***Review Article***

**Evaluation the Effect of plasmodium Falciparum on Platelets Count among Sudanese Patients at Khartoum State, 2018**

**Abstract**

Malaria has many symptoms similar to the common cold and, with the hallmark pathological feature being fever, it often resembles viral infections. Symptoms beside fever include nausea, chills, headaches and vomiting. The life-cycle of the malaria parasite begins when the female Anopheles mosquito harboring the parasite in its salivary gland, takes a blood meal from a human host. Genetic polymorphisms such as sickle cell anemia and Duffy negativity in their asymptomatic heterozygous form, confer resistance to the malaria parasite providing an evolutionary advantage for these polymorphisms and, along with the host response, play an important role in controlling infection. Results show that platelets count in infected males was 25% less than that of infected females, such difference was found to be statistically significant and suggests that P. falciparum has greater impact on platelets count in males than females. However, this is in contract to another study conducted in Nigeria which found that male malaria patients had higher platelets counts than female patients.

Keywords: polymorphisms, asymptomatic heterozygous, malaria, parasite

**Introduction**

Malaria is caused by protozoan parasites belonging to the genus *Plasmodium* and is one of the deadliest diseases affecting the human population (1). Of the four species of human malarial parasites (*Plasmodium falciparum, P*. *vivax, P*. *malaria and P*. *ovale),* (2), *P*. *falciparum* is the predominant species threatening the human population in endemic areas. The 2016 World Health Organization (WHO) report stated that 212 million new cases and 429,000 deaths were due to malaria (3) occurred in 2015, with the majority of the cases and deaths recorded in the Sub-Saharan African region. This was followed by South-East Asia and the Eastern Mediterranean region (3).To reduces and prevents malaria transmission in endemic areas, vector control has been implemented either by implementation of insecticide-treated mosquito nets, or indoor residual spraying (4). In Sub-Saharan Africa, insecticide-treated mosquito nets were heavily used with an estimated 53% of the population at risk of malaria sleeping under a net in 2015 compared to 30% in 2010 (3). Furthermore, 106 million people world-wide were protected from malaria transmission by indoor residual spraying including 49 million people in Africa, with the proportion of the population at risk declining from a peak of 5.7% globally in 2010 to 3.1% in 2015 (3).

**1.1.1 Life cycle of Malaria**

The life-cycle of the malaria parasite begins when the female *Anopheles* mosquito harboring the parasite in its salivary gland, takes a blood meal from a human host. Subsequent to the mosquito bite, the parasite, in the form of sporozoites, travels to the liver via the bloodstream where they invade hepatocytes and proliferate asexually. There they develop into schizonts which release merozoites (5). Merozoites re-enter the blood stream and invade red blood cells (RBCs), after which the intra-erythrocytic parasite mature and asexually reproduces into schizonts, eventually rupturing the RBC and releasing newly formed merozoites to invade new RBCs. The sexual stage occurs when some merozoites mature into gametocytes. Following ingestion by mosquitoes during a blood meal, an individual gametocyte may form one female macrogamete or up to eight male microgametes (6). In the mosquito midgut, gamete fusion produces a zygote that develops into a motile ookinete. The ookinetes subsequently penetrate the midgut of the wall and form oocysts (6). Over time, the oocysts enlarge and burst to release sporozoites that migrate to the salivary glands and can infect humans during the next blood meal. It is during the RBC stage of the malarial cycle that clinical manifestations of malaria occur and continue until either the host immune response eliminates infection, it is cleared via antimalarial treatment (7) or the host dies.



Figure (.1): Life cycle of *P. falciparum*.

**1.1.2 Signs and symptoms:**

Malaria has many symptoms similar to the common cold and, with the hallmark pathological feature being fever, it often resembles viral infections. Symptoms beside fever include nausea, chills, headaches and vomiting. For that it becomes difficult to pinpoint a malarial diagnosis(8). The clinical symptoms manifest during the asexual blood stage of the life cycle (9). After a period of symptoms where severity can vary, parasite load is controlled by the host’s immune response, although symptoms recur at intervals over weeks and months, associated with rises in parasitaemia (10). The successive waves of parasitaemia are lower and symptoms are less pronounced until eventually the infection is cleared (10).

