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To Study Haematological Profile In Patient Of Pulmonary Tb With And Without Hiv Co-Infection

Dr. Mahendra Tilkar¹, Dr. UmeshPratap Singh², Dr. AnkitAnoop Maravi³, Dr. Praveen K. Baghel⁴

¹M.D., Associate Professor, Department of Medicine, S.S. Medical College, Rewa, Madhya Pradesh, India.

²M.D., Assistant Professor, Department of Medicine, S.S. Medical College, Rewa, Madhya Pradesh, India.

³Resident 3rd Year, Department of Medicine, S.S. Medical College, Rewa, Madhya Pradesh, India.

⁴M.D., Professor & Head Department of Medicine, S.S. Medical College, Rewa, Madhya Pradesh, India.

email-³ankitmaravi@gmail.com

Corresponding Author:

Dr. AnkitAnoopMaravi PG 3rd Year RMO, Department of Medicine, Shyam Shah Medical College, Rewa (M.P.) 486001

Abstract

Background: TB and HIV form a lethal combination, as each fuels the progress of the other in the infected patients. This study assessed the haematological parameters of pulmonary tuberculosis (PTB) patients with and without HIV infection attending the shyam shah medical college, Rewa. Aims: To study hematological parameter namely Hb (Hemoglobin), total RBC count, Total WBC count, ESR (Erythrocyte Sedimentation Rate) and platelets in pulmonary tuberculosis. Methods: To analytical study of all 120 (TB with HIV 60 / TB without HIV 60) TB patients who were attending Department of Medicine, Shyam Shah Medical College, Rewa (M.P.). And patientsrefered from Anti-retroviral therapy centre, with sputum positivity for AFB (acid fast bacillius). Results: In our study, 83.3% were males and 16.6% were females in the TB with HIV group. 70% of patients were in the age group of 25 – 45 years in the TB with HIV group, whereas 86.6% of patients were in age group of 25 - 45 years in the TB without HIV. 90% of patients were underweight with BMI less than 18.5, in TB with HIV group, and 73.3% of patients were underweight in TB without HIV group. 80% were anemic in the TB with HIV and 66.6% were anemic in TB without HIV group. 63.4% of patients with TB and HIV had thrombocytopenia, whereas only 10% of patients had thrombocytopenia in TB without HIV group. Patients with tuberculosis per se have increased ESR count, whereas TB-HIV coinfection has drastically reduced the ESR count. Among patients with TB and HIV 83.3% of patients had ESR less than 60 mm/hr., whereas 96.6% of TB without HIV patients had ESR greater than 60 mm/hr. since, ESR is a marker of chronic inflammatory states like TB and HIV is a immunosuppressive state, the co-infection of TB with HIV has drastically reduced ESR values in these patients. Conclusion: ESR values are drastically reduced in TB patients with HIV, rather TB patients per se. hence, an ESR less than 60

mm / hr in pulmonary tuberculosis patients should arouse a suspicion of underlying immunocompromised state.

Keywords: Pulmonary Tuberculosis, Human Immunodeficiency Virus, Haematological Parameters, New TB Patients, Follow up TB Patients, Erythrocyte Sedimentation Rate.

Study Design: Observational Study.

1. INTRODUCTION

Consequently, the estimated prevalence worldwide is 16 to 20 millions of whom 8-10 million are sputum smear positive and highly infectious The number of persons infected with TB bacillus is estimated to be 6-7 billion, of which 1.3 billion live in developing countries. In India, more than 40% of adults are infected with TB and approximately 1.5 million cases are put on treatment every year. An estimated 5 lakh death from TB occur every year.

Haematological changes have been observed with pulmonary, extrapulmonary and disseminated TB and usually reversible with ATT. Anemia is common in TB. The extent of anemia depends on the extent of the disease; when TB is localized to only one organ eg. Lung. The Hb level is usually normal until the disease has made considerable progress, when a mild to moderate normochromic normocytic or slightly hypochromic anemia may develop. Severe anemia is rare in the absence of complications of TB like disseminated TB, ulceration of bowel etc.

