INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CLINICAL STUDY ON HAEMATOLOGICAL AND BIOCHEMICAL PROFILE OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS PATIENTS AND ITS RELATIONSHIP WITH PATIENTS SOCIOECONOMIC STATUS AND BODY MASS INDEX

Respiratory Medicine

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ABSTRACT

In the present study bacteriologically confirmed and/or clinico-radiologically diagnosed new or recurrent cases of pulmonary and extrapulmonary tuberculosis attending the OPD and IPD of Dept of Respiratory Medicine of I.P.G.M.E & R /S.S.K.M hospital Kolkata from December 2017 to May 2019 were studied for socioeconomic status using Modified B.G.Prasad scale 2017 and Nutritional status using their Body Mass Index. The various haematological and biochemical parameters were determined and correlation of these parameters with body mass index and Socioeconomic class were evaluated. 79.25 % patients of Pulmonary tuberculosis and 27.08% patients of Extrapulmonary Tuberculosis had anaemia, showing increasing prevalence of anaemia in pulmonary than extrapulmonary tuberculosis. In both pulmonary and extrapulmonary tuberculosis having anaemia, normocytic normochromic type is more common than microcytic hypochromic type. 49.05% cases of pulmonary tuberculosis and 41.67 % cases of extrapulmonary tuberculosis had Hyponatremia while 28.3% cases of pulmonary tuberculosis and 25% cases of extrapulmonary Tuberculosis had Hypokalaemia, though they showed no statistically significant correlation.

KEYWORDS

Haematological, Biochemical Profile, Pulmonary And Extrapulmonary Tuberculosis, Socioeconomic Status And Body Mass Index

INTRODUCTION

Tuberculosis is a great menace to mankind since ancient times. The genus *Mycobacterium* was known to originate 150 million years ago. The skeletal deformities of tuberculosis have been demonstrated in Egyptian mummies [1]. But the causative agent of this dreadful disease was not known for longer periods. The discovery of *Mycobacterium tuberculosis*, the causative agent for tuberculosis was by Robert Koch in 1882 using light microscopy and a special staining technique [2]. Tuberculosis related deaths are rising in the world in an alarming trend. No wonder that this chronic infection is setting the major brakes in human resources and economy of a nation particularly the developing ones.

Reversible peripheral blood abnormalities are commonly associated with pulmonary tuberculosis and these hematological changes act as marker for the diagnosis, prognosis and response to therapy. TB cause profound bone marrow and peripheral blood abnormalities by modulating normal hematopoiesis and the disease become more severe when it is co-infected with HIV because of weakened immunity [3]. In pulmonary tuberculosis many hematological and biochemical abnormalities are common and they are valuable aids to diagnosis. A variety of haematological changes have been described in patients with tuberculosis such as anemia, increased erythrocyte sedimentation rate, low serum albumin level and leukocytosis [4]. In active TB cases, anemia and iron deficiency erythropoiesis was observed. A close relationship was found to be exist between severity of tuberculosis and hematological abnormalities. During antituberculous treatment improvements in the hematological values such as, rise in hemoglobin and hematocrit values, were used as indicators reflecting good response to the treatment [5]. Furthermore, fall in values of platelet, white cell and erythrocyte sedimentation rate (ESR) were regarded as markers of good disease control [6]. India has a major share of the global incidence of tuberculosis (TB) (including MDR-TB) and TB related mortality. According to estimates for 2010, TB incidence was 185 per 100,000 with 320,000 TB-related deaths. HIV infection plays a relatively minor role in the TB epidemic in India, whereas under-nutrition, smoking, and diabetes are considered more important risk

factors. Recent systematic reviews have established the role of under-nutrition as an important risk factor for reactivation of latent TB infection to TB disease, while obesity has been found to be protective against TB.

Tuberculosis can lead to or worsen pre-existing under-nutrition, by decreasing appetite, and by increased catabolism. High prevalence of under-nutrition in TB patients has been reported in other settings, and has been linked to excess deaths, and increased risk of relapse. There have been few reports on prevalence, severity and implications of under-nutrition in Indian patients with TB, particularly from India's rural areas, where the majority of Indians live, and which have a higher prevalence of poverty, under-nutrition and self-reported TB than urban areas [7-10].

