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Original Article

Hematological and biochemical alterations in malaria patients with clinical correlation in a tertiary care hospital.

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ABSTRACT

Back gound and objectives : - Malaria is a major health problem in India being one of the biggest burdens in terms of morbidity and mortality among all infectious diseases. Malaria is the most important parasitic infection which poses major health challenges. Malaria pathogenesis is based mainly on extensive changes of Hematological and biochemical parameters. To find out clinical and laboratory findings in malaria caused by various plasmodium species. Materials & Methods: The present study for a period of two years from Oct 2010 to Nov 2012 was done in the department of pathology, Santhiram Teaching Hospital, Nandyal, Kurnool (DT) A.P. Study includes all the patients presenting with blood film proven malaria. This study includes frequency of changes in Hematological and Biochemical parameters with clinical correlation. The frequencies of various symptoms and signs of malaria caused by various Plasmodium species were determined. Mean,S.D, minimum, maximum values of laboratory alterations were calculated .Results:- One hundred and thirteen patients were enrolled for study .Out of the 113 cases 66 (58.4%) were males and 47 (41.5%) were females, and male to female ratio 1.4:1 that is 66 vs 47.Out of the 113 cases 52 (46%) had falciparum malaria, 26 (23.6%) had vivax malaria and 35 (30.9%) had mixed Infection. Anemia was seen in 68 cases (60.17%) of the patients and Thrombocytopenia was seen in 79 cases (69.9%,Leucopenia was seen in 29(25.66%) cases. Mean Hemoglobin was 11.06gm/dl, mean TLC was 6243.36, mean platelet count was 1,23309. Fevers, chills, sweating were leading clinical presentation in all three forms. Splenomegaly was leading sign in all forms. Anemia and jaundice were more common in plasmodium falciparum and mixed infections as compared to plasmodium vivax. Serum urea, creatinine, plasma glucose were with in normal limits in all the patients with malaria and raised serum bilrubin in some patients. conclusion: Malaria must be considered as a leading differential diagnosis in acute febrile patients with more abnormalities like splenomegaly, fall in Hemoglobin level, platelet count and raised bilrubin. It is suggested that the index of suspicion for malaria should be kept high in patients presenting with fever associated Anemia and thrombocytopenia.

1. Introduction

Malaria is the world's most important parasitic infection which poses major health challenges. Around 40% of the global population at risk of malaria resides in South-East Asian region and accounted for 8.5% of the local and around 4.1% of the global mortality due to malaria in 2008 (1). In spite of intensive world efforts to reduce its transmission, malaria remains the most serious and widespread protozoal infection of humans. Malaria is a protozoal disease caused by infection with parasites of the genus plasmodium and transmitted to man by certain species of infected female Anophelious mosquito. Best estimates currently describe

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the annual global burden of malaria as 300-500 million cases and 1-2 million deaths (2) . Four species of malaria parasite cause this disease (p. faciparum, p. vivax. P. malaria, p. ovale) but p. faciparum is the main cause of malaria and death. Malaria is not a uniform disease, it encompasses many manifestations and its impact varies on epidemiological setting. In 2008, there were an estimated 243 million (190-311 million) cases of malaria worldwide. A vast majority, about 85% were in African Region followed by the south –East Asian Region (10%) and East Mediterranean (4%). Still 80% of the Populated areas are malaria prone and nearly 60% of total malaria cases are of faciparum variety, and it contains to remain one of the most important causes of mortality infant child and adults(3). Malaria continues to poses a major public health threat in India due to p. faciparum. About 88% of malaria cases and 97% of death due to malaria is reported from North- Eastern states, Chhattisgarh, Jharkhand, Madhya- Pradesh, Orissa, Andhra Pradesh, Maharashtra, Gujarat, Rajasthan, West Bengal and Karnataka. In a Classical European text book of hematology published in the 1930 s, malaria was defined as a "typical blood disease" characterized by fever, anemia and Splenomegaly(4). It is currently considered a typical example of a hemolytic anemia in more recent hematology textbooks, due to an acquired extra-corpuscular cause. Malaria begins 8-30 days after infection; clinical presentation of malaria caused by various species resembles each other. Clinical features include fever, chills, sweating, headache, vomiting diarrhea, abdominal pain and distension, cough, Splenomegaly and hepatomegaly (5,6,7) . Laboratory alterations associated with malaria are well recognized but specific changes may vary with level of malaria endemicity , demographic factors and malaria immunity (8). Malaria causes different hematological changes anemia and thrombocytopenia being the most common.