AIDS is a chronic, life-threatening condition caused by the human immunodeficiency virus (HIV). By damaging or destroying the cells of immune system, HIV interferes with body's ability to effectively fight off viruses, bacteria and fungi that cause disease.

HIV infection is associated with numerous abnormalities of hematopoiesis, affecting both the myeloid and lymphoid lineages derived from the hematopoietic stem cell. Thus, as many as 70% to 80% of HIV-infected patients develop anemia during the course of infection, while neutropenia may be seen in more than 50% of individuals with more advanced HIV-related immunodeficiency. Thrombocytopenia is also common, occurring in approximately 40% of patients, and serving as the first symptom or sign of infection in approximately 10% of HIV-infected patients.

The bacterium responsible for TB, *Mycobacterium tuberculosis*, can affect different organs in the human body. The demonstrable changes that PTB plus HIV, PTB, and HIV seropositive patients have in their hematological and metabolic values showed varied pictures as a result of the phase of the infection and the causative agents, *M. tuberculosis* and HIV¹.

The hematopoietic system is seriously affected during TB infection. Both myeloid and lymphoid cell lines and plasma components are affected². Specifically, in pulmonary tuberculosis many hematological abnormalities are common and they are valuable aids to the diagnosis³.

These abnormalities are useful indicators providing a clue to diagnosis, assessing the prognosis, and indicating the complication of underlying infection and response to therapy⁴.

Although anemia is the most common complication of both TB and HIV infections, leukocytosis, thrombocytosis, monocytosis, and lymphocytosis are the frequent reported abnormalities^{2,3,5,6.} This suggests a systemic response of a patient to active inflammatory responses^{7,8}. HIV associated hematological abnormalities are dependent on the level of virus replication, and severe abnormalities are observed in the late stage of AIDS with high viremia. This is worsened when there is TB coinfection where all blood cell lineages are involved^{2,9}.

Aim of the study to hematological parameter namely Hb (Hemoglobin), total RBC count, Total WBC count, ESR (Erythrocyte Sedimentation Rate) and platelets in pulmonary tuberculosis. To compare the study in HIV-TB co-infected patients, to find out variations among HIV positive and negative patients.

2. METHODS

To analytical study of all 120 (TB with HIV 60 / TB without HIV 60) TB patients who were attending Department of Medicine, Shyam Shah Medical College, Rewa (M.P.). And patients refered from Anti-retroviral therapy centre, with sputum positivity for AFB (acid fast bacillius).

A total of 120 cases were taken for the study. They were divided in to two groups. The first group was sputum smear positive pulmonary tuberculosis, which consist of sixty patients and they were HIV ELISA negative, the second group was sputum smear positive pulmonary tuberculosis, which consist of sixty and they were HIV ELISA positive.

Inclusion criteria

In the pulmonary tuberculosis group, all patients with active tuberculosis will be selected for this study. Then according to ELISA positivity they will be divided into TB and HIV-TB co-infected patients. The patients selected will be above the age group of 15 years.

Exclusion Criteria

- 1. Old healed pulmonary tuberculosis lesion.
- 2. Diabetes and other metabolic disorder.
- 3. Malignancy
- 4. Collagen vascular disorder
- 5. Gross organ disorder.
- 6. Patients on steroid, iron therapy, or vitamin therapy.
- 7. Patients with bleeding disorder.
- 8. Tobacco and alcoholics.
- 9. Pregnancy
- 10. Past and current intake of ATT (anti tuberculosis therapy)
- 11. CD4+ < 200 cells / microlitre and HIV RNA copies >1,00,000/ ml.

Methods of Data Collection:

Tuberculosis patients were diagnosed by clinical examination, X-ray chest (PA view) and sputum smear examination. The sputum smear examination was done by Ziehl- Neelson technique. Sputum specimen was collected on the spot when a patient is suspected to of having tuberculosis. This is called a spot specimen. The patient is then given a sputum container to collect an early morning specimen before his second meeting, this is called early morning specimen. When the patient returns with the early morning specimen, a second spot specimen is also collected.

