ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-7 | JULY-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

THE ASSOCIATION BETWEEN ANEMIA AND DELAYED SPUTUM CONVERSION: EVIDENCE FROM A COHORT OF PULMONARY TUBERCULOSIS PATIENTS ATTENDING DIRECTLY OBSERVED TREATMENT SHORTCOURSE (DOTS) CENTRE FROM NEW DELHI

Community Medicine

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ABSTRACT

BACKGROUND: Sputum Smear Positive(SSP) Pulmonary Tuberculosis (TB) is the infectious form of TB and is associated with reversible peripheral blood abnormalities.
OBJECTIVES: To determine the hematological and serum ferritin profile and its association with delayed sputum conversion (DSC).
METHODS: The prospective study was conducted among 200 newly diagnosed smear positive pulmonary TB patients at DOTS centre, Najafgarh, New Delhi between 2015-16. Hemoglobin and serum ferritin were measured at the start and the end of Intensive Phase (IP). Data was entered in MS-Excel. Multi-variate logistic regression was applied using Predictive Analytics SoftWare.
RESULTS: The prevalence of DSC was 21.5%. In multi-variate logistic regression, it was found that odds of delayed sputum conversion were significantly higher if the TB patients had anemia at the end of IP.
CONCLUSIONS: Not only the drug therapy, but a multi-pronged strategy can help in prevention and control of tuberculosis infection.

KEYWORDS:

DOTS-centre, Delayed Sputum Conversion, Anemia, Hemoglobin.

Introduction:
Tuberculosis (TB) is a major global health problem and ranks as the second leading cause of death from infectious diseases, after Human Immunodeficiency Virus.[1] Sputum Smear Positive(SSP) Pulmonary TB is the infectious form of TB and is mainly responsible for transmitting the disease via cough or sneeze which expel droplet nuclei carrying infectious bacilli.[2] In spite of various serological markers, detection of Acid Fast Bacilli (AFB) remains an important measure for the diagnosis and treatment response.[3]

Pulmonary TB is commonly associated with reversible peripheral blood abnormalities. The prevalence of anemia among TB patients ranges between 30–94%.[4-8] It has been shown that anemia is more likely to occur among TB patients compared to healthy controls.[9] More importantly, anemia is associated with more severe forms of TB and poorer TB outcomes, including death.[5,7,10] Iron deficiency Anemia (IDA) is the most common cause of nutritional deficiency anemia in the developing world.[11] It is important to establish the presence of IDA in the patients of TB and other chronic inflammatory or infectious disease, as even mild iron deficiency (ID) causes a significant impairment in the immunological status and reduces the capacity of such patients to control infections.[12] Bone marrow examination for iron is the gold standard for detecting Iron Deficiency in such conditions.[13,14] Being an invasive procedure, it causes patient discomfort and anxiety. Hence, serum ferritin (SF), a non-invasive parameter reflecting iron stores, is being extensively studied. However, SF is an acute phase reactant and is increased in inflammations and infections. In most cases of Chronic Disease (CD), SF is disproportionately increased relative to iron stores.[15,16] In such a clinical setting of CD it is, therefore, not reflective of bone marrow iron. To compensate for this inflammatory component, many authors have suggested higher cut-off values, predictive of ID in patients with anemia of chronic disorders.[17-20]

In India, both TB and anemia are public health problems but there is limited literature on association between anemia and delayed sputum conversion among TB patients. Hence, against this background, the present study was planned to determine the hematological and serum ferritin profile among the newly diagnosed TB patients and to explore the association between anemia and delayed sputum conversion. We conducted a prospective study to examine the effect of anemia on sputum smear conversion at the end of two months of anti-tuberculosis therapy (ATT).

Materials and Methods:
The prospective study was conducted at Directly Observed Treatment Shortcourse (DOTS) centre, of Rural Health Training Centre (RHTC), Najafgarh, New Delhi between December 2014 and May 2016. It has a Designated Microscopiy Centre (DMC) for TB, which functions under the chest clinic Rao Tula Ram Memorial Hospital, Jaffarpur, New Delhi.[21] The sample size was calculated by the formula $n = 4\ pq/\ l^2$, where p was 12.8% from a study conducted in Andhra Pradesh in 2013.22 With an absolute error of 5% and a no-response rate of 10%, the total sample size was found out to be 200. First 200 newly diagnosed smear positive category I pulmonary TB patients aged more than 15 years enrolled between February 2015 and January 2016 were included and previously diagnosed category I, category II and category IV pulmonary TB patients were excluded from the study.

