EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 7
75-78
Year: 2018

ASSOCIATION BETWEEN D- DIMER LEVEL AND MALARIA INFECTION AMONG SUDANESE PATIENTS IN KHARTOUM STATE 2017

Tarig A. M. Hamid[1*], Zeinab S. A. Alsayed[2], Sarah M. D. Ahmed[1], Hind A Mahmoud[1]

[1]Department of Hematology ond Immunohematology – AL Yarmouk Collage –Khartoum Sudan.
[2]Department of Hematology ond Immunohematology – Sharq Elnile College – Khartoum Sudan.

***Corresponding Author: Tarig A. M. Hamid**
Department of Hematology and Immunohematology – AL Yarmouk Collage –Khartoum Sudan.

Article Received on 03/05/2018 **Article Revised on 24/05/2018** **Article Accepted on 14/06/2018**

ABSTRACT
BACKGROUND This prospective case control study was aimed in assessing the presence, severity, and correlate the pathogenesis of blood coagulation disorder (hypercoagulability) often associated with malaria in patients that have the disease**.** AIM in order to evaluate the effect of hypercoagulability by using D-Dimer among various categories of Sudanese malaria patients in Khartoum state. METHOD Trisodium citrate anticoagulated venous blood was collected from patients with malaria and centrifuged for 15 minutes at 2000g and plasma was separated from the sample, the plasma sample was kept frozen at -20^{o}c for 2 weeks, thawing of plasma was performed at 37^{o}c for 15 minutes in order to obtain platelet poor plasma. The platelet poor plasma samples were measured by using d-dimer test device (Ichroma^{TM}) to evaluate the cross-linked fibrin degradation product containing D-Dimer in the patient plasma. RESULTS A total of 40 blood samples were included, 30 of these samples were collected from patient with malaria infection included as a case group and 10 samples were collected from apparently normal individuals included as a control group. The samples were collected from different age and sex groups, child >14 years and adult (15 – 37) years, 23 males and 17females. The study population divided into two group depend on the malaria parasite species, patient who's infected with P. *vivax*, and other twenty seven patient infected with P. *falciparum*. Present study showed a significant decrease of d dimer level associate with the age groups (P; 0.00), and was slightly decreased in a female group compared with male group with significant (P; 0.02). D dimer level was elevated in vivax group compared with falciparum group with statistical significant (P; 0.00) .CONCLUSION The present study concluded that Malaria patient have a hypercoagulable status, with increased risk of thrombosis which is more in female, adult and falciparum infected patient compare with males, child and vivax infected patient respectively.

KEYWORDS: Malaria infection, d-dimer.

1. INTRODUCTION

Malaria is a mosquito-borne infectious parasitic disease affecting humans caused by protozoans, commonly transmitted by an infected female *Anopheles* mosquito.[1] Malaria is a great health problem in some of the most areas of the world, and continues to cause significant morbidity and mortality worldwide.[2] In 2016, there were 216 million cases of malaria worldwide resulting in an estimated 731,000 deaths.[3] Also cases of malaria acquired by international travelers from industrialized countries have increased worldwide.[4] the most severe form of malaria is caused by *P. falciparum*; that can lead to patient death.[5] Severe manifestations of P. falciparum malaria include (cerebral malaria), renal failure, hepatic dysfunction, profound anemia, and abnormal bleeding.[6] Many of these complications are believed to be related to the coagulopathy and microvascular changes in this disease. Coagulation abnormalities are frequently found in patients with severe malaria. Clinically apparent bleeding or disseminated intravascular coagulation (DIC) is associated with very severe disease and a high mortality. Bleeding in severe malaria results from several pathological processes such as thrombocytopenia, consumptive coagulopathy, and impaired clotting factor synthesis.[7]

The activation of the coagulation system during severe complicated malarial infection leading to in vivo thrombin generation. The stimulation of the coagulation system is caused by various procoagulants present during malarial infection. Including exposed phosphatidylserine on the cell surface of infected erythrocytes, the lysis of activated platelets together with their secretory products, and the tissue factor (TF) released from damaged vascular endothelial cells.[7] Furthermore, histamine - are additional factors that promote fibrin formation.[8] The intrinsic pathway of the coagulation has also been shown to be activated in severe malaria.[9] Activation of the

coagulation cascade also occurs in mild malaria.[10] In addition Protein C, protein S, and AT levels were found to be low in P. *falciparum*, particularly in complicated cases, but were normal in P. *vivax* infection.[11] The reduction in the levels of protein C, protein S, and AT is attributed to increased consumption due to microvascular thrombosis rather than to reduced synthesis in the liver.[10] Plasma levels of plasminogen activator inhibitor-1 (PAI-1) were very high in cases of P. *falciparum* infection as compared to normal controls and P. *vivax* infection; this could contribute to impaired fibrinolysis.[11] Elevated fibrinogen degradation products (FDP) were demonstrated only in acute complicated P. *falciparum* infection. Their occurrence is mostly a compensatory mechanism secondary to increased Fibrin formation during malarial infection.[7]

