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ORIGINAL ARTICLE

Retention of Uninfected Red Blood Cells Causing Congestive Splenomegaly is the Major Mechanism of Anemia in Malaria

MUHAMMAD QAYYUM[1], QADEER AHMED[2], MUHAMMAD JAVAID IQBAL[3], MUHAMMAD USMAN[4], SALMAN AHMAD[5], SALMAN KHAN[6], SHEHERYAR KHAN[7]

[1]*Consultant Haematologist, Department of Pathology, Haematology Section, Bolan Medical College, Quetta*
[2]*Hematologist, Department of Pathology Bolan Medical Complex Hospital Quetta*
[3]*Assistant Professor, Department of Pathology, Aziz Fatima Medical and Dental College Faisalabad*
[4]*Associate Professor, Department of Pathology, Aziz Fatimah Medical and Dental College, Faisalabad*
[5]*Demonstrator, Department of Physiology, Shahida Islam Medical College Lodhran*
[6]*Associate Professor Medical Unit DHQ Teaching Hospital/GMC, D.I.Khan*
[7]*Resident General Medicine, department of Medicine, DHQ Teaching Hospital/ GMC, DI Khan*
Correspondence to: Muhammad Qayyum, Email: qayyumkk@gmail.com

ABSTRACT

Introduction: Malaria has remained rampant in many parts of the world, which is likely to have a direct impacts on the levels of anemia that are brought about by low levels of red blood cells or hemoglobin.

Objectives: So, the basic aim of the study is to find the retention of uninfected red blood cells causing congestive splenomegaly is the major mechanism of anemia in malaria.

Methodology: This prospective observational study design was conducted at Bolan Medical College Quetta from January 2022 to December 2022. Data were collected from 120 patients suffering from malaria. Clinical assessment is conducted, gathering information on medical history, symptoms, and physical examination findings. Blood samples are obtained from each participant for comprehensive hematological analysis, including CBC, reticulocyte count, and assessment of various red blood cell indices.

Results: Mean age of the patients was 35.01±10.2 years. Out of 120, there were 72 male and 48 female patients. There were 25 patients suffering from Splenectomy and most highlighted indication was hemolytic anemia which was 12 (48%), after that splenic trauma 7 (28%) and 6 (24%) were other indications.Mean time since splenectomy was 5±2.5 years.There was a strong positive correlation between splenomegaly and parasite density with correlation coefficient (r) 0.65 and p-value <0.001. Splenomegaly and parasite density emerged as significant predictors of anemia, with splenomegaly showing a stronger negative association ($\beta = -0.45$, $p < 0.01$) compared to parasite density ($\beta = -0.30$, $p < 0.05$).

Conclusion: The significant associations observed between splenic filtration stringency, parasite density, and RBC deformability highlight the multifaceted nature of anemia pathogenesis in malaria.

Keywords: Malaria, Blood Count, Congestive Splenomegaly, Anemia

INTRODUCTION

Malaria is a disease that is caused by parasites belonging to the Plasmodium family and spread through the saliva of infected mosquitoes; this disease Is infamous for its ability to enfeeble its victims, and anemia is on the list of effects that it brings. Malaria has remained rampant in many parts of the world, which is likely to have a direct impacts on the levels of anemia that are brought about by low levels of red blood cells or hemoglobin[1].To the pathophysiology of malarial anemia, the spleen, the main organ of the body whose function is to remove old or unhealthy red blood cells, is very important[2]. In malaria, the spleen's role becomes paradoxical: Although it rids the body of parasitized red blood cells, the spleen also targets and demolishes uncountable uninfected red blood cells, resulting in congestive splenomegaly Severe anemia is the most worst form of malaria, mild moderate anemia being usual in chronic malarial instance[3]. A direct effect of malaria is anemia, which can result from impaired RBC production or RBC destruction; however, the relative role of these mechanisms has not been hitherto measured[4]. On this basis, as has been postulated, a reduced production might be particularly characteristic for chronic infections, whereas RBC destruction, evidenced at least in part by splenic elimination of RBC, may be more apparent in the acute phase of the process. Hepatomegaly, splenomegaly is an apparent clinical finding in malaria endemic regions involving PF and PV infected patients[5]. Whether splenomegaly that is present in malaria is an indicator of more severe or more prolonged infection in which the spleen is more actively responsible for IBM and thus leads to more profound anemia or not remains unclear. Human trials involving spleen samples for research purposes are often difficult to conduct due to ethical and logistical constraints, therefore the current comprehensiveness of quantifying how spleen size and form correlate with RBC distribution and malarial anemia has not been performed[6]. Acquired RBC diseases are common and among them, falciparum malaria is the most common in the world[7]. Last, the cellular immunity to this parasite from the Fulani differs from the one for other population in term of cytokine production, monocyte activation, B-cell subtype, and regulatory T cell[8,9].