A pre-tested interviewer administered questionnaire was used in Hindi language to collect data from study participants. The questionnaire included the questions on socio-demographic characteristics (age, education, occupation, etc); information related to TB and anemia. This was followed by a general physical examination, anthropometric assessment and systemic examination of the study participants. Blood was collected from the cubital vein, with the help of 26 Gauge needle and a vacutainer and then transferred into 2 labeled vials, a plain vial and an EDTA coated vial. Hemoglobin (Hb) was measured by Hematology Automated Analyser and peripheral smear was done by thin blood smear and SF was measured by ELISA method.

The sputum grading was scanty, 1+, 2+ and 3+. Scanty means 1 to 9 AFB in 100 oil immersion fields.1+ means 10-99 AFB in 100 oil immersion fields. 2+ means 1 to 10 AFB per oil immersion field in at least 50 fields. 3+ is more than 10 AFB per oil immersion field in at least 20 fields as per RNTCP guidelines.[23] Anemia is defined per WHO guidelines as hemoglobin <13 g/dl (males) or <12 g/dl (female). Anemia was further categorized according to severity with the following hemoglobin cut off points: mild anemia; 11.00 – 13 g/dl (male) and 11.00 – 12 g/dl (female); moderate anemia 8.00 – 11 (both sexes); severe anemia hemoglobin less than 8 g/dl for both sexes as per WHO guidelines.[24] Delayed Sputum Conversion: As per the Revised National Tuberculosis Control Program (RNTCP), response to treatment for TB is assessed by sputum smear examination for AFB, which is done at the end of 2, 4 and 6 months of DOTS therapy. For the purpose of our study if a patient remained sputum smear positive at the end of 2 months of intensive phase treatment, we labelled him or her as a case of delayed sputum conversion. The reference range for BMI as recommended for Indian population by ICMR,2011 is as follows: Under-weight- <18.5 kg/m^2, Optimal-weight- 18.5 - 22.9 kg/m^2, Over-weight- 23 – 24.99 kg/m^2 and Obese- >25 kg/m^2. Serum ferritin values ≤10 µg/l were diagnostic of low Bone Marrow iron stores and therefore

of Iron deficiency.[25] In a study conducted by Kotru M,[26] revealed that raising the cut- off levels of SF to ≤30 µg/l was most effective in predicting absent bone marrow iron. SF level of ≤30 µg/l, which is higher than the usual cut-off of ≤10 µg/l used in uncomplicated iron deficiency, was recommended to reasonably diagnose iron deficiency in a setting of TB. For the purpose of our study, a cut-off value of ≤ 30 µg/l was used for the iron deficiency status for the TB patients.26 Anthropometric assessments, blood sample collection and sputum smear examination were done at the start and the end of 2 months of IP of anti-tuberculosis treatment.

Data was entered in MS Excel and analysis was done using Predictive Analytics SoftWare (PASW) licensed version 21. The variables were analyzed using descriptive statistics to calculate frequencies, mean, range etc. Bi-variate analysis was done and Chi square test and Fisher Exact test were applied to determine the association between Delayed Sputum Conversion and the determining factors. Multi-variate logistic regression was applied to the variables that has p- value < 0.05 during bi-variate analysis.

Approval from Institutional Ethical Committee of VMMC & Safdarjung Hospital and written informed consent from the TB patients were taken before the start of the study. The TB patients with iron deficiency were counseled about the diet, started on iron therapy and those who required specialist care for management were referred either to VMMC and Safdarjung Hospital, New Delhi; or to Rao Tula Ram Memorial Hospital, Jaffarpur, which is the nearest health care center from the DOTS Centre, Najafgarh.

Results:

The study was conducted among 200 newly diagnosed Tuberculosis patients.

Socio demographic characteristics: The age of the participants ranged from 15 to 76 years and the median age was 30 years. Majority (98%) of study participants were Hindu by religion. Among the unemployed (68%), 43 (21.5%) study participants were house wives while 39 (19.5%) were students. Among the employed (32%), most of them (32, 16%) were unskilled workers. The maximum number (86, 43%) of study participants belonged to SE Class III of modified B.G. Prasad's classification, 2014. Half of them (106, 53%) belonged to nuclear family and overcrowding was present in families of 129 (64.5%).