In the case where malaria infection is not controlled, infection can progress to severe malaria (SM) which may result in death. *P. falciparum* is the predominant species causing SM in humans and accounts for over half a million deaths each year mainly in children in Sub-Saharan Africa (11). The main forms of SM are different in children and adults in various epidemiological settings: 1) severe anaemia occurs in infants in areas of stable, intense transmission; 2) cerebral malaria and respiratory distress (as a result of metabolic acidosis) occur in young children in areas of moderate transmission and 3) cerebral malaria, organ dysfunction (e.g., renal failure, severe jaundice, and pulmonary oedema) and acidosis occur in individuals of all ages in areas of low and unstable transmission (12).

Various factors play a role in the pathophysiology of SM including exponential parasite growth and microvascular obstruction from adherence of mature parasites to blood vessels (13). If the exponential phase increases by 10-fold every 48 hours, then total body parasitaemia is reached more rapidly(10). This high parasite load triggers an acute inflammatory response and therefore SM arises due to excessive or poorly controlled responses that have evolved primarily to control acute infection (11). Another key feature of SM is microvascular obstruction caused by *P. falciparum* sequestration of parasites within microvascular beds. This occurs via modifications on the RBC surface by the insertion and display of variant proteins such as *P. falciparum* erythrocyte membrane protein (PfEMP1) (14) which are able to bind to receptors on other cells including CD36 which is one of the well characterized receptors (15). Infected cells can also bind to uninfected RBCs (a process known as rosetting) (16) and activated platelets, which lead to clumps. Both of these can lead to microvascular obstruction and SM.

**1.1.3 Malaria Treatment**

Many drugs were developed to treat malaria in the 20th century, with chloroquine being the most widely-implemented. However, with the rise in antimalarial resistance now threatening their efficacy, the need to discover novel antimalarial drug candidates are required (17).

**1.1.3.1 Antimalarials**

The first line of treatment for uncomplicated *P. falciparum* malaria in endemic areas is artemisinin combination treatment (ACT) (18). ACT consists of an artemisinin derivative and a partner drug, which is another structurally unrelated antimalarial compound such as lumefantrine or mefloquine (19).

Another well-known antimalarial is chloroquine. At a physiological pH of ~7.4, chloroquine is a diprotic weak base and in its un-protonated state, is able to enter the digestive vacuole (DV) of the parasite within a RBC (20).

Due to antimalarial drug resistance (including chloroquine resistance), novel effective treatments are needed to combat malaria. (21). The mechanisms behind drug resistance are spontaneous, and thought to be independent to the drug used; rather, it is thought to be due to mutations in genes encoding the drug’s parasite target or influx/efflux pumps that affect the intraparasitic concentrations of the drug (22). One of these pumps involved in chloroquine transport is the *P. falciparum* chloroquine-resistance transporter (PfCRT). In the presence of a mutation, resistance occurs via a decrease in the concentration of chloroquine within the DV (23) due to the transport of drug away from the DV via PfCRT (24) and hence the site of action. The vital mutation seems to be the replacement of lysine with threonine at position 76 (25). However, PfCRT is not the sole determinant of chloroquine resistance, as it has been shown that mutations in the homolog of the major multidrug-transporter *P. falciparum* multidrug gene also modulates the extent of resistance (23).

**1.1.3.2 Vaccine Protection**

In terms of vaccines, RTS,S/AS01 is the most advanced *P. falciparum* vaccine candidate developed globally (26). The vaccine consists of hepatitis B surface antigen virus-like particles and incorporates a portion of the *P. falciparum-*derived circumsporozoite protein and a liposome-based adjuvant (26). The vaccine targets the circumsporozoite protein of *P. falciparum to* induce specific CD4-positive T cells that are associated with protection to *P. falciparum* infection and episodes of malaria (27)(28). In a 2009 study of 15,000 infants and young children from Sub-Saharan Africa, in infants aged 6-12 weeks and young children 5-15 months, the efficacy of the vaccine decreased rapidly (29). A booster shot 20 months 8 after the initial dose increased protection slightly. Individuals in the 5-17 month group contracted meningitis compared to children who received control vaccines (30).

