

HEMATOLOGICAL IMPACTS OF MALARIA: COAGULATION PATTERNS IN SEMI-URBAN POPULATIONS

Ifeoma Ngozi Okonkwo

Department of Medical Laboratory Science, Faculty of Health Sciences and technology College of Medicine, University of Nigeria, Enugu Campus;

Abstract: Malaria remains a significant public health challenge in endemic regions, impacting various physiological parameters, including haemostasis. This study investigates the haemostatic parameters among malaria-infected patients in a semi-urban setting within a malaria-endemic region. By examining these parameters, the research aims to enhance the understanding of malaria's impact on blood clotting mechanisms and identify potential complications related to haemostasis. The study involved a cohort of patients diagnosed with malaria, from whom blood samples were collected and analyzed for key haemostatic markers. The findings reveal alterations in several haemostatic parameters, suggesting a correlation between malaria infection and disrupted blood clotting processes. These insights underscore the importance of monitoring haemostatic parameters in malaria management and provide a basis for further research into mitigating haemostasis-related complications in malaria-infected individuals.

Keywords: Malaria, Haemostatic Parameters, Blood Clotting, Endemic Region, Semi-Urban Setting

INTRODUCTION

Reports have showed that Vector borne diseases (VBDs) are posing threat to global health thus accounting for 17% of the global infectious disease burden and are responsible for substantial morbidity and mortality worldwide (London School of Hygiene & Tropical Medicine, 2021; Ramalho-Ortigao & Gubler, 2020; World Health Organization, 2020). Among the VBDs, Mosquito-borne infectious disease account for the majority of cases reported as well as mortality, and disability-adjusted life years. Malaria is one of the mosquito-borne infection with high global burden (Franklin et al., 2019). Despite Nigeria Government intervention towards eradication of malaria, the country is still counted among endemic countries (World Health Organization, 2021) Children under the age of 5 years and pregnant women are the major group greatly affected by malaria infection (Oyibo et al., 2021; Oladimeji et al., 2019; Cohee & Laufer, 2018). The major route of acquiring the infection by human host is through the bite of infected female anopheles' mosquito during their blood meal (Wells & Andrew, 2019). Transfusion transmission of Plasmodium species had also been documented (Alho et al., 2017; Allain, 2010; Owusu-Ofori et al., 2010), but less attention had been paid to this in endemic region (Allain, 2010). Though rare health workers needlestick injury and sharing of need by drug addicts had been reported as another route of transmission of malaria infection (Minard et al., 2021; Alho et al., 2017; Chau et al., 2002; Weir, 1997). Another rare cases of malaria transmission is through congenital transmission, here parasitized erythrocytes can be transfer from infected mother to the fetus either transplacentally or during labor (Bilal et al., 2020; Omer et al., 2020; Olupot-Olupot et al., 2018; Sotimehin et al., 2008).

Alteration in haematological parameters had been documented as one of the major effects of malaria on human host (Al-Salahy et al., 2016; Osaro et al., 2014; Squire et al., 2014; Kayode et al., 2011; Maina et al., 2010; Wickramasinghe & Abdalla, 2000), the disease also altered some biochemical parameters as well (AlSalahy et al., 2016; Kayode et al., 2011; Adeosun et al., 2007). Major study on malaria and its associated

haemostatic parameter had been majorly on platelet count (Gupta et al., 2019; Peprah et al., 2020; Sakzabre et al., 2020), and when other parameter was done it is usually on pregnant women. In this study, changes in haemostatic parameters in symptomatic malariuos and asyptomatic malarious subjects were compared. This is to asserting the possible effect of the presented symptom of malaria infection such as fever and raised body temperature on haemostatic parameters.

METHODS

Study area

This study was conducted in Owo-Ondo State. The town Owo, lies at latitude 710'59.988"N and longitude 534'59.988" E with an altitude of 360m. Owo is less dense town with an estimated population of about 276.593(National Population Commission (2007). It is located within the low rain forest zone of Nigeria and has two seasons, dry and wet. The dry season lasts from mid-October to March while the rainy season lasts from April to September.