Substance use: Out of the 200 study participants, 102 (51%) were current smokers, 115 (57.5%) were current users of smoke less form of tobacco and 94 (47%) were current user of alcohol in any form. Dietary history: Out of 200 study participants, 86 (43%) were vegetarian whereas, 114 (57%) were non-vegetarian who consumed Red meat. None of the study participants were on iron supplements or steroids or immunosuppressant at the time of interview.

BCG vaccination: More than half of the study participants 118 (59%) were not aware of whether they had ever been vaccinated with BCG vaccination. BCG scar was present in 78 (39%). History of TB contact: Out of 200 study participants, 69 (34.5%) gave history of contact with TB infection either among family members or neighborhood and none reported history of contact in both.

On being enquired about presenting symptoms related to TB and anemia, cough for more than 2 weeks was reported by all the study participants followed by loss of weight (183,91.1%) and shortness of breath (116, 58%).

Out of 75 female study participants, 65 (86.67%) were menstruating. All of them had regular cycles and menopause was attained by 10 (13.33%).

Out of 200 study participants, 13 (6.5%) of them had associated co-morbid conditions. Of which, 7 (3.5%) had known Hypertension, 5 (2.5%) had known Diabetes Mellitus, and none of them were HIV positive at the time of diagnosis of TB.

Figure 1. Distribution of study participants based on presenting symptoms related to Tuberculosis and Anemia at the start of intensive phase of treatment (N=200)

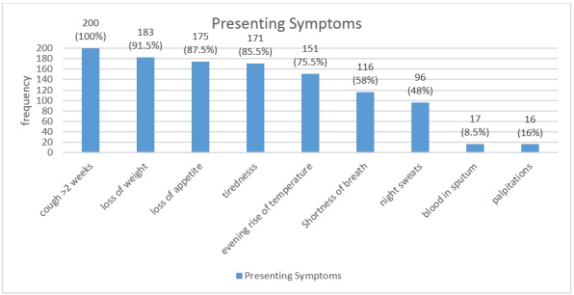

Table 1. Distribution of study participants based on Hemoglobin levels (N=200)

S. No.	ANEMIA*	At the start of the intensive phase, n (%)			At the end of the intensive phase, n (%)		
		Male	Female	Total	Male	Female	Total
1	No anemia	41 (67.2)	8 (10.7)	49 (24.5)	71 (56.8)	30 (40)	101 (50.5)
2	Anemia	84 (32.8)	67 (89.3)	151 (75.5)	54 (43.2)	45 (60)	99 (49.5)
	Total	**125 (100)**	**75 (100)**	**200 (100)**	**125 (100)**	**75 (100)**	**200 (100)**

*WHO criteria

Anemia was found in 151 (75.5%) of the study participants at the start of Intensive phase and in 99 (49.5%) of the study participants at the end of Intensive phase. The mean Hb was 11.16 g/dl (±1.97; minimum = 6.9 g/dl and maximum = 17.1 g/dl) at the start of Intensive phase and was 12.2 g/dl (±1.63; minimum = 7.9 g/dl and maximum = 16.4 g/dl) at the end of Intensive phase.

Among males, the mean Hb was 11.7 g/dl (±2.04; minimum = 7.4 g/dl and maximum = 17.1 g/dl) at the start of Intensive phase and was 12.6 g/dl (±1.7; minimum = 7.9 g/dl and maximum = 16.4 g/dl) at the end of Intensive phase. Among females, the mean Hb was 10.3 g/dl (±1.36; minimum = 6.9 g/dl and maximum = 13.6 g/dl) at the start of Intensive phase and was 11.4 g/dl (±1.2; minimum = 9.0 g/dl and maximum = 14.0 g/dl) at the end of Intensive phase.

Table 2. Distribution of study participants based on their serum ferritin value (N=200)

S. No.	Ferritin Levels (µg/l)	At the start of the intensive phase, n (%)	At the end of the intensive phase, n (%)
1	≤ 30	24 (12)	9 (4.5)
2	> 30	176 (88)	191 (95.5)
	Total	**200 (100)**	**200 (100)**

The mean serum ferritin level at the start of Intensive phase was 249.5 µg/l (±256.3 µg/l) and at the end of Intensive phase was 197.6 µg/l (±206.2 µg/l).

The prevalence of Delayed Sputum Conversion at the end of 2 months of intensive phase of anti-tuberculosis treatment was 21.5%.