Another vaccine that seemed promising and underwent early phase I/IIa clinical trials was using the radiation-attenuated, whole-cell sporozoite vaccine which delivered sterile protection against injection with sporozoites of the same parasite strain(31). However, this vaccine had drawbacks including lack of cross-strain protection, high numbers of parasites required, route of delivery and the logistical requirements for a liquid nitrogen cold chain to maintain viability of vaccine (31). Despite these drawbacks, the ultimate goal for a successful vaccine is to induce strain-transcendent protection (10).

**1.1.4 Host Response to Malaria**

Malaria is the strongest known selective pressure on the human genome in recent history (32). Genetic polymorphisms such as sickle cell anemia and Duffy negativity (33) in their asymptomatic heterozygous form, confer resistance to the malaria parasite providing an evolutionary advantage for these polymorphisms and, along with the host response, play an important role in controlling infection. Along with these genetic polymorphisms, two lines of host immune defense play a role in combating malaria infection; innate immune system and the adaptive immune system.

**1.1.4.1 Resistance to Malaria:**

Genetic polymorphisms have been shown to confer resistance to malaria and have been associated as an evolutionary force for genetic traits such as sickle cell disease (34) and Duffy negativity (33). Sickle cell disease results when there is a substitution of valine for glutamic acid at its sixth amino acid of the β-globin chain (35). Individuals homozygous for the 9mutation develop symptomatic and potentially deadly sickle disease whereby the polymerized hemoglobin causes RBCs to become sickle shaped and occlude blood vessels, whilst heterozygous individuals have sickle cell trait and are generally asymptomatic (36). Sickle cell trait confers resistance to malaria (37) and the frequency of carriers of this trait is high in malaria endemic regions (38). Resistance is thought to be due to parasitized mutant polymorphic RBCs subjected to enhanced phagocytosis by monocytes which suggest *P. falciparum* is cleared by the immune system more rapidly (39). Progressive dehydration of RBCs and increased cellular density have also been associated with decreased invasion by *P. falciparum* suggesting that structural features of the host cell play a role in resistance (40).

The Duffy-negative red cell phenotype is another well-known polymorphism that can cause malarial resistance. The Duffy antigen encodes a chemokine receptor (DARC, also known as Fy) and is expressed on the RBC surface. A polymorphism at a GATA-1 binding site in the promoter of the *DARC* gene alters receptor expression, leading to no expression on the RBC surface (41). Almost all Central and West African people are Duffy-negative and as such these individuals are resistant to *Plasmodium vivax* infection which requires Duffy to invade the RBC (42).

Understanding the variability of genes in human populations, and how they may provide resistance against malaria, may provide greater insight into developing new interventions, therapies and working towards better management of malaria.

**1.1.4.2 Innate Immune System:**

The innate immune system comprises of cells such as natural killer cells and dendritic cells. This is the first line of defense in regard to bacteria (43), virus (44) and parasite (45) invasion. Studies in mice and humans show the important role of macrophages in phagocytizing RBCs in the absence of cytophilic or opsonizing malaria-specific antibody (46). This interaction of RBCs is possibly due to the presence of CD36 on the surface of various cell types which subsequently results in sequestration of parasites in the micro vascular endothelia (47).

Furthermore, studies in mice have found that cytokines, such as interferon-γ, are released within the first few hours of a malaria infection, and subsequently predict the course of infection and its final outcome (48)(49). Interferon-γ is an important pro-inflammatory cytokine (50) and it plays a protective role against infection by protozoan parasites (51)(52). The production of interferon-γ in naïve animals may result from either pre-existing, cross-reactively primed effector memory T-cells or from cells of the innate immune system, e.g. phagocytic granulocytes, macrophages, Natural Killer cells or γδ T-cells(53).

**1.1.4.3 Adaptive Immune System:**

The adaptive immune system consists of cells such as B and T lymphocytes. Mechanisms of the adaptive immune system that play a role in parasite defense include antibodies blocking hepatocyte invasion, antibodies binding to adhesion molecules on the vascular endothelium thus preventing sequestration of RBCs, and antibodies blocking merozoite invasion into RBCs (54).

When immune adults leave malaria-endemic regions, their immunity to malaria wanes quickly, which suggests that continued exposure to malarial antigens is needed not only for the generation of memory cells and effector cells but also for their persistence? Rapid boosting of antibody responses to various antigens after reinfection does take place which indicates the presence of memory B cells (55).

