was put on anti-Koch's therapy, to which she responded well clinically.

## DISCUSSION

Hepatic tuberculosis is usually a disseminated disease associated with miliary tuberculosis. Most of the cases of hepatic tuberculosis reported in literature are in the form of localized tubercles or abscesses. These are usually misdiagnosed as primary or secondary liver tumors. Major risk factors include immunocompression (including AIDS), intravenous drug abuse, cirrhosis, alcoholism, steroid therapy, diabetes, neoplasia, endemic area dwellers, malnutrition and poor socio-economic status[1].

According to Levine[2], liver tuberculosis can be classified as (1) miliary tuberculosis, (2) pulmonary tuberculosis with liver involvement, (3) primary liver tuberculosis, (4) tuberculoma (abscess) and (5) tuberculous cholangitis. Hepatic tuberculosis is usually associated with tuberculous involvement elsewhere in the body. The gastrointestinal tract is the major route of infection in contrast to hematogenous spread of the miliary form. Liver involvement in disseminated tuberculosis occurs in up to 80% of cases[3].

Abdominal tuberculosis provides or presents a varied spectrum of clinical and radiological appearances, often requiring a high index of

suspicion of tuberculosis for making a correct diagnosis. Symptoms and signs can be non-specific and insidious and may mimic malignancy, with weight loss, abdominal masses and ascites. Chest radiographs may be normal in upto 50% of cases[3], as in the case described. Tubercle bacillus may never be cultured despite repeated sampling of stool, sputum, ascitic fluid, gastric washing, or even liver biopsy. Skin testing may also prove unhelpful if the patient is anergic[4].

Ultrasonography shows two different patterns: (1) hypoechoic lesions and (2) hypoechoic lesion with hyperechoic rims related to abscesses[5-6]. Hepatic tuberculomas appear usually on CT as round hypodense lesions. Contrast enhancement occurs in the peripheral granulomatous tissue, while the central low-density caseation necrosis shows less enhancement[5]. Calcification in the tuberculoma may increase in number, enlarge or remain unchanged at different stages of healing. The presence of calcification in a hepatic nodule may be the only clue to diagnosis of tuberculosis. The radiological diagnosis of hepatic tuberculoma remains difficult and pathological confirmation is required for diagnosis. The histological picture of hepatic tuberculoma is usually that of a large epithelioid tumor composed of conglomerate tubercles with central caseation necrosis[6]. The frequency of positive acid-fast smear is low, ranging from 0% to 45% and only 10% of cultures yield a positive result compared with a high positive rate (60%) in miliary tuberculosis[2].

In our case, the unusual finding was the association of hepatic tuberculomas with fatty metamorphosis of liver, which has never been reported to the best of our knowledge. We assume that fatty metamorphosis was due to malabsorption syndrome on account of long standing small bowel wall edema secondary to tuberculous gastrointestinal tract involvement, as was revealed on enteroclysis examination. The differential diagnosis on CT included – pyogenic and amoebic liver abscess, necrotic metastases, lymphoma and fibro-lamellar variety of hepatoma. The possibility of disseminated malignancy could be rejected in favour of diagnosis of abdominal tuberculosis on clinical findings and suggestive CT and US appearances.

Hepatic macronodular tuberculomas can mimic focal hepatic lesions, hence should be included in the differential diagnosis of hepatic focal lesions in endemic countries like India, especially with increasing spread of HIV leading to increased visceral and non-visceral tuberculosis. When associated with fatty metamorphosis of liver due to malabsorption syndrome, secondary to gastro-intestinal tuberculosis, the diagnosis becomes even more difficult . The importance of establishing the correct early diagnosis cannot be overstated, since untreated abdominal tuberculosis carries a 50% mortality rate, whereas with prompt effective treatment, the prognosis is very good.

