

FREQUENCY OF HEMOLYTIC ANEMIA IN PATIENTS PRESENTING WITH MALARIA AT TERTIARY CARE HOSPITAL, PESHAWAR

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ABSTRACT

Objective: To determine the frequency of hemolytic anemia in patients presenting with malaria at a tertiary Care hospital.

Material and Methods: This study was carried out at Department of Internal Medicine, Lady Reading hospital, Peshawar - Pakistan. The Study design used was descriptive cross-sectional study. Study duration was one year from July 2017 to July 2018 in which the total number of observed patients were 151. More over all of the patients having malaria at presentation, of either gender and with age ranging from 16 to 70 years were included. Patients in pediatric age group i.e. age up to 10 years, patients with hemolytic anemia due to causes other than malaria as evident by the history, family history and previous medical record were exempted. With thorough history and physical examination, all of the patients were cautiously checked out and screened. Laboratory tests were done in LRH laboratory. The whole data was analyzed using the SPSS version 20.

Results: The mean age shown by our study was 38 years \pm 11.77. Male patients were 58 % and female patients were 42%. The Mean duration of disease was 1 week \pm 1.56. More over 3% patients had hemolytic anemia while 97% patients didn't have hemolytic anemia.

Conclusion: The majority of our patients were young, hemolytic anemia in malaria was more common, which can be reduced with early diagnosis and effective management of malaria.

Keywords: Hemolytic anemia, adult, malaria.

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INTRODUCTION

Malaria is a parasitic infection caused by any of the plasmodia (Falciparum, Vivax, Ovale, Malariae or Knowlesi^{1, 2}. Historically malaria had epidemics with high mortality on mass scale but with current advances in medicine such epidemics have reduced significantly. With improved sanitation and insecticide sprays in the areas of high malaria prevalence, the disease cycle can be broken, as eradicating the mosquitos (female anopheles- vector for malaria spread) breaks the chain and thus helps in the prevention of disease^{3,4}.

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Malaria patients typically present with episodes of high-grade fever ($>=101^{\circ}\text{F}$) but can present with a variety of atypical presentations. In malaria patients, high parasitemia can result in hemolysis and thus pallor and jaundice can be a clue to diagnosis and further investigations. Laboratory diagnosis of malaria usually requires MP test. Hemolysis and thus hemolytic anemia are one of features of malaria with or without jaundice depending on severity of hemolysis. Hemolytic anemia is quite common having variety of causes but one of the significant causes in our set up is malaria.

Hematological changes related to malaria are anemia, thrombocytopenia and neutropenia^{5, 6}. Severe anemia i.e. hemoglobin (Hb) $<5\text{g/dl}$ can result with Plasmodium Vivax & P. Malariae, 12.2 % with mixed infection while P. Falciparum alone accounts for 15.1%. As hemolytic anemia (Hemolysis) is a cause of significant morbidity and possible mortality and the resulting

complications like black water fever, cerebral malaria and acute renal failure can have devastating effects on the patient's health³. Therefore, knowing the frequency of hemolytic anemia will help in preventing these complications and control of long-term sequels. According to recent advancement in research, different types of cytokine dysregulations are certain contributors in inducing and hastening the pathogenesis of hemolysis in malaria. They involve a remarkable rise in interleukin²⁻⁶, hypoxia inducing factor (HIF)-1 tumor necrosis factor (TNF)-alpha, interferon (IFN) gamma, IL-1, and decline in IL-12 and IL10 levels⁸. Drug-mediated anemia has also been postulated. However, the crucial aspect of treatment in malaria is that the extent of hemolysis is much higher caused by parasites than that observed in other diseases. Thus, there is suggestion of an immune regulated pathology underlying this pathogen⁹. There are trends having a sudden drop in hemoglobin after the treatment course is completed; necessitating a packed red blood cell transfusion. The peripheral smear and (complete blood count) CBC test are mostly negative for malarial parasite. Hence, a direct parasite mediated cell lysis could be ruled out. The raised reticulocyte counts along with a weak-positive direct Coombs' test point towards an immune-mediated cell destruction. Also corroborating these laboratory evidences is the clinical response after initiating corticosteroid therapy. A run through the literature reveals that a percentage of patients having malaria undergo immune hemolysis¹⁰⁻¹².

There are multiple factors which point to be precursors of immune hemolysis. The mechanisms include: a) serum antibodies directed against the antigens of parasites attaching to red cells b) deposition of immune complex progressing to a by-stander hemolysis because of a parasitic antigen or drug and antibody complex, or c) because of damage by oxidative process and clumping of anion channel protein of red cell, followed by coating of this particular denatured protein by the already naturally occurring autoantibody with subsequent removal by macrophages present in the reticuloendothelial system¹³⁻¹⁶. Adding to this, higher levels of cytokines, like TNF-alpha can activate macrophages, which subsequently in a hyperactive stage, may decrease their upper limit of threshold for the quantity of antibody coating required for phagocytosis. Other proposed mechanism includes a mislaying of complement regulatory proteins including CD-55 and CD-59 in cells those are parasitized; which are known to protect RBCs from inadvertent complement-mediated lysis. This combined with higher number of immune

complexes in malaria makes RBCs prone to complement induced lysis¹⁷⁻¹⁹.