The present study has been an attempt to investigate hematological and biochemical changes in patients with active pulmonary and extrapulmonary TB. An attempt has also been made to assess the relationship of these effect of these haematologic and biochemical abnormalities with the patients nutritional status measured by his/her body mass index and with their socioeconomic status.

To ascertain the association between the haematological and biochemical parameters of Tuberculosis (both Pulmonary and Extra Pulmonary) patients with their Body Mass Index and Socio Economic status.

MATERIALS AND METHODS

Place Of Study

Department of Respiratory Medicine, IPGME&R, KOLKATA, West Bengal from December 2017 to May 2019.

Ethical Consideration

Ethical and research clearance was obtained from the Ethical Committee IPGME&R, KOLKATA, West Bengal, and Permission to conduct the study was sought from the respective hospital department authorities. Personal interview was conducted by the author to every patient. A standard proforma was filled up at the time of interview and

informed consent was obtained from the patients before enrollment to the study.

Inclusion Criteria:

Bacteriologically confirmed and Clinically diagnosed New or Recurrent cases of Pulmonary and Extrapulmonary tuberculosis by

- Smear microscopy
- Quality assured molecular tests (Gene Xpert Test or Cartridge Based Nucleic Acid Amplification Test)
- Culture of Mycobacterium Tuberculosis from Pulmonary or Extrapulmonary samples
- Appropriate Imaging technique
- Appropriate biochemical tests and Clinical profit

Exclusion Criteria:

- Patients of age <12 years
- Presence of pre-existing renal disease, liver disease, bleeding and haematological disorders.
- Patients requiring Modifying ATD regimen excluded from the final analysis.
- Drug Resistant Tuberculosis.
- HIV co-infection.
- Refusing to give consent.

Parameters To Be Measured:

Clinical Parameters: History and physical examination as per case format.

Statistical Analysis

Data was first entered into a Microsoft excel spread sheet and then analysed by on graphpad.com by Graphpad software. Data have been summarized by routine descriptive statistics namely mean & SD for numerical variables where these variables are met normally distributed & counts percentage for categorical variables. Univariate comparisons between patients with Pulmonary tuberculosis and those with Extrapulmonary tuberculosis were performed using Fischers exact test for categorical variables and the Student's t test for continuous variables. All tests of significance were two sided, and the p value of less than 0.05 was considered significant.

RESULTS AND ANALYSIS

Our study showed that 53 cases of newly diagnosed adult Pulmonary Tuberculosis and 48 cases of adult Extra Pulmonary Tuberculosis attending the Chest Department of a Tertiary Medical College were evaluated for their Haematological, Biochemical profile and its relationship with their Body Mass Index and Socioeconomic Status. Out of total 101 cases of Tuberculosis studied, 53 cases are having Pulmonary Tuberculosis, and remaining 48 cases are of Extrapulmonary.

We found that out of total 53 cases of Pulmonary Tuberculosis, 69.81 % (37/53) cases are bacteriologically confirmed while 30.18 % (16/53) cases are clinicoradiologically diagnosed cases. Again, out of 48 total cases of Extra Pulmonary Tuberculosis, 16.66% (8/48) are bacteriologically confirmed while 83.33 % (40/48) are clinicoradiologically diagnosed cases. The mean age of Pulmonary Tuberculosis was 42.36 years with standard deviation of 13.97 years. About 49 % belong to age group of 17 – 40 years, 37.7% belong to 41 – 60 years and 13.2% in geriatric age group (>60 years).

We showed that the mean age of Extra pulmonary tuberculosis was 36.54 years with standard deviation of 11.54 years. About 62.5 % belong to age group of 17 – 40 years, 35.4 % belong to 41 – 60 years and only 2 % in geriatric age group. So, the most common age group for both Pulmonary and Extra Pulmonary tuberculosis was 17 – 40 years regarded as the most productive age group from socioeconomic point of view.