A full blood, blood count was carried out in a 5ml anticoagulated blood sample. A thick and thin stained blood film was prepared for examination of morphology of the different cells and by specific stains red blood cell, white blood cell and platelet count was determined.

The examination of stained blood film is most important and by this the red cells are examined to access their degree of haemoglobinisation and their shape. If both are normal, they are called as normochromic and normocytic pale staining which suggests under

haemoglobinisation is called as hypochromia and reduction in the size of RBC is called as microcytosis.

One ml of blood is introduced in to automated cell counter. Specific values like Haemoglobin, RBC count, WBC (total) count, Differential count (D.C), Platelet count, are obtained which are the basic parameters to be studied.

3. INVESTIGATION DETAILS

Hb, TLC, DLC, MCV, MCHC, PC, ESR, Platelet count, CD4 Count, Chest Xray, HIV sputum

4. STATISTICAL METHODS

Data will be collected and managed on an excel work sheet. All values are expressed as mean. Data will be calculated by appropriate statistical test.

5. RESULTS

	<25 yea	rs	25 – 45 y	/ears	> 45 years			
Status	males	females	males	females	males	females		
TB with HIV	0	2	34	8	16	0		
TB without HIV	0	0	42	10	4	4		
BMI	< 18.5		18.5-24.9	9	>24.9			
	n	%	n	%	n	%		
TB with HIV	54	90	6	10	0	0		
TB without HIV	44	73.3	12	20	4	6.6		

Table 1- Characteristic Profile

TABLE: 2 CorrelationOf Haematological Parameters According To TB With HIV And Without HIV Status

Parameter	Total	PTV/HIV	PTB without HIV					
Haemoglobin								
< 11 gm / dl	88	48 (54.54%)	40 (45.46)					
>11 gm / dl	32	12 (37.5%)	20 (62.5%)					
PLATELETS (in cells/cu mm)								
<1,50,000 cells/cumm	44	38 (63.4%)	06 (10.0%)					
1,50,000-3,90,000 cells/cumm	54	22 (36.6%)	32 (53.4%)					
>3,90,000 cells/cumm	22	0	22 (100.0%)					
ESR mm / hr								
0 - 30 mm / hr	32	32 (53.4%)	0 (0%)					
31 – 60 mm / hr	20	18 (30.0%)	02 (3.3%)					
61 – 90 mm / hr	36	4 (6.6%)	32 (53.3%)					
91 – 120 mm / hr	32	6 (10.0%)	26 (43.4%)					

Haemoglobin	< 1	< 11 gm / dl						>	> 11 gm / dl										
_		Ma	les			Fen	nale	s		Μ	[ales				Fe	ma	les		
TB with HIV		42		70%		6	1() %	6	8]	3.3 %	%		4		6	5.6%	6
TB without HIV	7	30		50%		10	10	5.6	5%	16	5 2	26.6%	, D		4		6	5.6%	6
RBC	<3.8 million RBC/ cumm 3.8-5.8 y					million RBC / cumm													
			Males				Females			Μ	Males				Females				
TB with HIV		42		70%		6	1()%)	8]	3.3%	Ď		4		6	5.6%	6
TB without HIV	7	40		66.69	6	10	10	6.6	5%	6]	0%			4		6	5.6º	6
WBC		< 3	,500	cells	'cun	nm	3,	,50	0-10,	000)	ce	lls>	>10	,00)0 c	ells	5 /c	umm
			- -				/c	ur	nm										
		Ma	les		Fen	nales	s M	[a]	les]	Fema	ales	ľ	Ma	les]	Fen	nale	es
TB with HIV		4	8.	0%	0	0%	40	5	92%	-	10 1	00%	C)	0%) ()	0	%
TB without HIV	7	0	09	%	0	0%	44	4	95.65	%	12 8	35.71	% 2	2	4.3	5 2	2	14	4.29%
PLATELETS	<1.5	5 lacs/	cu n	nm			1.5	-3.	.9 lacs	s/cu	mm	l	>3	.9	lac	s / (cu 1	nn	1
(in cells/cu	Ma	les		F	ema	les	Ma	le	s	Fei	male	s	M	ale	S		Fe	ma	les
mm)																		-	
TB with HIV	32		53.3%	6	10)%	18	3	30%	4	6.6	5%	0	()		0)
TB without	6		10%	0	0		24	4	-0%	8	13	.3%	16	2	26.6	5%	6		10%
HIV																			
ESR	0-30)mm/hr 31			31-	-60mm/hr 6			61-	61-90mm/hr				91-120mm/hr					
	Ma	les	Fen	nales	Ma	ales	F	'en	nales	Ma	ales	Fer	nal	es	Ma	ales	5	Fe	males
TB with HIV	28	47.5%	<u>5</u> 4	6.5%	514	23%	64		6.5%	4	6.5%	60	0		6	109	%	0	0
TB without	0	0	0	0	2	3%	0		0	26	43%	6	10	%	18	309	%	8	14%
HIV																			