MATERIALS AND METHODS

This study was carried out at Department of Internal Medicine, Lady Reading Hospital, Peshawar - Pakistan. The study design used was descriptive cross-sectional study. Study duration was one year from July 2017 to July 2018 in which the total number of observed patients were 151 keeping 50% prevalence of hemolytic anemia in malaria, 95% confidence interval and 8% margin of error. The technique used for sample collection was non-probability consecutive sampling technique. More over all patients presenting with malaria, diagnosis being confirmed with positive MP test, of either gender and with age ranging from 16 to 70 years were included. While patients in pediatric age group i.e. age up to 10 years, patients with hemolytic anemia due to causes other than malaria as evident by the history, family history and previous medical record were excluded. With thorough history and physical examination all of the patients were cautiously checked out. Certain laboratory test like Peripheral Smear, Lactate Dehydrogenase (LDH) level, Liver Function Tests (LFTs) and thick and thin smear for malaria were carried out on all of the patients. The blood tests were done in LRH laboratory by qualified lab technician. Data was analyzed using SPSS version 20. For quantitative variables like age & duration of disease, mean and standard deviation was calculated. For gender and hemolytic anemia which are qualitative variables, frequency and percentages were calculated. Hemolytic anemia was stratified with age, gender and duration of disease to see the effect modification. After the application of post stratification chi square test, the P value came out to be ≤ 0.05 which was considered to be a significant value. All the results were presented in the form of tables and charts.

RESULTS

In this particular study, for age distribution 151 patients were graphed according to age. Scrutinized in following age ranges: 103 patients (68%) were in age range 16 to 40 years while 48 patients (32%) were in in age range 41 to 70 years. Thirty-eight years was mean age with SD ± 11.77 . Male and female patients were 58% and 42% respectively. One hundred thirteen (75%) patients had duration of disease ≤ 1 week while 38 (25%) patients had duration of disease >1 week. Mean duration of disease was 1 week with SD ± 1.56 . Hemolytic anemia among 151 patients was analyzed as 5(3%) patients had hemolytic anemia while 146(97%) patients didn't had hemolytic anemia.

Frequency of hemolytic anemia in patients presenting with malaria at tertiary care hospital, Peshawar.

Table 1: Hemolytic Anemia.

Hemolytic Anemia	Frequency	Percentage
Yes	5	3%
No	146	97%
Total	151	100%

Table 2: Hemolytic Anemia Stratification According To Age Distribution (n=151).

Anemia	6-10 Years	11-16 Years	Total
Yes	3	2	5
No	100	46	146
Total	103	48	151

Table 3: Hemolytic Anemia Stratification According To Gender Distribution (n=151).

Anemia	Male	Female	Total
Yes	3	2	5
No	85	61	146
Total	88	63	151

Table 4: Hemolytic Anemia Stratification According To Duration Of Disease (n=151).

Anemia	≤ 1 week	>1 week	Total
Yes	0	5	5
No	113	33	146
Total	113	38	151

DISCUSSION

Malaria is a parasitic infection caused by any of the plasmodia (Falciparum, Vivax, Ovale, Malariae or Knowlesi)^{1, 2}. Historically malaria had epidemics with high mortality on mass scale but with current advances in medicine such epidemics have reduced significantly. With improved sanitation and insecticide sprays in the areas of high malaria prevalence, the disease cycle can be broken, as eradicating the mosquitos (female anopheles- vector for malaria spread) breaks the chain and thus helps in the prevention of disease^{3,4}.

In our study mean age was 38 years having SD \pm 11.77. Male and Female patients were 58% and 42% respectively. The disease mean duration of length was 1 week having SD \pm 1.56. More over 3% patients had hemolytic anemia while 97% patients didn't have hemolytic anemia. In another study conducted by Gosling RD et al, had reported that hematological changes related to malaria other than anemia are thrombocytopenia and neutropenia. Severe anemia i.e. hemoglobin (Hb) <5g/dl can result with Plasmodium Vivax & P. Malariae, 12.2 % with mixed infection while P. Falciparum alone

accounts for 15.1%⁵. While in a study conducted by Munir A H, Nadeem S, Amina A and Ashraf Z, in KTH showed that 51%, 51%, 8% and 3% patients had anemia, thrombocytopenia, leukopenia and pancytopenia respectively²⁰.

There were similar trends in the present case. The sudden drop in hemoglobin was noted after the treatment course was completed; necessitating a packed red blood cell transfusion. The raised reticulocyte counts along with a weak-positive direct Coombs' test point towards an immune-mediated cell destruction^{10, 11}.

While hemolysis had been reported in patients of Plasmodium falciparum malaria; both immune and non-immune; an association with P. vivax has seldom been reported. To the best of our knowledge, in association of malaria and autoimmune hemolysis two single cases have been reported, from Korea and Canada¹⁷. Despite a high degree of prevalence of malaria in India, only sporadic case reports have surfaced. This scarcity in literature may be attributed to the rarity of this phenomenon or due to under-recognition of this clinical phenomenon.

CONCLUSION

The majority of our patients were young. There is no statistically significant difference regarding hemolytic anemia due to malaria, with respect to gender. This can be reduced with early diagnosis and prompt management of malaria.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Nowsherwan: Study idea concept and design.

Khan AM: Study supervision and drafting.

Iqbal N: Statistical data analysis.

Mehr MT: Data Collection.

Iqbal F: Critical revision of the article for important intellectual content.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.