Study population

The study was conducted at Federal Medical Centre, Owo which serve as a tertiary institution in Ondo State. A total number of 100 samples were collected. Fifty (50) samples were collected from symptomatic malarious patients with signs and symptoms of malaria (this includes; headache, fever, malaise, chill, nausea, vomiting and body temperature above 37OC). Fifty (50) blood samples were also collected from apparently healthy subjects with no sign or symptom of malaria but stained thin film of their blood samples shows malaria parasites (subjects in this group are asymptomatic).

Clinical thermometer was used to determine the body temperature of all subjects. Subjects with symptoms such as headache, fever, malaise, chill, nausea, vomiting and body temperature above 37OC were grouped symptomatic while those without any symptom were grouped asymptomatic.

Inclusion criteria

Patients with sign and symptom of malaria and also positive to malaria parasitive testing using microscopy. This group serves as symptomatic malarious patients Individual with no sign and symptom of malaria parasites served as asymptomatic malarious subject and their thin blood film were positive to malaria parasite.

Exclusion criteria

In Both groups of subjects, individual with liver disease such as Hepatitis-B and C infection or liver cancer were excluded. Patients on antimalaria drugs were excluded. Subjects without malaria parasites were also excluded from this study

Specimen collection

About nine 9ml of blood was collected from each participants and 4.5 ml were dispensed into a pre-labeled bottle containing 1.5ml Sodium citrate. The remaining blood was dispensed into pre-labeled bottle of Ethylene Diamine tetra acetic acid (EDTA).

Sample Analysis

The blood samples were analysed within 4 hours of collection. Thin blood films were made for malaria parasite screening as described by Chesbrough (2006). Platelet count were analysed by diluting with ammonium oxalate and using standard manual methods (Chesbrough, 2006). While Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) were estimated using Calcium Rabbit Brain Thromboplastin and Kaolin platelet substitute mixture respectively (Dace & Lewis, 2001; Ramnik, 2009).

Statistical analysis of data

The mean values obtained from the control and test groups were recorded and compared statistically using the unpaired T-Test and Symmetric Measured Test of the Statistical Package for Social Sciences (SPSS).

RESULTS

A total of one hundred (100) subjects were involved in this study, comprised of fifty (50) symptomatic malaria patients and 50 asymptomatic individual without sign and symptom of malaria for two weeks. There was prolong in prothrombin time of malaria symptomatic patients compared to asymptomatic (Table 1, Figure 1). Activated Partial Thromboplastin time of the symptomatic patients was also found to be prolong when compared with asymptomatic subjects (Table 1, Figure 2). However, the Mean Platelet counts of the symptomatic patients was significantly lower ($p < 0.05$) compared to asymptomatic group (Table 1, Figure 3). These results show that there was a significant difference in haemostatic parameters of symptomatic and asymptomatic malarious subjects.

DISCUSSION

Haematological and haemostatic abnormalities are considered hallmarks of malaria, and are reported to be most pronounced in *Plasmodium falciparum* infection, probably as a result of the higher levels of parasitemia found in these patients (Facer, 1994). The findings presented in previous study shows that in malaria, there are several peripheral blood changes, including anemia which is a common presentation and complicated malaria has been observed to be a consequence of *Plasmodium falciparum* infection (Mohapatra et al., 2013). In this present study, the effect of malaria on prothrombin time, Partial thromboplastin time with kaolin (PTTK), and platelet counts were considered.

The result of this study showed that malaria infection debilitates prothrombin time (PT) by causing prolongation in prothrombin time this is in line with Mohamed and Mubarak (2009) report. This effect therefore is an indication that malaria patients may have deficiency of factor I, II, VII and X when it is prolonged.

The result of this study showed that malaria infection debilitates partial thromboplastin time with kaolin (PTTK). This is line with findings of Erhabor et al. (2020) on pregnant women with malaria infection. This increase could be due to the effect of malaria parasite on clotting factors either directly or by affecting the hepatocytes which are responsible for the most of the clotting factors thereby, leading to prolonged bleeding in the patients with malaria parasite (Lillicrap et al., 2009). This disorder of coagulation factors could lead to an increased risk of bleeding (haemorrhage) or obstructive clotting (thrombosis) (Lillicrap et al., 2009).