TABLE: 3 Gender wise correlation of Haematological Parameters according to TB with HIV and without HIV status

TABLE: 4 Reference Range Of Haematological Parameters

HAEMOGLOBIN gm%	RANGE	MEDIAN	MEAN
TB WITH HIV	6.4 – 12.6 Gm	9.1 Gm	9.2 Gm
TB WITHOUT HIV	6.0 – 12.8 GM	9.9 Gm	9.74 Gm
RBC (millions/cumm)	RANGE	MEDIAN	MEAN
TB with HIV	2.3 - 4.2	3.3	3.3
TB without HIV	2.2 - 4.2	3.0	3.1
WBC (in cells /cu mm)			
TB with HIV	3400 - 10000	6500	6538
TB without HIV	3600 - 10950	6500	6696
PLATELET (in cells/cu	mm)		
TB WITH HIV	40,000 - 3,00,000	1,60,000	1,54,333
TB WITHOUT HIV	1,00,000 - 5,60,000	3,05,000	3,31,666
ESR (IN MM / HR)			
TB WITH HIV	20 - 120	30	38
TB WITHOUT HIV	60 - 120	98	102

6. INTERPRETATION OF THE ABOVE TABLES

In our study, 83.3% were males and 16.6% were females in the TB with HIV group. Whereas 76.6% were males and 23.3% were females in the TB without HIV group. Hence males dominated in both groups.

In our study, 70% of patients were in the age group of 25 - 45 years in the TB with HIV group, whereas 86.6% of patients were in age group of 25 - 45 years in the TB without HIV. Hence, both the disease predominantly affect adults.

In our study, 90% of patients were underweight with BMI less than 18.5, in TB with HIV group, and 73.3% of patients were underweight in TB without HIV group. Since both disease causes chronic wasting, co-infection of TB with HIV may have deleterious effect in BMI.

In our study, 80 % were anemic in the TB with HIV and 66.6% were anemic in TB without HIV group. Among those anemic patients, male patients were more (70 % vs 34%) anemic.

In our study, WBC count was not much altered in both the study groups, in which more than 65% of patients had normal WBC count in the TB with HIV groups and 70% of patients had normal WBC counts in TB without HIV. Since HIV was in early stages, the WBC count has not drastically reduced.

In our study, 63.4% of patients with TB and HIV had thrombocytopenia, whereas only 10% of patients had thrombocytopenia in TB without HIV group. Instead, 36.6% of patients had thrombocytosis in the TB without HIV group.

Since isolated thrombocytopenia is a well documented feature in HIV patients, and either normal platelet counts or thrombopoeisis occur in pulmonary tuberculosis patient per se, the co-infection TB and HIV has drastically reduced the platelet count in these patients.