In Pulmonary Tuberculosis 81.13 % (43/53) were male and 18.86% (10/53) were female individuals.

In our study showed that extra Pulmonary Tuberculosis 64.58% (31/48) were male and 35.41% (17/48) were female individuals. So there is a male preponderance for both Pulmonary and Extra Pulmonary Tuberculosis. In Pulmonary Tuberculosis cases (n=53), 54.7 % (29/53) cases were suffering from MALNUTRITION with BMI <18.5 kg/m², 43.3% (23/53) have Normal nutrition status with BMI within normal range (18.5-25 kg/m²), and 1.8 % (1/53) were of Over Nutrition status having BMI >25 kg/m². In Extra Pulmonary Tuberculosis cases (n=48) 10.4 % (5/48) cases were suffering from

MALNUTRITION, 81.2 % (39/48) have Normal nutrition status, and 8.33 % (4/48) were of Over Nutrition status.

We found that malnutrition was more prevalent in Pulmonary Tuberculosis than the Extra Pulmonary one. In fact, about 34 cases (33.66% of total) are suffering from Malnutrition, of which 29 cases (85.29%) are having Pulmonary tuberculosis and 05 (14.7%) are having Extra Pulmonary tuberculosis. Out of 61 cases belonging to Lower Middle class, 46 (75.41%) cases have Pulmonary tuberculosis, and 15 (24.59%) cases have Extra Pulmonary tuberculosis. Out of 21 cases belonging to Middle socioeconomic class, 4 (19.05%) cases have Pulmonary tuberculosis and 17 (80.95%) cases have Extra Pulmonary tuberculosis. Out of 16 cases belonging to Upper middle socioeconomic class 3 (18.75%) cases have pulmonary tuberculosis and 13 (81.25%) cases have Extra Pulmonary tuberculosis.

We showed that the remaining 3 cases belonged to Upper socioeconomic class and all of them have Extra Pulmonary tuberculosis. So Pulmonary Tuberculosis is associated more with Lower Socioeconomic Class (46 out of 53 ie, 75.41%) compared to Extra Pulmonary Tuberculosis (15 out of 48 ie, 24.49%). Anaemia defined as (Hb<9 gm/dl in females and Hb<10 gm/dl in males) was present in 79.25 % (42/53) cases of Pulmonary Tuberculosis and 27.08 % (13/48) cases of Extra Pulmonary Tuberculosis. Anaemia defined as (Hb<9 gm/dl in females and Hb<10 gm/dl in males) was present in 79.25 % (42/53) cases of Pulmonary Tuberculosis and 27.08 % (13/48) cases of Extra Pulmonary Tuberculosis.

In our study Out of 42 cases of Pulmonary Tuberculosis having Anaemia, 30 (71.42%) cases are Normocytic Normochromic type and 12 (28.57%) patients are of Microcytic Hypochromic types. Whereas, out of 13 cases of Extra Pulmonary Tuberculosis having Anaemia, 9 (69.23%) cases are Normocytic Normochromic type and 4 (30.76%) patients are of Microcytic Hypochromic types. So the trend shows Normocytic Hypochromic type of anaemia to be more common than Microcytic Hypochromic type, both in Pulmonary and Extra Pulmonary Tuberculosis.

Out of total 61 cases belonging to Lower Middle socioeconomic class 43 (70.49%) are anaemic.

Our study showed that Out of total 21 cases belonging to Middle socioeconomic class 5 (23.81%) cases are anaemic. Out of total 16 cases belonging to Upper Middle socioeconomic class, 7 (43.75%) cases are anaemic. Whereas, no one of 3 cases belonging to Upper socioeconomic class are having anaemia. So among 55 cases having anaemia, 43 ie, 78.18 % belonged to Lower Middle class. Out of 33 cases of tuberculosis having Malnutrition 28 (84.84%) are having Anaemia. Out of 62 cases of tuberculosis, normally nourished, only 27 (43.54%) are having Anaemia. Out of 06 cases of tuberculosis, over nourished, only 01 (16.66%) is Anaemic.