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# POST-TEST COUNSELLING FOR HIV

With the uprising HIV epidemic in the country, it has become imperative for every physician to acquire knowledge and skills for HIV counselling comprising general post-test and HIV-positive patient counselling. The guidelines for post-test counselling are:

- ❑ Put the person at ease; establish personal rapport and begin by recapitulating what is remembered from pre-test session.

## If test is negative :

- ❑ Discuss meaning and significance of negative result.
- ❑ Go over the need for further testing, if necessary, without creating an alarm. Give priority to non-HIV tests.
- ❑ Reinforce information on HIV transmission and how chance acquisition of HIV can be prevented.

## If test is positive :

- ❑ Discuss meaning and significance of positive result.
- ❑ Go over the chances of a false-positive result and how confirmation can be obtained.
- ❑ Stress that a positive result does not mean AIDS, nor a prediction that AIDS will inevitably follow.
- ❑ Warn of the infectious status and the danger of passing on infection to spouse and casual sex-partners.
- ❑ Tell the person that the infectious status is life long, even if asymptomatic.
- ❑ Guide regarding occurrence of opportunistic infections and development of full blown AIDS.
- ❑ Discuss various preventive measures against infecting others and getting AIDS.
- ❑ Detail modes of treatment and cost of anti-viral therapy.
- ❑ Indicate and provide opportunities for future counselling.

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**Case Report** *Ind. J. Tub, 2003,50, 47*

# TUBERCULOUS MASTITIS: A REVIEW OF SEVEN CONSECUTIVE CASES

**Prem Parkash Gupta[1], K.B. Gupta[2], Rohtas K. Yadav[3] and Dipti Agarwal[4]****

*(Received on 29.8.02; Accepted on 8.12.02)*

***Summary***: Seven consecutive patients (6 females) with tuberculous mastitis among tuberculosis patients who attended PGIMS, Rohtak during a two year period, from January 2000 to December 2001 were reviewed. Investigations undertaken to confirm the diagnosis were a thorough clinical evaluation, tuberculin test, FNAC, biopsy, ultrasonography and mammography.

Only one patient had bilateral breast involvement, 5 belonged to the reproductive age group, 6 presented with a breast mass or nodule and one patient presented with a breast abscess. Constitutional symptoms were present in all the cases. All achieved cure after anti-tuberculosis treratment and only one patient required surgical intervention to get well.

## INTRODUCTION

Extra-pulmonary tuberculosis occurring in the breast is relatively rare despite one third of the world's population being infected with tubercle bacilli[1]. Tuberculosis of the breast was first documented in medical literature by Sir Astley Cooper[2] in 1829. Though cases of tuberculous mastitis have been reported worldwide[3-5], they are reported more frequently in India, probably due to a high prevalence of tuberculosis infection[6-7].

Tuberculous mastitis occurs far more frequently in women. In a review comprising 160 patients, only six were males[8] and a majority of the patients were in the reproductive age group of 21-40 years. Previously, tuberculous involvement of the breast was believed to be uncommon in older persons. However, in recent years it has been reported in the elderly also[9]. Two patients out of 7 of our patients were above 50 years of age.

Amongst the various risk factors considered to be associated with tuberculous mastitis are multiparity[10], lactation[11], trauma[11,12] and past history of suppurative mastitis[4,12]. Co-existing carcinoma of the breast has been reported in many studies[13,14] suggesting that even if tuberculous mastitis is identified, adequate tissue biopsy must be examined to rule out co-existing cancer.