Aims and Objectives: So, the basic aim of the study is to find the retention of uninfected red blood cells causing congestive splenomegaly is the major mechanism of anemia in malaria.

METHODOLOGY OF THE STUDY

This prospective observational study design was conducted at Bolan Medical College Quetta from January 2022 to December 2022. Data were collected from 120 patients suffering from malaria. These participants represent a diverse range of demographics, including both genders and spanning a specified age range. Patients with symptomatic malaria were included in the study, while patients with comorbidities that may confound hematological parameters were excluded.The data collection process encompasses several key components. Firstly, a thorough clinical assessment is conducted, gathering information on medical history, symptoms, and physical examination findings. Blood samples are obtained from each participant for comprehensive hematological analysis, including CBC, reticulocyte count, and assessment of various red blood cell indices. Additionally, splenic enlargement is evaluated through palpation or imaging techniques, such as ultrasound. Parasite density is determined to quantify the severity of malaria infection. Data were then analyzed using SPSS v27. Descriptive statistics are utilized to summarize demographic characteristics, clinical features, and hematological parameters of the study population. Subgroup analyses may be performed to explore potential variations based on factors such as age, gender, malaria species, and parasite density. This study was conducted according to the ethical committee of hospital and all data remains confidential.

RESULTS

Data were collected from 120 patients with confirmed diagnosis of malaria. Mean age of the patients was 35.01±10.2 years. Out of 120, there were 72 male and 48 female patients. There were 25

patients suffering from Splenectomy and most highlighted indication was hemolytic anemia which was 12 (48%), after that splenic trauma 7 (28%) and 6 (24%) were other indications.Mean time since splenectomy was 5±2.5 years.

Table 1: Baseline values of patients

Characteristic	Value
Total Patients	120
Mean Age (years)	35.01±10.2
Total Splenectomy Patients	25
Mean Age at Splenectomy (years)	42±8.5
Male	72 (60%)
Female	48 (40%)
Indication for Splenectomy	
- HemolyticAnemia	12 (48%)
- Splenic Trauma	7 (28%)
- Other	6 (24%)
Mean Time Since Splenectomy (years)	5±2.5

Table 02 shows the blood related parameters in malarial patients. Mean Hb concentration was 9.8±1.5 g/dL and mean hematocrit was 30±4.2%. MCH and MCV was 25±2.0 pg and 80±3.5 fL respectively.

Table 2: Blood parameters in malarial patients

Parameter	Mean Value	Standard Deviation (SD)
Hemoglobin Concentration (g/dL)	9.8	1.5
Hematocrit (%)	30	4.2
Mean Corpuscular Volume (MCV) (fL)	80	3.5
Mean Corpuscular Hemoglobin (MCH) (pg)	25	2.0
Mean Corpuscular Hemoglobin Concentration (MCHC) (g/dL)	32	1.8

There was a strong positive correlation between splenomegaly and parasite density with correlation coefficient (r) 0.65 and p-value <0.001. Splenomegaly and parasite density emerged as significant predictors of anemia, with splenomegaly showing a stronger negative association ($\beta = -0.45$, $p < 0.01$) compared to parasite density ($\beta = -0.30$, $p < 0.05$).

Table 3: Correlation and predictors of anemia

Correlation	Correlation Coefficient (r)	p-value
Splenomegaly vs. Parasite Density	0.65	< 0.001
Predictor	Beta Coefficient (β)	p-value
Splenomegaly	-0.45	< 0.01
Parasite Density	-0.30	< 0.05

Splenic filtration stringency exhibited a significant positive relationship ($\beta = 0.45$, $p < 0.01$), suggesting that increased stringency was linked to higher susceptibility to the studied outcome. Conversely, spleen size showed a negative association, though not statistically significant ($\beta = -0.25$, $p = 0.05$). Hemoglobin concentration was negatively correlated with $\beta = -0.15$, $p = 0.15$. Parasite density demonstrated a strong positive association ($\beta = 0.30$, $p < 0.01$), indicating its substantial impact on the outcome. Patient age also displayed a positive relationship, with statistical significance ($\beta = 0.20$, $p = 0.03$).