Previous study revealed that patients with malaria had low platelet count (Abro et al., 2009). In their report most of the patients had mild thrombocytopenia (Abro et al., 2009). A study carried out in Pakistan showed that overall, of malaria patients were found to have low platelet count (Sheraz et al., 2008). Malaria is usually associated with various degrees of thrombocytopenia (Sheraz et al., 2008). The result of this present study also supports the earlier claim by Horstmann et al., (Horstman & Dietrich, 1985) who reported that malaria infection has an adverse effect on platelet count. Similar result had also been reported earlier in previous studies that patients with malaria had low platelet count (Abro et al., 2009). Role of platelet in malaria parasite sequestration had been documented (Rowe et al., 2009), the interaction of *Plasmodium falciparum* infected erythrocytes affects platelets hence cause platelets clumping (autoagglutination) (Miller et al., 2002). In a review, suggestion had been made that oxidative stress might responsible for part in the pathogenesis of thrombocytopenia associated to malaria (Percário et al 2012). In earlier work, Erel et al. (2001) reported that the number of platelets and the activities of antioxidant enzymes—superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px)—in patients with *Plasmodium vivax* infection were reduced while lipid peroxidation of platelets was elevated. Thus

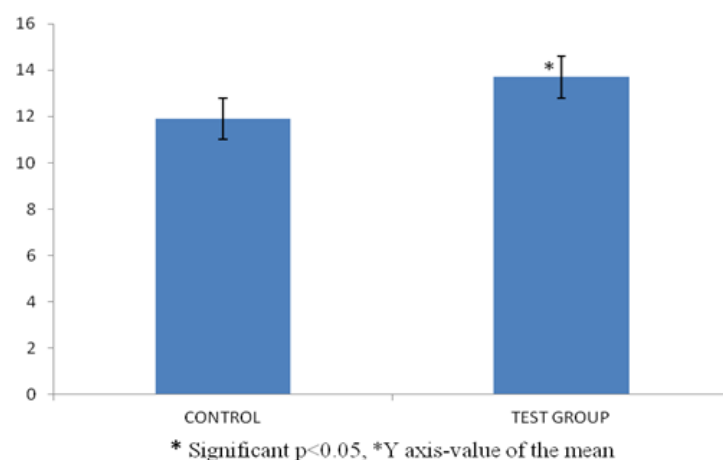
this suggests a negative correlation between platelet count and platelet level of lipid peroxidation. This might explain reduction in platelets experienced in this study.

CONCLUSION

This study revealed that malaria parasite debilitates haemostatic parameters by prolonging the prothrombin time (PT), Activated Partial Thromboplastin Time (APTT) and reducing platelet counts. Future study will investigate liver function in malaria infected patients in order to ascertain if the observed effects are directly on the clotting factors or on hepatic cells of the liver.

Table 1: The Mean $\pm$ Standard Error of Mean of Prothrombin Time, Partial Thromboplastin Time with Kaolin (PTTK) and Platelet Count of the Experiment

Parameters	Symptomatic	Asymptomatic	P Value
PT	13.70+ 0.19	11.90 + 0.23	P <0.05
PTTK	44.56 + 0.16	41.58+0.35	P<0.05
PLT COUNT	48.68 + 3.16	165.18 + 5.60	P<0.05



Legend:- there was a significant increase($p < 0.05$) in PT of malaria patients compared to control.

Figure1: Shows Difference in the Prothrombin Time (PT) of Malarious Patients and Control Human.