Of the two types, primary tuberculous mastitis is confined only to the breast and is rare. Even though the breast may appear to be the only organ involved, the term 'primary tuberculous mastitis' should be reserved for those unusual cases where direct inoculation of the breast by tubercle bacilli has taken place. Secondary tuberculous mastitis is when there is a co-existing tuberculous lesion elsewhere in the body. In these cases, the major routes of spread are lymphatic, contiguous spread and the hematogenous one. Lymphatic spread, generally, is by retrograde extension from regional lymph nodes, usually axillary, but also from cervical or mediastinal nodes. This route is most common and 50 to 75 per cent of patients have involvement of axillary nodes at the time of presentation[4]. Extension from contiguous structures occurs from ribs, sternum, costo-chondral junction, the pleural space, and even through the rectus sheath, from an intra-abdominal source. Hematogenous spread has been documented to occur from miliary tuberculosis[4]. In the present series, five out of seven cases had tuberculous lesions elsewhere and in patient No.7, involvement of breast was due to trauma followed by suppurative mastitis. Involvement

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of both breasts is, extremely rare[15]: in our series only one patient had bilateral tuberculous mastitis and left breast was involved twice as frequently as the right one.

Tuberculosis of the breast presents in one of three ways: a painless breast mass, generalized breast edema or localized abscess, with or without axillary involvement. Generalized edema of the breast is usually associated with extensive involvement of axillary nodes. Breast abscess, with or without sinus tract drainage, is the least common presentation. Due to proximity of the axillary nodes, upper outer quadrant of breast is the most frequently involved site, though any area of the breast can be involved.

Mammography, ultrasonography and Gd-DTPA-enhanced dynamic MRI have been used to study breast involvement[16]. Mammographic findings include a mass, calcification, asymmetric density with spiculated margins and axillary node enlargement. On ultrasonography, a smooth bordered mass with thin boundary and heterogeneous, intermediate internal echoes are most commonly demonstrated. On Gd-DTPA enhanced dynamic MRI, almost half of the lesions show a significant enhancement at the first minute after injection. The maximum enhancing is usually greater than 500 normalized units. The enhancing pattern is usually a smooth or irregular ring appearance.

The demonstration of acid-fast bacilli on Ziehl Neelsen stain or growth of *M. tuberculosis* on culture of the FNA specimen remains the gold standard for diagnosis despite 38% yield in a large series of 160 cases[8]

Earlier, the therapy used to be exclusively surgical resection of the infected tissue, but now anti-tuberculosis chemotherapy supplemented by limited surgery or aspiration of abscesses[9,12] is considered adequate treatment. Tuberculous mastitis should probably be treated as any other form of extra-pulmonary tuberculosis generally for six months (2HRZE/4HR) or nine months (2HRE/7HR, 2HRZ/7HR), unless drug resistance is present. Found mostly in young, reproductive age group multiparous, lactating women, the clinical and radiological features of the disease are often non-specific, mimicking those of many diseases. The disease is likely to be missed if a high level of suspicion is lacking. We describe 7 consecutive cases of tuberculosis of breast (6 female and one male) diagnosed over a period of 2 years, from January 2000 to December 2001(Table 1).

## REVIEW OF CASES

A total of 2,754 new cases were diagnosed as having pulmonary or extra-pulmonary tuberculosis at the Post-graduate Institute of Medical Sciences, Rohtak (PGIMS) during the period. Out of these 7 (0.04%) patients were diagnosed to have tuberculous mastitis. The diagnosis was based on (i) suggestive clinical history of a painless breast mass, low grade fever, loss of appetite and weight loss, (ii) a positive tuberculin test using 1 TU of PPD RT 23, (iii) detection of acid fast bacilli in the specimen obtained from the breast lesion or biopsy specimen suggestive of chronic caseating granulomatous lesion with epithelioid cells, lymphocytes and Langhans' type giant cells or fine needle aspiration cytology revealing chronic inflammatory cells, mainly epithelioid cells, lymphocytes and Langhans' type giant cells with a (caseous) necrotic background, (iv) a supportive past history of pulmonary tuberculosis or tuberculous lymphadenitis, and (v) a favourable response to anti-tuberculosis drugs.

Co-existing fibrocystic disease, other chronic inflammatory diseases or tumor of the breast were carefully excluded using appropriate investigations including mammography, ultrasonography and biopsy of the lesion.