The diagnosis of malaria is based on direct visualization of parasite in peripheral blood film (9, 10) . Other modalities being utilized in different parts of the world include fluorescent microscopy antigen detection test and HRP-2 (Histidine Rich Protein -2) based assays (11,12, 13) . Unfortunately most of the facilities are not available in all areas endemic for malaria.The objective of this study was to determine the common clinical features and laboratory parameters in malaria caused by various p. species in this part of world.

2. Materials & Methods

The present study for a period of two years from Oct -2010 to Nov 2012 was done in the department of pathology Santhiram Teaching Hospital, Nandyal , Kurnool (dt) A.p. Study included all the patents presenting with blood film proven malaria. Venous Blood samples of all suspected cases of malaria reported in the hospital were drawn for diagnosis. After establishing the diagnosis, clinical evaluation was done and recorded regarding to age , sex , Fever, Chills , sweating, Vomiting , Headache, Abdominal pain ,Cough , Jaundice & Splenomegaly was confirmed by Ultrasonography. Thick and thin smears were stained with Leishman stain and full blood counts were determined by using automated cell counter analyzer, Patients with history of bleeding disorder, cerebral Malaria, Acute renal failure and drugs intake such as quinine, sulfadoxine –pyrimethamin, thiazides, Co-trimoxazole, and other hemolytic agents were excluded from the study. This study includes frequency of changes in Hematological and Biochemical parameters with clinical correlation were done. The frequencies of various symptoms and signs of malaria caused by various p. species were determined. Mean S.D, minimum, Maximum values of laboratory alterations were calculated.

3. Results

One hundred and thirteen patients were enrolled for study. Frequency of Plasmodium species shown in Table.1. Out of 113 cases 52 (46.%) had faciparum malaria, 26 (23%) had vivax malaria and 35 cases (30.9%) had mixed infections. Age and sex wise distribution was shown in Table.2. The mean age of patient was 31.25 years (SD11.73). Out of the 113 cases 66(58.4%) were males and 47 (41.5%) were females. The highest affected age group were those between 20-40 yrs, at their third decade of life were most commonly affected 53 cases (46.9%) and male to female ratio 1.5:1 that is 66 vs. 47. Hematological alterations of subjects with malaria shown in Table 3. Anemia was seen 68(60.17%) of the patients and leucopenia was seen 29 (25.66%) of the cases and thrombocytopenia is 79(69.9%) of cases. In regard to hematological profile of subjects of malaria shown in Table4. Mean hemoglobin in faciparum group was 10.84 gm /dl. (SD 2.29) .In vivax group 11.36 gm/dl (SD1.77) and in mixed infection cases it was 10.7 gm/dl (SD 2.44). Mean white cell count in faciparum group was 6200 /cumm (SD 2322). in vivax group was 6340 / cumm (SD 2310) and mixed infections cases it was 6511 / cumm (SD 2153). Mean platelet count in falciparum group was 1,36,173 / cumm(SD 35066), in vivax group it was 1,28,461 / cumm (SD 37068) and in mixed infections cases it was 1,17,914 / cumm(SD 53360). In regard to biochemical profile of subjects with malaria show in Table 5. Serum urea , glucose, creatinine were within normal limits in all the patients with malaria and raised serum bilurubin in faciparum (31%) and mixed infection 42.8% in compared vivax infection(7.6%).Mean Blood urea in falciparum was in 24.94 (SD 6.26), vivax group was 23.76(SD 6.52) . and in mixed infection cases it was 25.85(SD 6.10). Mean Blood sugar in falciparum group was in 116.45 (SD 13.76) , vivax group was 107.5(SD 17.21),and in mixed infection cases it was 116.7 (SD 12.38). Mean Serum Creatinine in falciparum group was 0.86 (SD 0.22) and vivax group was 0.96 (SD 0.37) and in mixed infection cases it was 0.8 (SD 0.28). Mean serum bilurubin in faciparum was in 0.94 (SD 0.27) and vivax group was 0.71 (SD 0.23) and in mixed infection cases it was 1.19(SD 0.19).The detailed account of clinical presentation of various plasmodium species shown in Table 5. Fever Chills, Sweating were leading Clinical Presentations in three forms. (90%) Other main Symptoms were Headache, vomiting, abdominal pain diarhoea, cough in all species. Splenomegaly was the leading sign in all three forms plasmodium infection ranging from 59.6% to 65.7%.