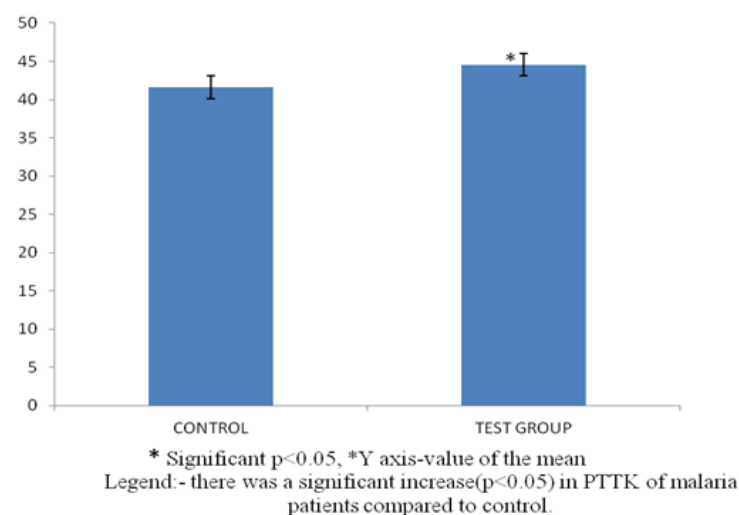
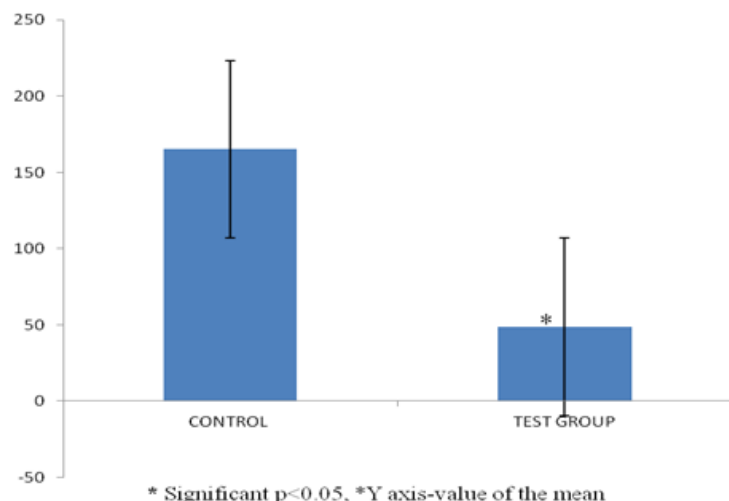


Figure 2: Show Difference in the Partial Thromboplastin Time with Kaolin (PTTK) of Malarious Patients and Control Human.



Legend:- the platelet count of malarious patients were a significant low($p < 0.05$) when compared to control group.

Figure 3: Shows difference in the Platelets count of malarious patients and control human.

REFERENCES

- Abro, A.H., Saleh, A.A., Abdou, A.S., Ustadi, A.M., Shuri, M. and Seliem, R.M., 2009. Thrombocytopenia in adults with acute malaria. *RMJ*, 34(2), pp.170-172.
- Adeosun, O.G., Oduola, T., Akanji, B.O., Sunday, A.M., Udoh, S.J. and Bello, I.S., 2007. Biochemical alteration in Nigerian children with acute falciparum malaria. *African Journal of Biotechnology*, 6(7). pp. 881–885
- Alho, R.M., Machado, K.V.A., Val, F.F., Fraiji, N.A., Alexandre, M.A., Melo, G.C., Recht, J., Siqueira, A.M., Monteiro, W.M. and Lacerda, M.V., 2017. Alternative transmission routes in the malaria elimination era: an overview of transfusion-transmitted malaria in the Americas. *Malaria journal*, 16(1), pp.1-14. <https://doi.org/10.1186/s12936-017-1726-y>
- Al Karsani, M.S. and Ali, M.S.M., 2009. Haematological Changes In Malaria Infected Blood Stored In Blood Bank Refrigerator (1-6° C). *Journal of Science and Technology*, 10(1), pp.1-11.
- Allain, J. P. (2010). Malaria and transfusion: A neglected subject coming back to the forefront. In *Clinical Infectious Diseases* 51(10), pp. 1199–1200. <https://doi.org/10.1086/656807>
- Al-Salahy, M., Shnawa, B., Abed, G., Mandour, A. and Al-Ezzi, A., 2016. Parasitaemia and Its Relation to Hematological Parameters and Liver Function among Patients Malaria in Abs, Hajjah, Northwest Yemen. *Interdisciplinary Perspectives on Infectious Diseases*, 2016, pp.5954394-5954394. <https://doi.org/10.1155/2016/5954394>