Out of total 16 cases belonging to Upper Middle socioeconomic class, only 03 (18.75%) cases are having Hypoproteinemia. Whereas, no one of 3 cases belonging to Upper socioeconomic class are having Hypoproteinemia. Out of 33 cases of tuberculosis having Malnutrition 25 (75.75%) are having HypoProteinemia. Out of 62 cases of tuberculosis, normally nourished, only 24 (38.70%) are having Hypo Proteinemia. Out of 06 cases of tuberculosis having over nutrition only 01 (16.66%) is HypoProteinemic. HypoAlbuminemia, defined as Serum albumin < 3.5 gm/dL was present in 35 out of 53 ie 66.04% cases of Pulmonary Tuberculosis and 13 out of 48 ie 27.08% cases of Extra Pulmonary tuberculosis.

We found that total 61 cases belonging to Lower Middle socioeconomic class 37 (60.66%) are having HypoAlbuminemia. Out of total 21 cases belonging to Middle socioeconomic class 08(38.10%) cases are having HypoAlbuminemia. Out of total 16 cases belonging to Upper Middle socioeconomic class, only 03 (18.75%) cases are having HypoAlbuminemia. Whereas, no one of 3 cases belonging to Upper socioeconomic class are having HypoAlbuminemia. So, out of 48 cases of HypoAlbuminemia, 37 ie, 77 % belonged to Lower Middle Class Family.

Our study showed that out of 33 cases of tuberculosis having Malnutrition 24(72.72%) are having HypoAlbuminemia. Out of 62 cases of tuberculosis, normally nourished, only 24 (38.70%) are having HypoAlbuminemia. Out of 06 cases of tuberculosis,

overnourished, only 2 (33.33%) are having HypoAlbuminemia. Hypocalcemia, defined as serum corrected calcium <8.5 meq/L was present in 27 out of 53 ie 50.94% cases of Pulmonary tuberculosis and 15 out of 48 ie, 31.25% cases of Extra Pulmonary tuberculosis, showing increasing prevalence of Hypocalcemia in pulmonary than extrapulmonary tuberculosis.

We found Out of total 61 cases belonging to Lower Middle socioeconomic class 30 (49.18%) are having HypoCalcemia. Out of total 21 cases belonging to Middle socioeconomic class 09(42.86%) cases are having HypoCalcemia. Out of total 16 cases belonging to Upper Middle socioeconomic class, only 03 (18.75%) cases are having HypoCalcemia. Whereas, no one of 3 cases belonging to Upper socioeconomic class are having HypoCalcemia. Out of 33 cases of tuberculosis having Malnutrition 23 (69.69 %) are having HypoCalcemia. Out of 62 cases of tuberculosis, normally nourished, only 17 (27.41 %) are having HypoCalcemia. And out of the remaining 06 cases of tuberculosis, overnourished only 01 (16.66%) case is having hypocalcemia.

We showed that HypoVitaminosis D3, defined as serum 25 (OH) vit D3 < 12 ng/mL was present in 24 out of 53 ie 45.26% cases of Pulmonary tuberculosis and 12 out of 48 ie, 25% cases of Extra Pulmonary tuberculosis. Out of total 61 cases belonging to Lower Middle socioeconomic class 28 (45.90%) are having Hypovitaminosis D3. Out of total 21 cases belonging to Middle socioeconomic class 07(33.33%) cases are having Hypovitaminosis D3. Out of total 16 cases belonging to Upper Middle socioeconomic class, only 01 (6.25 %) cases are having Hypovitaminosis D3. Whereas, no one of 3 cases belonging to Upper socioeconomic class are having Hypovitaminosis D3.

Out of 36 cases of HypoVitaminosis D3, 28 ie 77.77 % cases belonged to Lower Middle Class family.