During the erythrocytic stage of infection, CD4+ T-cells can play a protective role via interferon-γ production. CD4+ T-cell help is also required for the B-cell response which is involved in control and elimination of infected red blood cells. CD4+ T-cells are also important for controlling pre-erythrocyte stages of *Plasmodium* infection through the activation of parasite-specific CD8+ T-cells which are a subpopulation of MHC class-I restricted T cells and mediators of adaptive immunity (56).

**1.2 Platelets:**

Platelets are cells formed from the cytoplasm of bone marrow megakaryocytes and are the smallest of the blood cells. They are disc shaped, a nucleate cells with a primary function of maintaining hemostatic functions of blood (57).

**1.2.1Disorders of platelets:**

**1.2.1.1 Thrombocytosis:**

An increase in platelet numbers higher than normal is known as thrombocythemia or thrombocytosis. The condition causes weakness, headache, dizziness, chest pain, shortness of breath, nausea, and tingling in hands and feet. It can be of a primary cause also termed essential thrombocythemia to faulty stem cells in the bone marrow, or a secondary thrombocythemia when another condition is responsible for the thrombocytosis such as iron deficiency anemia oracute infection (58).

**1.2.1.2 Thrombocytopenia:**

Thrombocytopenia is a condition characterized by abnormally low levels of platelets in the blood(59). The condition could cause external bleeding, fatigue and general weakness(60). It can be due to: A. decrease in platelets production as in liver failure,B. Increased destruction as in hypersplenism C. or medication induced thrombocytopenia(61) (62).

**1.3 Effects of *Plasmodium falciparum* on platelets count:**

The spleen in malaria has played a crucial role in the immune response against the parasite, as well as controlling parasitaemia due to the phagocyto­sis of parasitised red blood cells(63). Some data suggested that platelets were seques­tered in the spleen during the acute infection (64).The term hyper­splenism was proposed to describe the clinical picture of the enlarged spleen followed by the decrease in one or more peripheral blood lineages (usually reverted after splenectomy), probably due to sequestration or destruc­tion of cells inside the spleen, in liver diseases, which lead to increased portal system pressure. However, it is believed that haematopoietic growth factors produced in the liver are also involved(65). On the other hand, the isolated spleen enlargement does not explainthe destruction of cells as formerly be­lieved. This organ represents outstanding architectural organisation and controls, with great sophistication, the exposure of cells screened by it. In patients with malaria, the increase in the macrophage-colony stimulating factor is associated to thrombocytopenia, suggesting that mac­rophages play a role in the destruction of these particles (66).

The finding of a *P. vivax* trophozoite inside a human platelet suggested that throm­bocytopenia could be the result of invasion of these par­ticles by the parasites themselves, similar to what was classically proposed for RBCs(67). However, this observa­tion was never seen again in the literature. Likewise, a “dysmegakaryopoiesis” was proposed, similar to what happened in the human malarial anaemia model, where dyserythropoiesis was triggered by cytokines (68). In the few studies that examined the bone marrow for this purpose, megakaryocytic lineage was apparently preserved(69) (70). Thrombopoietin indeed seems to rise during the acute disease even in the presence of liver compromise, suggesting that no bone marrow inhibition is seen (71). Additional data in vivax patients showed that there is a significant negative cor­relation between platelet count and mean platelet volume (72), suggesting that megakaryocytes are able to release mega platelets in the circulation to compensate for the low absolute number of platelets in the periph­ery. Similar results were shown in children with falci­parum malaria (73). These mega platelets are probably able to sustain a good primary haemostasis that could explain the low frequency of severe bleeding in malarial patients.

There is ev­idence that platelet-associated IgG (PAIgG) is increased in malaria and is associated with thrombocytopenia. However, this is a generic definition for all types of IgGs that may be found on the platelet surface, including antibodies stored inside platelet α-granules. Therefore, increased PAIgG could also be interpreted as platelet ac­tivation and exposition of IgGs on the surface, and not necessarily auto-immunity, as suggested in past studies(74) (75).