Table No.1 (Frequency of Plasmodium Species (113)

Species	Frequency	Percent %
p. vivax	52	46%
p. Falciparum	26	23.6%
Mixed	35	30.9%

TABLE NO.2 (Age & Sex wise Distribution of all Malaria proven cases)

AGE	10.20	21.30	31.40	41.50	51.60	Total
TOTAL	20	22	53	10	8	113
%	17.6	19.4	46.9	8.8	7.0	100%
M	11	13	31	6	5	63
F	9	9	22	4	3	47
M:F	1.2:1	1.4:1	1.4:1	1.5:1	1.6:1	1.4:1

TABLE NO -3 (Hematological alterations of subjects with Malaria)

Hematological Alteration	P.f(52)	P.V.(26)	Mixed Infection(36)
Anemia	44(84..6%)	9 (34.6.%)	15 (42.8%)
Thrombocytopenia	36 (69.23%)	18 (69.23%)	25(69.44%)
Leucopenia	13 (25%)	7 (26.9%)	9 (25.0%)

TABLE NO 4.(Hematological profile of subjects with Malaria)

	HEMATOLOGICAL PARAMETRES	N	MEAN	STD. DEV	MIN. VALUE	MAX VALUE
	FALIFARUM	52	10.84	2.29	6.2	14.2
HB	VIVAX	26	11.36	1.77	8.6	14.4
	MIXED	35	10.7	2.44	6.4	13.8
	FALIFARUM	52	6200	2322	3000	10100
WBC	VIVAX	26	6340	2310	2200	10200
	MIXED	35	6511	2153	2000	12000
	FALIFARUM	52	136173	35066	60,000	2,20,000
PLATELETS	VIVAX	26	128461	37068	35,000	2,51,000
	MIXED	35	117914	53360	75,000	2,15,000

TABLE NO.5.(Bio-chemical profile of subjects with Malaria

	BIO CHEMICAL PARAMETRES	N	MEAN	STD. DEV	MIN. VALUE	MAX VALUE
	FALIFARUM	52	24.94	6.26	40	60
B.UREA	VIVAX	26	23.76	6.52	38	65
	MIXED	35	25.85	6.10	36	68
	FALIFARUM	52	117.10	19.32	75	140
BLOOD	VIVAX	26	117.65	11.43	70	124
SUGAR	MIXED	35	118.40	9.53	78	130
SERUM	FALIFARUM	52	0.86	0.26	0.6	1.4
CREATININE	VIVAX	26	0.77	0.29	0.6	1.4
	MIXED	35	0.88	0.25	0.8	1.4
	FALIFARUM	52	0.64	0.27	0.2	2.6
S.BILIRUBIN	VIVAX	26	0.98	0.23	0.2	2.8
	MIXED	35	1.16	0.19	0.2	2.2

TABLE NO.6 (Clinical Presentation of Various plasmodium Species)

PARAMETRES	P. FALCIPARUM	P.VIVAX	MIXED
FEVER (%)	51(98%)	26(100%)	35(100%)
CHILLS (%)	47(90.3%)	24(92.3%)	32(91.4%)
SWEATING(%)	47(90.3%)	24(92.3%)	32(91.4%)
HEADACHE (%)	32(61.5%)	15(60%)	21(60%)
VOMITING (%)	20(38.4%)	6(23.07%)	17(45.7%)
DIARHOEA (%)	1(1.92%)	1(3.8%)	1(2.8%)
ABDOMINAL PAIN	3(5.7%)	1(3.8%)	2(5.7%)
COUGH %	1(1.92%)	1(3.8%)	1(2.8%)
SPCENOMEGALY %	31(59.6%)	16(61.5%)	23(65.7%)

4. Discussion

limited body of knowledge. Anemia and thrombocytopenia are the two most frequently found abnormalities in patients suffering from malaria (14). This study was carried out primarily to find impact of malaria infection on Hematological and Bio-chemical parameters. Anemia in Malaria is multi factorial in origin. These factors include hemolysis of parasitized as well as non parasitized cells, splenic and reticular hyperactivity, genetic factors and oxidative stress and bone marrow suppressions (14, 15). About 84.6% of the subjects with P. f and 42.8%% mixed infections cases were Anemic while 34.6% of vivax infected cases had this abnormality. Anemia was less frequently observed in other studies (16, 17).