One patient (No.6) gave a family history of breast cancer (elder sister underwent radical mastectomy with radiotherapy for breast cancer) and just one female patient had bilateral involvement. The most usual presentation was a painless breast mass or a painless breast nodule but one patient presented with a breast abscess. Five patients had received anti-tuberculosis treatment (ATT) in the past: three received treatment for pulmonary tuberculosis ( one for inadequate duration) and two for tuberculous lymphadenopathy (one for inadequate duratioin).

**Table**. Demographic and Clinical Profile of the Seven patients

| Case no. | Age & Sex | Possible risk factor(s) | Breast involved | Presentation | Constitutional symptom (s) | Clinical history | Tuberculin test | Diagnosis |
|---|---|---|---|---|---|---|---|---|
| 1 | 60 F | Multipara | Right | Painless breast nodule | Fever, decreased weight & appetite | ATT for 2 months for PTB 7 months back | 12x12 mm | HP-S<br>R-ATT |
| 2 | 25 M | Basket ball player<br>? trauma | Right | Painless breast nodule | Low grade fever | - | 20x20 mm | FNAC-S<br>R-ATT |
| 3 | 60 F | Multipara, underlying suppurative mastitis | Left | Breast abscess | Fewer, loss in weight & appetite | Adequate ATT 2 years back for PTB | 13x14 mm | FNAC-S<br>FNAC-MTB |
| 4 | 40 F | Multipara | Left | Painless breast nodule | Low grade fever, generalized weakness | Adequate ATT for 8 months for PTB | 18x18 mm | FNAC-S<br>R-ATT |
| 5 | 32 F | Multipara, lactating | Bilateral | Painless breast nodule | Low grade fever, generalized weakness | Adequate ATT for 8 months for PTB | 18x18 mm | FNAC-S<br>R-ATT |
| 6 | 28 F | Multipara, lactating | Left | Painless breast mass | Fever, decreased appetite | Tubercular cervical LAP Adequate ATT | 20x20 mm | HP-S<br>R-ATT |
| 7 | 24 F | Traumatic injury (fall) | Left | Painless breast mass | Fever decreased appetite | Suppurative mastitis after a fall | 15x15 mm | FNAC-S<br>FNAC-MTB |

M = Male, F = Female, ATT = Anti-tuberculosis Treatment, PTB = Pulmonary tuberculosis, LAP = Lymphadenopathy

HP-S :Biopsy with histopathology report showing chronic caseating granulomatous lesions with epithelioid cells, lymphocytes and Langhans' type giant cells

FNAC-S :Fine needle aspiration cytology revealing chronic inflammatory cells mainly epithelioid cells, lymphocytes and Langhans' giant cells against (caseous) necrotic background

FNAC-MTB: Detection of *M.tuberculosis* bacilli by fine needle aspiration cytology

R-ATT: Favourable response to therapeutic trial of anti-tuberculosis treatment

The presumptive clinical diagnosis in six out of seven cases was that of breast cancer and in case No.3, an inflammatory breast abscess. Mammography in patient no.6 with a family history of breast cancer was negative. All patients had a positive tuberculin test with 1 TU of PPD RT-23. Acid fast bacilli were detected in fine needle aspiration specimen in two patients, histopathological examination of biopsy specimen showed typical granulomatous lesions in three patients, and in two patients, suggestive diagnosis was based on fine needle aspiration cytology alone with a favourable response to therapeutic trial of ATT.

All the patients were given short course chemotherapy (2HRZE/4HR) and all but one had excellent improvement without requiring any surgical intervention. Non-dependent drainage of breast abscess was undertaken in patient No.3 to prevent a discharging sinus and subsequent scaring. with good recovery at the end of 6 months of ATT.