Table 3. Multi-variate logistic analysis of determinants of Delayed Sputum Conversion among Tuberculosis Patients (N=200)

S. No	Predictor	Uni-variate Analysis (95% CI) p- value	Multi-variate Analysis (95% CI) p- value
1	Family history of TB No Yes	0.046#*	0.529
2	Shortness of Breath No Yes	0.035#*	0.579

3	Anemia at the Start of IP No Yes	0.009##*	3.933
4	Anemia at the End of IP No Yes	<0.001##*	0.030*
5	Serum Ferritin <30 at the Start of IP No Yes	<0.001#*	0.336
6	Under-weight at the Start of IP No Yes	0.030#*	0.716
7	Under-weight at the End of IP No Yes	0.024#*	0.973
8	Bacilli Load at the Start of IP Low cohort (2+, 1+ and scanty) High cohort (3+)	<0.001#*	**3.440**

'#*' indicates significant p-value by chi-square test, '##*' indicates significant p-value by Fisher Exact test, '##' indicates p-value by Fisher Exact test, *p- value is significant

Bi-variate analysis shows that the factors such as history of tuberculosis infection in family members, shortness of breath, under-weight at the start and at the end of intensive phase of anti-tuberculosis treatment, initial high bacilli load of 3+, anemia at the start and at the end of intensive phase of anti-tuberculosis treatment and Serum ferritin level of ≤ 30 µg/l at the start of intensive phase were found to be associated with delayed sputum conversion.

In multi-variate logistic regression analysis of association factors, it was found that odds of delayed sputum conversion were significantly higher if the tuberculosis patients had anemia at the end of 2 months of intensive phase of anti-tuberculosis treatment.

Discussion:

In the present study, the prevalence of Delayed Sputum Conversion was 21.5% which is similar to the studies conducted by **Pajankar S,**[27] **Mota PC,**[28] **Kayigamba FR**.[29] A study by among 338 sputum smear positive tuberculosis patients revealed that the prevalence of Delayed Sputum Conversion was 35.5% which is slightly higher than our study.30 However, the prevalence of Delayed Sputum Conversion was found to be lower in the following studies, **Dudala SR**,[22] and **Nagu TJ**,[31] than the present study. Higher prevalence of delayed sputum conversion in our study may be due to increase in resistant tuberculosis in North India over the years.[32]

In the present study, the prevalence of anemia was 75.5% at the start of intensive phase. This result is similar to the studies conducted by **Yarnal PJ,**[33] **Thatoi PK**,[34] **Bhargava A,**[35] **Nagu TJ**,[31] Minchella PA,36 Oliveira MG37 and Isanaka S,5 where the prevalence of anemia was high among tuberculosis patients.

In the present study, there was a statistically significant association between delayed sputum conversion and anemia at the end of 2 months of intensive phase of anti-tuberculosis treatment ($p<0.05$). In the study by **Nagu TJ** among 1245 pulmonary tuberculosis patients, where anemia at the start of intensive phase of anti-tuberculosis treatment was three times more likely to have sputum positive smear at the end of two months of anti-tuberculosis treatment as compared to non-anemic patients.[31]

It has been observed that the serum ferritin may be elevated as a part of acute phase reaction in chronic diseases like tuberculosis and the same had been observed in the current study also. In the present study, the mean serum ferritin level at the start of IP was 249.5 µg/l which was higher than the normal for both males and females and at the end of IP was 197.6 µg/l, which was lower than the baseline value. The result is similar to the studies conducted by **Kumar S**[38] and **Oliveira MG**.[37] In a study by **Minchella PA** among 45 cases and they found that the mean serum ferritin was 164.5 µg/l (95.7–252) at the start and 24.0 µg/l (9.1–76.3) at the end of 2 month of tuberculosis treatment. The mean serum ferritin was reduced during anti-tuberculosis treatment.[36] There is paucity of studies which looks into the association between delayed sputum conversion and serum ferritin levels.

There is no scarcity of literature on the prevalence of anemia in tuberculosis patients in New Delhi and India, however our study is one of the longitudinal follow up study to show the importance of association of hemoglobin, serum ferritin levels and delayed sputum conversion. Our study has considered only sputum smear results only at the end of 2nd month of intensive phase, but not at the end of 3rd month and at the completion of treatment.