We found Out of 33 cases of tuberculosis having Malnutrition 20 (60.60 %) are having HypoVitaminosis D3. Out of 62 cases of tuberculosis, normally nourished, only 15 (24.19 %) are having HypoVitaminosis D3. And out of the remaining 06 cases of tuberculosis, over nourished only 01 (16.66%) case is having HypoVitaminosis D3. Out of total 53 cases of Pulmonary tuberculosis cases, 26 (49.05 %) cases have HypoNatremia, whereas out of total 48 cases of Extra pulmonary tuberculosis cases, 20 (41.67 %) cases have HypoNatremia. Out of total 53 cases of Pulmonary tuberculosis cases, 15 (28.3 %) cases have HypoKalaemia, whereas out of total 48 cases of Extra pulmonary tuberculosis cases, 12 (25 %) cases have HypoKalaemia.

DISCUSSION

All efforts were made to determine the haematological and biochemical parameters of the tuberculosis patients and to ascertain the correlation between these parameters and the patients nutritional status and socioeconomic class.

In this study total 101 cases of Tuberculosis attending the chest department (OPD and Indoor) of a tertiary medical college are studied, out of which 53 (52.47%) are having Pulmonary tuberculosis and 48 (47.52%) are having Extrapulmonary tuberculosis.

Among the 53 Pulmonary tuberculosis patients, 37 ie, 69.81% are bacteriologically confirmed while 16 ie, 30.18% are clinico-radiologically diagnosed cases. Again, among the total 48 extrapulmonary tuberculosis patients, 08 ie 16.66 % are bacteriologically confirmed and 40 ie, 83.33% are clinico-radiologically diagnosed.

In this study 49 % cases of pulmonary tuberculosis and 62.5% cases of extrapulmonary tuberculosis belonged to age group of 17- 40 years, 37.7% of pulmonary and 35.4% of extrapulmonary tuberculosis belonged to age group of 40-60 years while 13.2 % of pulmonary and 2.08% of extrapulmonary cases belonged to geriatric age group. So 17-40 years is the most common age group for both Pulmonary and Extrapulmonary cases of tuberculosis.

In pulmonary tuberculosis cases 81.13% were males while 64.58% cases are males in cases of extrapulmonary tuberculosis. So male is most preponderant in both pulmonary and extrapulmonary cases of tuberculosis.

Saket kumar Mondal, Laxmikant Chavan studied 100 patients above 12 years of age without HIV coinfection of newly diagnosed cases of

pulmonary tuberculosis and extrapulmonary tuberculosis for haematological analysis, out of which 63 (63%) were under 40 years of age (range 12 to 39), whereas, 37 (37%) were more or equal to 40 years of age (range 40 to 78). Mean age of young 3.7 years adults (below 40 years) was 32.71 & 1.03 elderly (more than or of 40 years) was 67.57 respectively. In their study there were 64 males(64%) and 36 (36%) females, showing male preponderance of tuberculosis among males.

Parasappa Jotteppa Yaranal, Toolhally Umashankar, Sadula Govindareddy Harish studied 100 patients of fresh pulmonary tuberculosis with sputum positive for AFB. There were 71 males and 29 females with mean age of 41 years. Mean age for males was 42 years and mean age for females was 35 years. 61% of patients were in age group of 20 – 50 years, 8% of the total population was below the age of 20 years and 31% of the total population was above 50 years.

In the study by Anurag Bhargava, Madhuri Chatterjee, Yogesh Jain, Biswaroop Chatterjee et al in a consecutive cohort of 1695 adult patients with pulmonary tuberculosis in rural India during 2004 – 2009 using multivariable logistic regression to obtain adjusted estimates of the association of nutritional status with deaths during treatment. At the time of diagnosis, median BMI and body weights were 16.0 kg/m² and 42.1 kg in men, and 15.0 kg/m² and kg in women, indicating that 80% of women and 67% of men had moderate to severe under-nutrition (BMI < 17.0 kg/m²). Fifty two percent of the patients (57% of men and 48% of women) had stunting indicating chronic under-nutrition.