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# FIFTY SEVENTH NATIONAL CONFERENCE ON TUBERCULOSIS AND CHEST DISEASES: A BRIEF REVIEW

**M.M. Singh***

The 57th National Conference on Tuberculosis and Chest Diseases was held in Panaji (Goa) from 26th to 29th September, 2002, under the joint auspices of the Tuberculosis Association of India (TAI) and the Goa TB Association, and the overall leadership of Dr. Arvind V Salelkar, Director of Health Services, Goa and Dr.D. Bhounsule, Hony. Secretary, Goa TB Association. Nearly 525 delegates attended the Conference. Dr. S.N. Tripathy, was President of the Conference.

A CME preceded the Conference. Two of the topics covered related to management of difficult asthma and community acquired pneumonia. The other two dealt with an overview of tuberculosis and RNTCP implemented very recently in the State of Goa. Besides, there was a separate session on immuno-modulators in TB & HIV under the chairmanship of Dr. M.M. Singh and Dr. S.N. Tripathy. The speakers discussed the role of "immuvac" *(Myco. W* vaccine*)* in the routine treatment of tuberculosis and MDR-TB. The results showed quicker conversion of sputum by about a month, without any drug side effects, and hopefully reducing the spread of infection. The results were equally good in new and re-treatment cases and with all grades of sputum positivity. This session was followed by Dr.P.K. Sen - TAI Oration "Private Public Mix - a prioritization under RNTCP - An Indian perspective" delivered by Dr. V.K. Arora, Director, LRS Institute of TB & Allied Diseases, Delhi.

The main conference was inaugurated by His Excellency Shri Mohd. Fazal, Governor of Goa and Dr. Suresh Amonkar, Hon'ble Health Minister of Goa. In his key note address, Dr. S.P. Agarwal, DGHS and Chairman, TAI discussed the high prevalence of tuberculosis and its socio-economic effect on the problem of HIV and MDR-TB and the efforts being made to combat the disease. He further informed the audience that about half the country had been covered under RNTCP and currently about 500 NGOs and nearly two thirds of medical colleges were providing services under the RNTCP. Dr.S.N. Tripathy, President of the Conference stressed the need for involvement of general practioners and NGOs in TB control, besides imparting of training regarding control programmes in the medical curriculum and strengthening of IEC activities. Dr. Suresh Amonkar,Hon'ble Health Minister of Goa suggested possible combined use of allopathic, homeopathic and ayurvedic medicines. The Minister further highlighted the problem of patients from neighbouring States who never turn up for further treatment after initial treatment in Goa.

Then followed the Awards Giving ceremony. Dr. M.M. Singh read out the citations and His Excellency the Governor of Goa presented the awards; Dr. P.K. Sen-TAI Gold Medal Oration Award went to Dr.V.K. Arora, the Ranbaxy-Robert Koch Oration award was given to Dr.R.C. Jain, former Director, LRS Instt. of TB and Allied Diseases, New Delhi, for "Story of Successes, Failures and Hopes", the Lupin-TAI Oration award went to Dr.I. Ranga Rao, former Dy. Director of Health Services, Hyderabad, for "TB Control Services in India: evaluation, progress and future", and the Dr.O.A. Sarma Guest Lecture Award was given to Dr.P.A. Deshmukh, Superintendent of the AD Memorial Hospital, Jamshedpur for "Emerging spectrum of chronic airways diseases". The Governor also felicitated Dr. Damodar Bhounsule, Hony. Secretary of the Goa TB Association for his long association with activities of the Goa Association. The Programme Committee had selected about 57 papers for presentation at the scientific session. The panel discussion on "RNTCP" was moderated by Dr.V.K. Arora, Director, LRS Instt. of TB and Allied Diseases, New Delhi. Dr.S. Sahu (WHO), Dr. Rani Balasubramanian (TRC), Dr. Prahlad Kumar, (NTI), Dr.P.B. Mehta (State TB Officer (STO) Gujarat) Dr.S.K. Srivastava (STO UP) and Dr. Rohit Sarin, (LRS Instt., Delhi) were the panelists.