In our study 46% patients had Faciparum malaria, 23% had vivax and 30.9% had mixed infections. In our study 60.17% patients had anemia and 69.9% patients had thrombocytopenia. The nature of hematological abnormalities depends on the time after infection. A recent study has revealed a role of interleukins (IL – 4) and interferon's (IFN – gamma) in erythropoietin suppression. (18, 19). In appropriately low reticulocytosis has been observed in malaria patients' suggesting that insufficient erythropoiesis is major factor. Exact mechanism of erythropoiesis suppression is still under study. About 69.23% pf the subjects with p.f and 69.44% mixed infection cases had thrombocytopenia while 69.23% of vivax infected cases had this abnormality. The cause of thrombocytopenia is poorly under stood, but the immune mediated lysis, sequestration in the spleen, and a dyspoietic process in the marrow with diminished platelet production have all been postulated. Abnormalities in platelet structure and function have been described as a consequence of malaria and in rare instances, platelets can be invaded by malaria parasites them selves. Two types of changes in platelet dysfunction are seen in malaria. Initially there is platelet hyper activity followed by platelet hypo activity. Platelet hyper activity results from various aggregating agents like immune complexes, surface contact of platelet membrane to malaria red cells and damage to endothelial cells. The injured platelets undergo lysis intra vascularly.. The release of platelet contents (an activate the coagulation cascade and contribute to DIC., Transient platelet hypo activity is seen following this phase and returns to normal in 1 to 2 weeks.. This Hematological alteration due to result of peripheral destruction and consumption. Immune complexes

generated by malaria antigen tend to sequestration of injured platelets by macrophages in spleen (20) .Fever, chills, sweating were leading Clinical presentation in three forms and this triad was found in about 90% of subjects with p.falciparum, P.vivax, and mixed infection subjects. This traid was found in about 91% of vivax of subjects in Colombia (21). Vomiting was noted more commonly in 23.07% of subjects with p. vivax infection as compared to 22% in previous studies (16). Similar complaint was observed in 38.46%of P. faciparum infected subjects as compared to 37% in Western Thailand study 16. White cell counts are also found reduced in about 20% of the subjects infected with various plasmodium species. This Hematological alteration is certainly not unprecedented, neither for p.f (23) nor p. vivax (23). Jaundice is a common feature attributed on part to liver damage and haemolysis of both parasitized and non-parasitized erythrocytes (24). Serum bilrubin was found raised more frequently in p. faciparum (3i%)

The study focuses on clinical and laboratory findings in various plasmodium species infection in this part of world. Though these Clinical and laboratory alterations in association with malaria are not new to subject, this data adds more detailed information to the and mixed infection (42.8%) as compared to p. vivax (7.6%). A study from Thailand (25) reported about 6.5% of p. vivax infected cases to be mildly jaundiced. Splenomegaly was recorded in 61.5% of p. vivax 59.6% of p. faciparum and 65.7% mixed infected patients. This high proportion of Splenomegaly is contrast to international studies showing Splenomegaly in 6.5 to 13% patients. (21, 25).

5. Conclusion

Malaria has a significant impact on Hematological profile, most marked being thrombocytopenia and anemia .clinical presentation of various plasmodium species is almost similar with few differences. Malaria must be considered as a leading differential diagnosis in acute febrile patients with more abnormalities like splenomegaly, fall in hemoglobin level, platelet count and raised bilirubin levels. Patients with acute febrile illness having combination of thrombocytopenia and anemia should alert the treating physician about the possibility of malaria infection which can be confirmed with specific tests. Peripheral smear study is the gold standard investigation for identification of different forms of parasites and determination of parasitemia level.

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