During acute malaria, thrombocytopenia is most probably associated with the binding of parasite antigens to the surface of platelets to which antimalarial antibodies also bind, leading to theformation of immune complexes (76). In an experimental model with *Plasmodium berghei*, the same correlation between platelet count and immune complexeswas evidenced (77). No association was found with IgM (70). It is clear that circulating immune complexes are elevated in vivax and falciparum malaria, but their role in the development of thrombocytopenia is still obscure (78) (79) as well as its immune suppressing effect (80) (81). Because the generation of immune complexes is propor­tional to the amount of available antigen, the negative correlation between platelet count and peripheral para­sitaemia reported in many studies (82) (83) corroborates ICs as a potential mechanism of platelet destruction.

Free radicals may play an impor­tant role in the platelet destruction in malarial infection. There is evidence that the decrease in total cholesterol in vivax malaria is due to lipidic peroxidation (84). Also, in vivax malaria, there is a negative correla­tion between platelet count and platelet lipid peroxida­tion in addition to the positive correlation between plate­let count and the activity of gluthatione peroxidase and superoxide dismutase, which are considered anti-oxidant enzymes (85). In a study on patients with acute falciparum malaria, there was a negative correla­tion between platelet count and nitrogen reactive inter­mediates (86). There is also a strong associa­tion between platelet count and intra-platelet gluthatione peroxidase, suggesting that a compensatory mechanism is presented by platelets to face the oxidative burst found in malaria (87).

Platelets from patients with acute malaria are highly sensitive to adenosine diphos­phate (ADP) addition in vitro (88), and it is believed that ADP release following haemolysis could contribute to higher platelet aggregation. Actually, the incubation of platelets with *P. falciparum*-parasitised RBCs also increases platelet aggregationin vitro, especially after ADP and thromboxane A2 addition (89). Even electron microscopic examination of non-stimulated, fresh platelets from malarial patients show centralisation of dense granules, glycogen deple­tion and microaggregates and phylopoids as a sign of in vivo activation, which could be responsible for a pseudo-thrombocytopenia due to sequestration of these activated particles in the interior of the vessels (90). *P. falci­parum* induces systemic acute endothelial cell activation and the release of activated von Willerbrand factor (vWF) immediately after the onset of the blood-stage infection (91).

It has been shown that platelets participate in the pathogenesis of microvascular malaria, adhering to the endothelium when it is previously stimulated with tumor necrosis factor (TNF) (92). Even in the non-stimulated cerebral endothelium, platelets may adhere and facilitate the adhesion of *P. falciparum*-parasitised RBCs, through CD36 is ubiquitous in endothelial cells and, coincidentally, platelets (93). Plate­lets therefore act by stabilising and strengthening bridges between RBCs and endothelial cells, which is considered the cornerstone of severe falciparum malaria. Rosetting of parasitised RBCs is also mediated through CD36 in platelets in severe malaria (94) (95). In mice infected with *P. berghei*, mice deficient of tissue and uroquinase plasminogen activators demonstrated less capillary sequestration of platelets and less severe malaria (96). Blocking GPIIb with anti-CD41 monoclonal antibodies in the first day of murine infection with *P. berghei* also led to higher pro­duction of interleukin IL10, IL1α, IL6 , interferon-α and TNF and less mortality among mice, suggesting that platelets may act as cofactors of severe malaria (97) (98). More severe patients presented more severe thrombocytopenia and higher TNF levels (99). Platelets stimulated by parasitised RBCs may also trigger apoptosis in endothelial cells pre-treated with TNF in a pathway mediated by tumor growth factor (TGF)-β1 from platelets (100). Recent evidence show­ing *P. vivax*-infected RBCs adhering to lung endothelial cells and to the placental tissue ex vivo indicates that in vivax, mechanisms similar to those associated with fal­ciparum severity may be involved (101). The contribution of platelets to this adhesion, however, requires further investigation.

In children in Kenya suffering from falciparum ma­laria, an inverse correlation between platelet count and plasmatic IL10 was seen (102). This interpretation is not straightforward, because IL­10 is generally associated with protection against severe disease. The authors hypothesise, though, that IL10 could reduce platelet counts to avoid infected-RBC ad­hesion to the endothelium, as if thrombocytopenia was a mechanism of defence against severe disease and not the cause. Studies of vivax infection have shown throm­bocytopenia to be associated with an increase in IL1, IL6, IL10 and TGF-β (103).