*Vice-Chairman, Tuberculosis Association of India

**Review of Scientific Sessions**

The session on 'HIV and TB' covered 7 papers. A rising trend of HIV infection in tuberculosis patients (2.82%) as compared to the previous years was reported from Aligarh. The effectiveness of DOTS in TB & HIV co-infection was brought out in a study from Bombay. Among the HIV +ves, 86.27% were suffering from TB and the rest had non-tuberculous conditions, according to a paper from Kanpur. Another study reported 4% mycobacteremia among the HIV positives.

In the session on 'Epidemiology', the TRC, Chennai reported the rates of ARI found in three districts of Maharashtra (National Sample Survey) and the role of Community DOT Providers. Community participation in RNTCP was highlighted by Dr.V.K. Arora, while a study from Delhi reported the extent of default under RNTCP as 8.4%, mainly in the intensive phase of treatment.

In the session on 'extra-pulmonary tuberculosis and COPD', a study assessed the role of ultrasound guided FNAC for peripheral lesions in the chest and another presented retrospective review of the post-operative radiological findings. A paper from Chennai found increased sputum positivity in sputum negative pulmonary tuberculosis cases after bronchodilator therapy. Dr.K.B. Gupta from Rohtak maintained that typical *M.tuberculosis* were the only organisms found in histopathologically proved TB cervical adenitis cases.

In the session on 'NTP & RNTCP', the prevalence of initial drug resistance was reported to be 2.2% from Bangalore City. A study brought out the reduction of cost to patients on DOTS therapy. Category l regimen was found to be equally effective in children and adolescents in a study. Dr. P.P. Mandal presented various schemes for involvement of general practitioners, as proposed by the Central TB Division, Ministry of Health & Family Welfare. Good results with Category l regimen were claimed by Dr.K. Rajaram from Chennai in non-insulin dependent diabetes mellitus (NIDDM) cases. A random sample survey in Tamil Nadu found ARI of 1.8%. Over 94% of the patients from Delhi under DOTS expressed satisfaction with the services provided but also pointed to the less than optimal infrastructure facilities and need for augmentation of supervision of DOTS centres and the staff.

In the session on "Social aspects", one NGO study reported 92% success using financial incentives with RNTCP regimens. Another paper presented experience with combining private practitioners and RNTCP with the help of an NGO. A new health related quality of life scoring method for cases of tuberculosis for follow up under RNTCP was presented by Dr. Dhingra from the New Delhi Tuberculosis Centre. An external quality assurance scheme for sputum microscopy implemented in Bombay in collaboration with an NGO found much higher levels of false positives and negatives in the reported results under DOTS pointing to the need for better training.

In the session on MDR-TB, a study among Armed Forces personnel estimated drug resistance to one or more drugs as 13.7%. Only 42% favourable response was reported among multi-drug resistant tuberculosis cases by using individually tailored regimens. A paper from Calcutta reported that doing culture and sensitivity tests had no advantage over assessment of the patient's previous drug history in selecting the treatment regimen.

In the concluding session on "Diagnostic procedures and treatment - Miscellaneous papers", pharmacokinetics of Ofloxacin, when administered alone or in combination with other drugs, showed no difference in MIC values. A study from Armed Forces showed that the diagnostic yield from transthoracic needle aspiration was 61.2% as compared to 23.6% from fibroptic bronchoscopy. A paper from TRC, Chennai presented estimates of *in vitro* activity of different quinolones against clinical isolates of *M.tuberculosis*. Under poster presentations, a paper reported 32.4% hypercalcemia among patients of tuberculosis. Another depicted fall in default rates with the implementation of DOTS strategy and relative efficacy of fast plaque TB test vis-a-vis smear and culture on LJ medium. A noteworthy feature of the Conference was that a number of papers were presented by young workers who showed keen interest in presenting papers of good quality.