Conclusion:

To conclude from our study, three out of four newly diagnosed tuberculosis patients were anemic at the time of diagnosis of tuberculosis. Delayed sputum conversion was found in 21.5% of the newly diagnosed tuberculosis patients. Multi-variate analysis shows that anemia at the end of intensive phase of anti-tuberculosis treatment was found to be associated with delayed sputum conversion. It is recommended that the universal screening for anemia at the time of diagnosis of tuberculosis should be done to improve the treatment outcome of the tuberculosis patients and further studies should be done to find out the mechanism of anemia among tuberculosis patients and to assess the efficacy of treating anemia in a randomized setting so as to improve the treatment outcomes. Hence, not only the anti-tuberculosis drug therapy, but a multi-pronged strategy which takes all the mentioned association factors into consideration can help in prevention and control of tuberculosis infection in India.

Conflicts of interest:

There are no conflicts of interest.

References:

1. World Health Organisation. Global Tuberculosis Report 2015. Available from: http://www.who.int/tb/publications/global_report/en/. [Accessed on November 10, 2016].
2. Centers for Disease Control and Prevention. Guidelines for preventing the transmission of Mycobacterium tuberculosis in healthcare settings, 2005. MMWR 2005;54[RR-17]:1-141.
3. Epstein MD, Schluger NW, Davidow AL, Bonk S, Rom WN, Hanna B. Time to detection of Mycobacterium tuberculosis in sputum culture correlates with outcome in patients receiving treatment for pulmonary tuberculosis. Chest 1998;113(2):379-386.
4. Lee SW, Kang YA, Yoon YS, Um SW, Lee SM, Yoo CG, et al. The Prevalence and Evolution of Anemia Associated with Tuberculosis. J Korean Med Sci 2006;21(6):1028–1032.
5. Isanaka S, Mugusi FM, Urassa W, Willett WC, Bosch RJ, Villamor E, et al. Iron Deficiency and Anemia Predict Mortality in Patients with Tuberculosis. J Nutr 2012;142(2):350–357.
6. Saathoff E, Villamor E, Mugusi F, Bosch RJ, Urassa W, Fawzi WW, et al. Anemia in adults with tuberculosis is associated with HIV and anthropometric status in Dar es Salaam, Tanzania. Int J Tuberc Lung Dis 2011;15(7):925–932.
7. Hussain SF, Irfan M, Abbasi M, Anwer SS, Davidson S, Haggee R, et al. Clinical characteristics of 110 miliary tuberculosis patients from a low HIV prevalence country. Int J Tuberc Lung Dis 2004;8(4):493–499.
8. Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. Afr J Med Med Sci 2003;32(3):239–242.
9. Karyadi E, Schultink W, Nelwan RHH, Gross R, Amin Z, Dolmans WM, et al. Poor Micronutrient Status of Active Pulmonary Tuberculosis Patients in Indonesia. J Nutr 2000;130(12):2953–2958.
10. Kourbatova EV, Borodulin BE, Borodulina EA, del Rio C, Blumberg HM, Leonard MK, et al. Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. Int J Tuberc Lung Dis 2006;10(11):1224–1230.
11. Hansen TM, Hansen NE. Serum ferritin as indicator of iron responsive anemia in patients with rheumatoid arthritis. Ann Rheum Dis 1986;45(7):596–602.
12. Cook JD, Lynch SR. The liabilities of iron deficiency. Blood. 1986;68(4):803–809.
13. Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, eds. Wintrobe's clinical hematology. 10th ed. Baltimore: Williams & Wilkins; 1999. p. 920–933
14. Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, eds. Wintrobe's clinical hematology. 10th ed. Baltimore: Williams & Wilkins; 1999. p. 1012–1014.
15. Konijn AM, Hershko C. Ferritin synthesis in inflammation. I. Pathogenesis of impaired iron release. Br J Hematol 1977;37(1):7–16.
16. Kurer SB, Seifert B, Michel B, Ruegg R, Fehr J. Prediction of iron deficiency in chronic inflammatory rheumatic disease anemia. Br J Hematol 1995;91(4):820–826.
17. Ahluwalia N, Lammi-Keefe CJ, Bendel RB, Morse EE, Beard JL, Haley NR. Iron deficiency and anemia of chronic disease in elderly women: a discriminant analysis approach for differentiation. Am J Clin Nut 1995;61(3):590–596.
18. Blake DR, Waterworth RF, Bacon PA. Assessment of iron stores in inflammation by assay of serum ferritin concentration. Br Med J 1981;283(6300):147–148.
19. Coenen JL, van Dieijen-Visser MP, van Pelt J, van Deursen CT, Fickers MM, van Werch JW, et al. Measurements of Serum ferritin used to predict concentrations of iron in bone marrow in anemia of chronic disease. Clin Chem 1991;37(4):560–563.
20. Krause JR, Stolc V. Serum Ferritin and bone marrow iron stores. I. Correlation with absence of iron in biopsy specimens. Am J Clin Pathol 1980;74(5):817–820.
21. The Tuberculosis Association of India. DOTS clinics in India. Available from: http://tbassnindia.org/DOTSClinicsinIndia.html. [Accessed on November 10, 2016].
22. Dudala SR, Reddy KR, Bolla CR, Rao AR, Prabhu RG. Sputum Grading as a predictor of treatment of new sputum smear positive tuberculosis patients in Khammam Tuberculosis Unit. Nat J Res Com Med 2013;2(2):79-148.
23. Revised National Tuberculosis Control Programme (RNTCP). Training Module for Medical Practitioners. Central TB Division Directorate General of Health Services Ministry of Health and Family Welfare Nirman Bhawan New Delhi. 2010:1-128.
24. World Health Organisation (2011) Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva, Switzerland.
25. National Institute of Nutrition, Dietary guidelines for Indians. Indian Council of Medical Research, 2011. Available from: http:// ninindia.org/ dietaryguide linesforn inwebsite.pdf. [Accessed on November 10, 2016].
26. Kotru M, Rusia U, Sikka M, Chaturvedi S. Evaluation of serum ferritin in screening for iron deficiency in tuberculosis. Ann Hematol 2004;83(2):95-100.
27. Pajankar S, Khandekar R, Al Amri MA, Al Lawati MR. Factors Influencing Sputum