- Biggam, A.G., 1929. Malignant malaria associated with the administration of heroin intravenously. Transactions of The Royal Society of Tropical Medicine and Hygiene, 23(2), pp.147-153. [https://doi.org/10.1016/S0035-9203\(29\)90473-9](https://doi.org/10.1016/S0035-9203(29)90473-9)
- Bilal, J.A., Malik, E.E., Al-Nafeesah, A. and Adam, I., 2020. Global prevalence of congenital malaria: A systematic review and meta-analysis. European Journal of Obstetrics & Gynecology and Reproductive Biology, 252, pp.534-542. <https://doi.org/10.1016/j.ejogrb.2020.06.025>
- Chau, T.T.H., Mai, N.T.H., Phu, N.H., Luxemburger, C., Chuong, L.V., Loc, P.P., Trang, T.T.M., Vinh, H., Cuong, B.M., Waller, D.J. and Sinh, D.X., 2002. Malaria in injection drug abusers in Vietnam. Clinical infectious diseases, 34(10), pp.1317-1322. <https://doi.org/10.1086/340053>
- Cheesbrough, M. 2006. District Laboratory Practice in Tropical countries, part 1, Cambridge Low price Edition. Pp. 248-250. Cambridge University Press
- Cohee, L. and Laufer, M., 2018. Tackling malaria transmission in sub-Saharan Africa. The Lancet Global Health, 6(6), pp.e598e599. [https://doi.org/10.1016/S2214-109X\(18\)30197-9](https://doi.org/10.1016/S2214-109X(18)30197-9)
- Dace, J. and Lewis, S., 2001. Basic Haematological techniques.
- In Practical haematology 9th edition. Edited by Barbara JB,
- Mitchell LS, Imelda B. London:, pp 487-490. Churchill Livingstone
- Erel, O., Vural, H., Aksoy, N., Aslan, G. and Ulukanligil, M., 2001. Oxidative stress of platelets and thrombocytopenia in patients with vivax malaria. Clinical biochemistry, 34(4), pp.341-344.
- Erhabor, O., Abdulrahman, A. and Erhabor, T., 2020. Effects of malaria parasitaemia on some haemostatic parameters among pregnant women of African descent in Specialist
- Hospital Sokoto, Nigeria. Human Antibodies, 28(1), pp.21-28. <https://doi.org/10.3233/HAB-190389>
- Facer CA (1994). Hematological aspects of malaria. In: Infection and hematology. Oxford:, pp. 259-294. Butterworht Heinmann ltd
- Franklinos, L.H., Jones, K.E., Redding, D.W. and Abubakar, I., 2019.
- The effect of global change on mosquito-borne disease. The Lancet
- Infectious Diseases, 19(9), pp.e302-e312.
- [https://doi.org/10.1016/S1473-3099\(19\)30161-6](https://doi.org/10.1016/S1473-3099(19)30161-6)

Gupta, P., Guddattu, V. and Saravu, K., 2019. Characterization of platelet count and platelet indices and their potential role to predict severity in malaria. *Pathogens and global health*, 113(2), pp.8693. <https://doi.org/10.1080/20477724.2019.1600855>

Horstmann, R.D. and Dietrich, M., 1985. Haemostatic alterations in malaria correlate to parasitaemia. *Blut*, 51(5), pp.329-335.

Khan, S.J., Khan, F.R., Usman, M. and Zahid, S., 2008. Malaria can lead to Thrombocytopenia. *Rawal Medical Journal*, 33(2), pp.183-185.