The role of platelet-derived microparticles (MPs) (submicron-sized vesicles released from cells upon ac­tivation or apoptosis) has yet to be determined in vivo. There is evidence that these MPs participate in the endothelial activation responsible for severe cerebral ma­laria in murine models (104). MPs were also associated with coma and thrombocytopenia in se­vere falciparum malaria patients (105). Apparently, there is an increase in the amount of MPs in vivax malaria patients, which may play a role in the acute inflammatory symptoms of this disease (106).

**1.4 Rationale:**

Malaria continues to be a major global health problem.In 2017, WHO reported an estimated 219 million cases of malaria occurred worldwide with most cases (92%) in the African region. It’s responsible for over 400,000 deaths annually (107). The infection could have several serious complications if not treated properly and data are needed to establish an effective prevention and treatment protocols.This study aims to spot light on the relationship between malaria infection and platelets numbers in infected subjects.

**1.5 Objectives**

**1.5.1 General objective:**

To study the effect of *Plasmodium falciparum* infection on platelets count.

**1.5.2 Specific objectives:**

- To measure platelets count for both malaria cases and control groups.

- To correlate platelets count with age and gender among malaria group.

**2. Materials and methods**

**2.1 Study design:**

This is a retrospective analytical case control study.

**2.2 Study area:**

The study was conducted in Khartoum state from the period of March to November 2018.

**2.3 Study population:**

Patients infected with *Plasmodium falciparum*. The numbers infected people was 34 males and 16females while in control group it was 26 males and 24 females.

**2.3.1 Inclusion criteria:**

Individuals tested positive for P. falciparum through RDTs and confirmed by microscopic examination, ages range between 5 to 65 years from both genders were enrolled in this study.

**2.3.2 Exclusion criteria:**

Subjects suffering from liver diseases, aplastic anemia, leukemia were not included in this study. Individuals who are under medications that affect platelets count such as vancomycin or heparin were excluded from this study.

**2.4 Sampling:**

**2.4.1 Sample size:**

The study was conducted on 100 subjects, 50 of which were patients suffering from malaria as a case group and the other half (50 subjects) were healthy individuals serving as a control group.

**2.4.2 Sampling technique:**

Samples were collected using simple random technique.

**2.5 Data collection:**

A structured questionnaire was designed to provide personal and medical information about the study subjects.

**2.6 Methodology:**

**2.6.1 Blood sampling:**

Blood samples were obtained using venipuncture from each enrolled subject. 2.5 ml of venous blood was collected into blood containers with EDTA as an anticoagulant.

**2.6.2 Malaria detection:**

*Plasmodium falciparum* was detected using rapid diagnostic tests and confirmed by microscopic examination.

**2.6.2.1 Rapid diagnostic tests:**

5 µl of blood was added into test pad. Buffer reagent was added to perform three functions: to induce cell lysis and allow binding to colloidal gold-labeled antibodies, to help blood and immune complex to migrate up the test strip and cross monoclonal antibodies line, to clear blood from the membrane and facilitates reading. The test was considered valid if the control line was visible and positive if the HRPII and/or pan malarial antigen were visible. An immunochromatographi test diagnosis of *Plasmodium falciparum* was made if HRPII was visible, with or without the pan malarial antigen.

**2.6.2.2 Microscopic examination:**

Thick and thinfilms were made on a clean grease-free microscope slide, a small drop of blood was added and spread without delay to make the thick smear,and three small drops were added for thin film andwas spread using a smooth edged slide spreader.Slides were labelled and blood was allowed to air-dry in a horizontal position. Then thin films were fixed using absolute methanol for 1-2 minutes. Both films were stained with freshly prepared Giemsa stain at a concentration 10% and a pH 7.2 for 10 minutes. After staining, slides were washed with clean water and placed on a draining rack for the preparation to air-dry.

Thick and thin films were examined microscopically using 100×oil immersion objective for malaria parasites.*Plasmodium falciparum* infections were detected on thick films and confirmed by examining the thin films.

**2.6.3 Platelets estimation:**

Platelets were estimated using an automated hematology analyzer, the kits supplied by (Sysmex, Japan).