Smear Conversion at One and Two Months of Tuberculosis Treatment. Oman M J 2008;23(4):263-268.
28. Mota PC, Carvalho A, Valente I, Braga R, Duarte R. Predictors of delayed sputum smear and culture conversion among a Portuguese population with pulmonary tuberculosis. Rev Port Pneumol 2012;18(2):72-79.
29. Kayigamba FR, Bakker MI, Mugisha V, Gasana M, Schim van der Loeff MF. Sputum completion and conversion rates after intensive phase of tuberculosis treatment: an assessment of the Rwandan control program. BMC Res Notes 2012;5:357.
30. Tiwari S, Kumar A, Kapoor SK. Relationship between sputum smear grading and smear conversion rate and treatment outcome in the patients of pulmonary tuberculosis undergoing dots–a prospective cohort study. Indian J Tuberc. 2012;59(3):135–140.
31. Nagu TJ, Spiegelman D, Hertzmark E, Aboud S, Makani J, Matee MI et al. Anemia at the Initiation of Tuberculosis Therapy Is Associated with Delayed Sputum Conversion among Pulmonary Tuberculosis Patients in Dar-es-Salaam, Tanzania. PLoS One 2014;9(3):e91229.
32. Sethi S, Mewara A, Dhatwalia SK, Singh H, Yadav R, Singh K, et al. Prevalence of multidrug resistance in Mycobacterium tuberculosis isolates from HIV seropositive and seronegative patients with pulmonary tuberculosis in North India. BMC Infect Dis 2013;13:137.
33. Yaranal PJ, Umashankar T, Harish SG. Haematological Profile in pulmonary Tuberculosis. Int J Health Rehabil Sci 2013;2(1):50-55.
34. Thatoi PK, Khadanga S. Pulmonary Tuberculosis and its Hematological correlates. Transworld Medical Journal. 2013;1(1):11-13.
35. Bhargava A, Chatterjee M, Jain Y, Chatterjee B, Kataria A, Bhargava M, et al. Nutritional Status of Adult Patients with Pulmonary Tuberculosis in Rural Central India and Its Association with Mortality. PLoS One 2013;8(10):e77979.
36. Minchella PA, Donkor S, Owalabi O, Sutherland JS, McDermid JM. Complex Anemia in Tuberculosis: The Need to Consider Causes and Timing When Designing Interventions. Clin Infect Dis 2015;60(5):764-772.
37. Oliveira MG, Delogo KN, de Oliveira HM de MG, Ruffino-Netto A, Kritski AL, Oliveira MM. Anemia in hospitalized patients with pulmonary tuberculosis. J Bras Pneumol 2014;40(4):403-410.
38. Kumar S, Singh UN, Saxena K, Saxena R. Hematological and Biochemical abnormalities in case of pulmonary Tuberculosis patients in Malwa region (Indore). Int J Pharm Bio Sci 2013;3(3):237-241.