Kayode, O.T., Kayode, A.A.A. and Awonuga, O.O., 2011. Status of selected hematological and biochemical parameters in malaria and malaria-typhoid co-infection. *Journal of Biological Sciences*, 11(5), pp.367-373. <https://doi.org/10.3923/jbs.2011.367.373>

Lillicrap, D., Key, N., Makris, M. and O'Shaughnessy, D. 2009. *Practical Hemostasis and Thrombosis*. Pp. 1-5. Wiley-Blackwell

London School of Hygiene & Tropical Medicine. 2021. The Global Challenge of Vector-Borne Diseases and How to Control Them |

LSHTM. Retrieved June 4, 2021, from

<https://www.lshtm.ac.uk/study/courses/short-courses/free-onlinecourses/vector-borne-diseases>

Maina, R.N., Walsh, D., Gaddy, C., Hongo, G., Waitumbi, J., Otieno, L., Jones, D. and Ogutu, B.R., 2010. Impact of *Plasmodium falciparum* infection on haematological parameters in children living in Western Kenya. *Malaria journal*, 9(3), pp.1-11.

<https://doi.org/10.1186/1475-2875-9-S3-S4>

Miller, L.H., Baruch, D.I., Marsh, K. and Doumbo, O.K., 2002. The pathogenic basis of malaria. *Nature*, 415(6872), pp.673-679.

Minard, G., Touche, S., Delavelle, A.C., Bonnet, M., Huguenin, A. and

N'Guyen, Y., 2020. Case Report: Could Artemisinin-Based Combination Therapy Prevent Occupational Malaria following Blood Exposure?. *The American Journal of Tropical Medicine and*

Hygiene, 104(1), pp.240-242. <https://doi.org/10.4269/AJTMH.20-0717>

Mohapatra, S., Samantaray, J.C., Arulselvi, S. and Ghosh, A., 2013. Disseminated intravascular coagulation following malaria due to *Plasmodium vivax*: a thromboelastography-based study. *Malaria journal*, 12(1), pp.1-4. doi:10.1186/1475-2875-12-336

National Population Commission, 2007: 2006 Population and housing

Census Enumerator's Manual. Federal Republic of Nigeria, Abuja Nigeria. <https://www.nationalpopulation.gov.n>

Oladimeji, K.E., Tsoka-Gwegweni, J.M., Ojewole, E. and Yunga, S.T., 2019. Knowledge of malaria prevention among pregnant women and non-pregnant mothers of children aged under 5 years in Ibadan, South West Nigeria. *Malaria journal*, 18(1), pp.1-12.

<https://doi.org/10.1186/s12936-019-2706-1>

Olupot-Olupot, P., Eregu, E.I., Naizuli, K., Ikiror, J., Acom, L. and Burgoine, K., 2018. Neonatal and congenital malaria: a case series in malaria endemic eastern Uganda. *Malaria journal*, 17(1), pp.1-5.. <https://doi.org/10.1186/s12936-018-2327-0>

Omer, S.A., Adam, I., Noureldien, A., Elhaj, H., Guerrero-Latorre, L., Silgado, A., Sulleiro, E. and Molina, I., 2020. Congenital Malaria in Newborns Delivered to Mothers with Malaria-Infected Placenta in

Blue Nile State, Sudan. *Journal of tropical pediatrics*, 66(4), pp.428-

434.. <https://doi.org/10.1093/TROPEJ/FMZ083>

Osaro, E., Jamilu, M.H., Ahmed, H. and Ezimah, A., 2014. Effect of plasmodium Parasitaemia on some haematological parameters in children living in Sokoto, North Western, Nigeria. *International Journal of Clinical Medicine Research*, 1(2), pp.57-64. <http://www.aascit.org/journal/ijcmr>

Owusu-Ofori, A.K., Parry, C. and Bates, I., 2010. Transfusiontransmitted malaria in countries where malaria is endemic: a review of the literature from sub-Saharan Africa. *Clinical Infectious Diseases*, 51(10), pp.1192-1198. <https://doi.org/10.1086/656806>

Oyibo, W., Ntadom, G., Uhomoibhi, P., Oresanya, O., Ogbulafor, N., Ajumobi, O., Okoh, F., Maxwell, K., Ezeiru, S., Nwokolo, E. and Amajoh, C., 2021. Geographical and temporal variation in reduction of malaria infection among children under 5 years of age throughout Nigeria. *BMJ global health*, 6(2), p.e004250. <https://doi.org/10.1136/bmjgh-2020-004250>