In our study, yet another finding is that, patients with tuberculosis per se have increased ESR count, whereas TB-HIV coinfection has drastically reduced the ESR count. Among patients with TB and HIV 83.3% of patients had ESR less than 60 mm/hr., whereas 96.6% of TB without HIV patients had ESR greater than 60 mm/hr. since, ESR is a marker of chronic inflammatory states like TB and HIV is a immunosuppressive state, the co-infection of TB with HIV has drastically reduced ESR values in these patients.

7. DISCUSSION

Sixty patients were chosen randomly in each group to avoid selection bias. Patients less than 15 years and more than 60 years were excluded.

These sputum positivity patients were further subjected to clinical examination.

Those patients who gave sexual promiscuity and high risk group for sexually transmitted diseases were further subjected to HIV screening test after written consent.

The high risk group patients belong to commercial sex workers, lorry / truck drivers, multiple sex partners, child abuse, ex – prisoners, etc.

Those patients with HIV ELISA test positivity were isolated, and HIV was further confirmed using the gold standard test namely WESTERN BLOT.

These TB patients with HIV positivity were subjected to CD 4 + cells count assay and HIV RNA copies were measured. Those patients with CD 4 + cell count between 200 - 350 and HIV RNA copies between <1,00,000 were only chosen for this study.

Hence the HIV patients chosen for this study were mostly asymptomatic or in the early stage of HIV infection.

Clinically some of these patients had oral candidasis in our study group 28 patients had oral candidasis. But for that, they had only symptoms and signs of pulmonary

tuberculosis as mentioned before.

Routine baseline investigations were done in these patients, which include renal function test, liver function test, random blood glucose. A chest X- Ray PA view was taken in all these patients.

5 ml of anti-coagulated blood was taken after venipuncture. This blood was subjected to automated analyzer counting and peripheral smear examination.

From results obtained from complete haemogram, these two sets of patients namely TB with HIV and TB without HIV were compared with respect to haematological profile.

Our study clearly shows that both HIV and TB affect the adult age group.

Among patients belonging to TB with HIV 70 % were in the age group of 25 - 45 years, whereas it is 86.6% in patients belonging to TB without HIV.

This is further confirmed by study conducted by Abay F, et al⁸, in Tanzania, in which 74% of patients belong to age group of 25 - 45 years. Hence both TB and HIV have great impact in patients of adult age group.

Regarding the sex distribution between these two sets of patients, both HIV and TB is more common in male sex. In our study, 83% were males and 16.6% were females in patients with TB with HIV, whereas it is 76.6% males and 23.3% females in TB without HIV.

This finding cannot be taken as fool proof, as the female patients attending the thoracic medicine OP is very less, due to social stigma and taboos.

Regarding BMI, majority of patients in both the group belong to underweight i.e, BMI < 18.5 around 90 % of patients in TB with HIV group and 73.3% of patients in TB with out HIV were under weight.

According to study by Morris, Bird and $et.al^{10}$ the basic pathogenesis for anaemia in HIV and TB patients was due to cytokines IL-1, IL-6, and TNF – alpha.

Among the various haematological abnormality noted in these patients, anemia, thrombocytopenia, and variation in ESR were very significant,

Anemia:

In our study anemia was found in both groups. In case of patients of TB with HIV 80% had haemoglobin less than 11gm / dl and 66.6% of TB without HIV patients had Hb less than 11 gm/dl. Among the anemic patients belonging to TB with HIV 87.5% were males and 12.5 % were females.

In case of anemic patients belonging to TB without HIV, 75% were males and 25 % were females.

Our study is well comparable to the study done by Morris, sharma et al,¹⁰ in which anemia was seen in 80% of patients with TB and HIV coinfection.

Our study coincide with that study conducted by Sullivan PS¹¹ in HIV infected males, i.e, around 70% of male patients are anemic in the category of TB with HIV. Mostly these patients belong to HIV infection or immunological AIDS, which are cases chosen particularly for this study.

Since the HIV patients chosen for this study belong to early stage of HIV infection, there were no remarkable changes in WBC counts. According to Murphy M, Metcalfe et.al¹², neutropenia occur in late stage of CLINICAL AIDS, whereas lymphocytopenia may occur before neutropenia as HIV infection mostly attacks lymphocytes.