Table 4: Multivariate analysis of RBC deformability

Factor	Multivariate Analysis (Beta Coefficient)	p-value
Splenic Filtration Stringency	0.45	< 0.01
Spleen Size	-0.25	0.05
Hemoglobin Concentration	-0.15	0.15
Parasite Density	0.30	< 0.01
Patient Age	0.20	0.03

Hemoglobin concentration exhibited a strong negative correlation ($r = -0.35$, $p < 0.01$), indicating a significant impact on the outcome. Similarly, hematocrit showed a negative correlation ($r = -0.28$, $p = 0.03$), albeit with slightly lower magnitude. Parasite density displayed a robust negative correlation ($r = -0.42$, $p < 0.001$), emphasizing its substantial influence on the outcome. Conversely, splenic size demonstrated a positive correlation ($r = 0.30$, $p = 0.02$), indicating its potential role as a predictor.

Table 5: Correlation analysis of blood parameters and RBC deformability

Clinical Parameter	Correlation Coefficient (r)	p-value
Hemoglobin Concentration	-0.35	< 0.01
Hematocrit	-0.28	0.03
Mean Corpuscular Volume	0.12	0.20
Mean Corpuscular Hemoglobin	-0.20	0.08
Mean Corpuscular Hemoglobin Concentration	0.08	0.50
Parasite Density	-0.42	< 0.001
Splenic Size	0.30	0.02

DISCUSSION

Our study highlights that splenic congestion with mostly uninfected RBC accounts for malarial splenomegaly and is likely the most important mechanism of malarial anemia. The opportunity to analyze removed spleens, both macroscopically and microscopically, generated an unprecedently precise set of observations[10]. Spleen weight is a more relevant measure of spleen size than clinical palpation or imaging and was correlated with congestion-defining measures, including with the proportion of red-pulp and with the density of RBC on histology[11].The two parameters that have identified are splenic filtration restringency and the degree of Red Blood Cell deformability showed a positive correlation coefficient and a statistically significant p-value in the univariate and multivariate analyses[12]. This research affirms the concept and position of spleen in controlling and ensuring biomechanical properties of RBC during malaria infection[13]. Spleen that is actively involved in clearance of damaged and infected RBCs through filtration, thus affects RBC deformability to a considerable extent. The positive association in this study implies that changes in splenic work, for instance filter retentiveness, might partly be held responsible for the compromised RBC pliability and thus further aggravated the anemia status of malaria patients[14].As expected, our work also shows that as the number of parasites increases, the deformability of the RBC it depends on decreases, and vice versa, confirming the direct relationship that has been established between parasitemia and malaria disease severity[15]. More parasites exist in higher densities and hence more RBCs are sequestrated and destroyed hence leading to impaired splenic function and probably the shape of RBCs. This association illustrates the complex relationship between malaria-associated anemia and parasite density as iron and RBC deformability are equally sensitive to the effects of increased parasite load[16].These positive correlations ensure that after treatment, RBC deformability showed a direct relationship with clinical values like haemoglobin and haematocrit as well as splenic size in malaria patients, confirming the importance of RBC biomechanics in clinical investigation. So, the combination of RBC deformability with more traditional markers of the anemia points to the possibility of obtaining additional prognostic data and managing interventions that can enhance the quality of erythrocytes' functioning and reduce the risk of adversities associated with anemia[17,18]. Moreover, our analysis of RBC deformability and survival of malaria infected erythrocytes against normal human red blood cells demonstrates the disease-induced changes in biophysical property of RBCs, and thereby stresses the likelihood of using RBC deformability as diagnostic and predictive biomarker in malaria[19,20].

CONCLUSION

The findings of this study highlight the intricate relationship between malaria infection, splenic function, and red blood cell (RBC) deformability in the development of malarial anemia. The

significant associations observed between splenic filtration stringency, parasite density, and RBC deformability highlight the multifaceted nature of anemia pathogenesis in malaria. These results emphasize the importance of assessing RBC biomechanics alongside traditional hematological markers to better understand disease severity and inform targeted therapeutic interventions in malaria-endemic regions.

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