Peprah, S., Ogwang, M.D., Kerchan, P., Reynolds, S.J., Tenge, C.N., Were, P.A., Kuremu, R.T., Wekesa, W.N., Masalu, N., Kawira, E. and Kinyera, T., 2020. Mean platelet counts are relatively decreased with malaria but relatively increased with endemic Burkitt Lymphoma in Uganda, Tanzania, and Kenya. *British journal of haematology*, 190(5), pp.772-782. <https://doi.org/10.1111/bjh.16700>

Percário, S., Moreira, D.R., Gomes, B.A., Ferreira, M.E., Gonçalves, A.C.M., Laurindo, P.S., Vilhena, T.C., Dolabela, M.F. and Green, M.D., 2012. Oxidative stress in malaria. *International journal of molecular sciences*, 13(12), pp.1634616372.

Ramalho-Ortigao, M., & Gubler, D. J. (2020). Human Diseases Associated With Vectors (Arthropods in Disease Transmission). In *Hunter's Tropical Medicine and Emerging Infectious Diseases* pp. 1063–1069. Elsevier.

<https://doi.org/10.1016/b978-0-323-55512-8.00147-2>

Ramnik S (2009). Medical Laboratory Technology Methods and Interpretations 6th edition, Jaypee Brother Medical Publishers Ltd, New Delhi, pp380-383. Jaypee Brother Medical Publishers Ltd, New Delhi

Rowe, J.A., Claessens, A., Corrigan, R.A. and Arman, M., 2009. Adhesion of Plasmodium falciparum-infected erythrocytes to human cells: molecular mechanisms and therapeutic implications. Expert Reviews in Molecular Medicine, 11(e16), pp.26-2009.doi:10.1017/S1462399409001082

Sakzabre, D., Asiamah, E.A., Akorsu, E.E., Abaka-Yawson, A., Dika, N.D., Kwasi, D.A., Ativi, E., Tseyiboe, C. and Osei, G.Y., 2020. Haematological Profile of Adults with Malaria Parasitaemia Visiting the Volta Regional Hospital, Ghana. Advances in Hematology, 2020, pp.9369758-9369758. <https://doi.org/10.1155/2020/9369758>

Sotimehin, S.A., Runsewe-Abiodun, T.I., Oladapo, O.T., Njokanma, O.F. and Olanrewaju, D.M., 2008. Possible risk factors for congenital malaria at a tertiary care hospital in Sagamu, Ogun State, South-West Nigeria. Journal of Tropical Pediatrics, 54(5), pp.313-320.

<https://doi.org/10.1093/tropej/fmn016>

Squire, D.S., Asmah, R.H., Brown, C.A., Adjei, D.N., ObengNkrumah, N. and Ayeh-Kumi, P.F., 2016. Effect of Plasmodium falciparum malaria parasites on haematological parameters in Ghanaian children. Journal of parasitic diseases, 40(2), pp.303-311. <https://doi.org/10.1007/S12639-014-0501-Z>

Weir, W., 1997. Two cases of malaria: four messages. Weekly releases (1997–2007), 1(12),

p.1077.<https://doi.org/10.2807/esw.01.12.01077-en>

Wells, M.B. and Andrew, D.J., 2019. Anopheles salivary gland architecture shapes plasmodium sporozoite availability for transmission. mBio, 10(4), pp.e01238-19. <https://doi.org/10.1128/mBio>

Wickramasinghe, S.N. and Abdalla, S.H., 2000. Blood and bone marrow changes in malaria. Best Practice & Research Clinical Haematology, 13(2), pp.277-299.

<https://doi.org/10.1053/beha.1999.0072>

World Health Organization. 2020. Vector-borne diseases.

<https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases> (accessed 4th June 2021)

World Health Organization. (2021). Malaria. 2021.

<https://www.who.int/news-room/fact-sheets/detail/malaria> (accessed 3rd June 2021)