In our study also both the group of patients i.e. TB with HIV and TB without HIV had normal WBC count in 93%.

In case of differential count, 23% of TB with HIV patients had lymphocytopenia.

In patients with tuberculosis, there was no significant alteration in terms of total WBC

counts, and differential counts. 12% of patients with Tuberculosis per se had lymphocytosis.

PLATELETS:

According to a study conducted in 350 pulmonary TB patients, thrombopoeisis is seen 33% of patients, 3% had thrombocytopenia and 64% had normal to low normal level of platelets (Dr. Sharma MD AIIMS, JIMA, 2006)

In HIV positive patients, according to Sullivan PS, Hanson DL et al¹¹, and isolated thrombocytopenia may be early consequences of HIV infection and if CD 4 count is less than 250, this may increase upto 40 % due to direct toxic effects of HIV on the megakaryocytes.

According to Vijay Babu C et al^{13} HIV and haematological problems, thrombocytopenia is common in HIV disease and only if persistent, cause bleeding.

In our study, 63.3% of patients belonging to TB with HIV positive status had thrombocytopenia, whereas only 10% of patients had thrombocytopenia among TB without HIV status.

In the contrary, 53.3% of patients had normal platelet counts and 36.6% had thrombocytosis in patients with TB per se.

Among the patients with thrombocytopenia I TB with HIV study group, 84.2% were males and 15.7% were femalesAmong patients with thrombocytosis in TB with HIV negative status, 72.7% were males and 27.2% were females.

ERYTHROCYTE SEDIMENTATION RATE

ESR is a marker of ongoing inflammatory reaction. It may be elevated in gross situations. The tuberculosis patients had high ESR value compared HIV positive TB patients.

According to the study of KamaleshSarkaret al¹⁴, ESR may be an indicator for screening of tuberculosis patients for underlying HIV infection, particularly in poor resource settings.

They had taken 34 patients with TB positive and HIV positive in one group and 25 patients with TB without HIV in another group. They have done routine investigation which included Total count (TC), Differential count DC), haemoglobin (Hb), ESR for both group of patients.

The data were compared between the two groups. According to the study, there was not much difference in basic investigations between these two groups except in ESR values. Most tuberculous patients with HIV infection had a much lower ESR value compared to the control group.

TB with HIV Mean value of ESR 38.5 mm/hr Median value of ESR 30 mm/hr TB without HIV Mean value of ESR 142 mm/hr Median value of ESR 108mm/hr.

In our study, 96.6% of patients belonging to TB without HIV negative status had ESR more than 60 mm / hr., in which 73.3% were males and 26.3% were females. Only 3.3% of patients in TB with out HIV had ESR less than 60 mm / hr.

In our study, 83.3% of patients belong to TB with HIV had ESR in the range of 0-60 mm/hr. and only 16.6% of patients in this group had ESR in range of 61 - 120 mm / hr.

Among these 66.6% of males had ESR less than 60 mm / hr and 16.6% of females had ESR less than 60mm / hr.

Hence **p** value is 0.001, which is significant, we can conclude that ESR is drastically reduced in patents with TB- HIV co-infection rather TB alone.

8. CONCLUSION

Boththediseasespredominantlyaffectthemalesex. Both the diseases affect the economically productive age group of the nation, namelyadults belonging to 25 - 45 years. Anemia is common in both diseases, but the combination further worsens this scenario.

There is not much reduction in WBC count, as the patients chosen for this study belong either to asymptomatic AIDS orimmunological AIDS. TheplateletcountsaredrasticallyreducedeveninasymptomaticAIDSpatients, hence this parameter can be used as marker of early HIV infectionamongthe pulmonary tuberculosis patients. ESR values are drastically reduced in TB patients with HIV, rather TB patientsper than mm / hr hence. an ESR less 60 in pulmonary tuberculosis se. patientsshouldarouseasuspicionofunderlyingimmunocompromised state.

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