Variables Measured:

Demographic details, general living conditions, household ownership of luxury items, and weekly consumption of four proteins (meat, fish, chicken and cheese). Three socioeconomic indices were constructed from the above variables. No significant differences were found between cases and controls on most of the variables. Overall significant differences were found on the pattern of language groups (chi-square; $p = 0.031$), employment groups (chi-square; $p = 0.029$) and meat (chi-square; $p = 0.012$) and chicken consumption (chi-square; $p = 0.034$). A tendency was observed for more employed cases than controls to have a primary school education. However, no conclusive evidence was found on the association between socioeconomic factors and risk of developing TB. The development of a more appropriate socioeconomic measure for developing countries is a necessary step for further research.

In this study 42 out of 53 ie 79.25% cases of pulmonary tuberculosis had anaemia, while 13 out of 48 ie, 27.08% cases of extrapulmonary tuberculosis cases had anaemia, with statistical analysis showing increasing in the prevalence of anaemia in pulmonary than extrapulmonary tuberculosis is a significant one with Fischers exact test 2 tailed p value < 0.001 .

Out of 42 cases of pulmonary tuberculosis having anaemia, 71.25% were normocytic normochromic type and 28.57% were microcytic hypochromic type. Again out of 13 cases of extrapulmonary tuberculosis, 69.23 % are of normocytic hypochromic type and 30.76 % are microcytic hypochromic type. So normocytic hypochromic type of anaemia is the more common type than microcytic hypochromic type in both pulmonary and extrapulmonary tuberculosis.

All chronic infections including TB can cause anemia. Various pathogeneses have been suggested in TB-associated anemia, but most studies have shown suppression of erythropoiesis by inflammatory mediators as a cause of anemia. Nutritional deficiency and malabsorption syndrome can deepen the severity of anemia.

It was studied here that anemia was present in 70.49% cases in lower middle class, 23.81% in middle class, and 43.75% in upper middle class, thus showing a decreasing trend in the prevalence of anaemia while moving up the socio economic class. The chi-square for the trend is < 0.001 which is statistically significant one.

In this study Leucocytosis was present in 9 out of 53 ie, 16.98% cases of Pulmonary tuberculosis and 8 out of 48 ie, 16.66% cases of Extrapulmonary tuberculosis.

ESR was more than 30 in 83.01% cases of Pulmonary and 16.98 % cases of extrapulmonary tuberculosis. The trend of increasing prevalence of high ESR in pulmonary tuberculosis than extrapulmonary type is statistically significant with Fischers exact test 2 tailed p value 0.04.

It was found in the study that hypoproteinemia was present in 63.93% cases in lower middle class, 33.33 % in middle class, and 18.75% in upper middle class, thus showing a decreasing trend in the prevalence of hypoproteinemia while moving up the socio economic class. The chi-square for the trend is <0.001 which is statistically significant correlation.

Hypoproteinemia was also seen in 75.75 % cases of patients having Malnutrition and there was a decreasing trend in the prevalence of hypoproteinemia with the improvement of nutritional status which revealed statistically significant with chi-square for trend p value <0.001.

HypoVitaminosis D3 was also seen in 60.60% cases of patients having Malnutrition and there was a decreasing trend in the prevalence of HypoVitaminosis D3 with the improvement of nutritional status which revealed statistically significant correlation with chi-square for trend p value 0.0014.

In this study, among Pulmonary tuberculosis 49.05 % cases have hyponatremia and 28.3 % have Hypokalaemia while among Extrapulmonary tuberculosis 41.67% have Hyponatremia and 25% have Hypokalaemia respectively.

CONCLUSION

The present study shows that patients of Pulmonary Tuberculosis suffers more from anaemia, hypoproteinemia and hypovitaminosis D3 compared to cases of Extrapulmonary Tuberculosis.

Also presence of these parameters namely anaemia, hypoproteinemia and hypovitaminosis D3 is correlated to poor nutritional and socioeconomic status of the patient. The impact of deranged haematological and biochemical parameters on outcome among cases of tuberculosis needs to be addressed in a larger study in future.

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