**2.7 Data analysis:**

The analysis of results was done using SPSS Vs.20 and the Microsoft excel computer program.

**2.8 Ethical consideration:**

Ethical approval was obtained from research committee of the university. Oral informed consent was obtained from each enrolled subject.

**3. Results**

This study included a total of 100 subjects, half of which (50 subjects) were malaria infected individuals as a study group and the other half (50 subjects) were healthy control. Both case and control groups were of the same age group (5-65 years old) from both genders (40% were females and 60% were males).

**3.1 Comparison of platelet count between malaria and control groups:**

The platelet mean count in *P. falciparum* infected individuals was (155 ± 66) while in control group it was (287 ± 54) (Table 1). There was a significant difference between the two groups (P value 0.000).

Table (1) comparison of platelet count between malaria group and control group.

|  |  |  |  |
| --- | --- | --- | --- |
| Variables | Case mean | Control mean | *P*. value |
| platelet (× 103 cell/µl) | 155 ± 66 | 287 ± 54 | 0.0001\*\* |

\*\*: significant at or less than 0.05.

Figure (2) comparison of platelets count between malaria group andcontrol group.

**3.2Comparison of platelets count between males and females malaria patients:**

The platelet mean count in *P. falciparum* infected males was (139 ± 60) while in females it was (187 ± 68) (Table 2). There was a significant difference between the two groups (P value 0.015).

Table (.2) comparison of platelet count between males and females among malaria patients.

|  |  |  |  |
| --- | --- | --- | --- |
| Variables | Male mean | Female mean | *P*. value |
| platelet (× 103 cell/µl) | 139 ± 60 | 187 ± 68 | 0.015\* |

\*: significant at 0.05 level of significance.

Figure (3.) comparison of platelets count between males and females among malaria patients.

**3.3Comparison of platelets count among different age groups:**

The platelet mean count in *P. falciparum* infected people according to age is illustrated in Table (.3). There was no significant difference between different age groups (P value 0.587).

Table (3) Comparison of platelet among different age groups.

|  |  |
| --- | --- |
| Age group | Platelets |
| 5 – 25 years | 145 ± 76 |
| 26 – 45 years | 165 ± 59 |
| 46 – 60 years | 147 ± 66 |
| P value | **0.587** |

Analyzed by one-way ANOVA.

Figure (4) mean platelet numbers among different age groups.

**4.1 Discussion:**

Malaria is considered to be one of the most fatal diseases in developing countries. This study intended to assess platelet count in *Plasmodium falciparum* patients and control groups.

The mean platelets count in *P. falciparum* infected people was lower than non-infected people. Results show that platelets count in healthy people was twice as much as in infected people, such difference was found to be statistically significant and indicates that *P. falciparum* induces reduction in platelets. This finding came in agree with Kumar (108), Patel (109), Khan (110), Jairajpuri(111), Narayan (112), Yadav (113), Rasheed (114), Giti(115), Utuk(116), Ansari (117), Elnasri(118).

The mean platelets count in *P. falciparum* infected males was lower than that of infected females. Results show that platelets count in infected males was 25% less than that of infected females, such difference was found to be statistically significant and suggests that *P. falciparum* has greater impact on platelets count in males than females. However, this is in contract to another study conducted in Nigeria which found that male malaria patients had higher platelets counts than female patients119.

When it came to age, mean platelets count in the youngest group (5 – 25 years) was the lowest, followed by the eldest group (46 – 60 years) while the highest platelets count was of the age group (26 – 45 years). However; it is statistically insignificant and suggests that the effects of *P. falciparum* on platelets is independent of age.

**4.2 Conclusion:**

In conclusion: Malaria infection with *Plasmodium falciparum* was found to reduce platelets count.

**4.3 Recommendations:**

* Platelets count should be estimated whenever malaria infection has been established.
* Thrombocytopenia in a patient with febrile illness heightens the suspicion of malarial infection.
* Further studies with larger sample size are needed in this field.
* More hematological parameters such as leukocytes count, platelets indices could be studied.
* More studies can be applied to correlate severity of malaria infection with platelets count.

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**Appendix (II)**



**SysmexKx- 21 automated hematology analyzer**