Malaria is diagnosed by the microscopic examination of parasite in the blood, or with antigen-based rapid diagnostic tests. Also techniques that use the polymerase chain reaction (PCR) to detect the parasite's DNA are available, but these are not widely used in malaria-endemic areas due to their cost and complexity.[12]

2. MATERIAL AND METHODS

2.1 Study area and population: This case-control study was conducted in Al-Tagana laboratory in Khartoum state where malaria infection was diagnosed, during January to June 2017. Included forty blood samples, thirty of these samples were collected from patient with malaria infection included as a case group and ten samples were collected from apparently normal individuals as a control group.

2.2 Sample collection Blood samples were taken from patient with malaria parasite infection. A total of 2.5 ml blood samples were collected in container containing 3.8 % of tri-sodium citrate to obtain platelets poor plasma that used to measure d dimer using ichroma™.

2.3 Statistical analysis: Data was analyzed using SPSS version 14 for windows 7 ultimate to obtain mean, standard deviation and P value. P value less than 0.05 consider clinically significant and more than 0.05 considered clinically insignificant.

2.4 Methodology: D-dimer concentration was investigated by quantitative determination of cross-linked fibrin degradation product containing D-dimer using ichroma™. The method comprise of four processes. Firstly apply 50µl of washing solution to the Test device, Avoid touching the membrane with the pipette and allow the washing solution to soak into the membrane, and then added 50µl of undiluted platelet-free citrated plasma or control to the Test device. The sample should be absorbed into the membrane in less than 50 seconds by Apply 50µl of conjugate to the Test device. The conjugate should be absorbed into the membrane in less than 50 seconds, finally apply 50µl of washing solution in the Test Device and read the result.

3. RESULT

The study has been done on 40 participants, 30 with malaria parasite infection considered as a case group (17 male and 13 female with different ages) in which 27 patient infected with P. *falciparum* species and 3 remaining cases infected with P. *vivax* species. Remaining 10 were apparently healthy individuals, 6 males and 4 females was considered as a control group.

Table No (1): Demographic/Clinical data of two studied group.

Age	Case group		Control group	
	Number	**Percent**	**Number**	**Percent**
< 14 yrs	10	25%	3	7.5%
>14 yrs	20	50%	7	17.5%
Total	30	75%	10	25%

Table No (2): Gender of two studied group.

Gender	Case group		Control group	
	Number	**Percent**	**Number**	**Percent**
Male	17	42.5%	6	15%
Female	13	32.5%	4	10%
Total	30	75%	10	25%

Table No (3): Number of cases infected with different species of Plasmodium Malaria.

species	Number	Percent
Falciparum	27	90.1%
Vivax	3	9.9%
Total	30	100%

Table No (4): Severity of malaria infection among case group.

Parasite density	Number	Percent
< +1	5	16.7%
+1	14	46.6%
+2	11	37.7%
Total	30	100%

A five number of cases with less than one cross parasitemia, and remaining 25 cases with one and two crosses of parasite density.

Table No (5): Comparison of means and SD of d-dimer among different ages of a case group.

Age	N	Mean	Std. Deviation
< 14 yrs.	10	990	1307.63
>14 yrs.	20	750	822.38

P Value 0.00

There is a significant decrease of d dimer among Adult compared with child group with a mean (750± 822.38, 990±1307.63 ng/ml) and (P; 0.00) respectively.

Table No (6): Correlation between d-dimer level and Gender among case group.

Gender	N	Mean	Std. Deviation
Male	17	835.3	1142.33
Female	13	823.1	803.28

P value 0.026

There was a significant decreased of d dimer level among female compare with male groups with a means (823.1±803.28, 835±1142.33 ng/ml) respectively, and (P; 0.026)

Table No (7): Correlation between d-dimer among different Species within case group.

Parasite Species	N	Mean	Std. Deviation
Falciparum	27	825.9	1029.78
Vivax	3	866.7	723.42

P-Value 0.000

There was a significant decrease of d dimer among patient infected with Falciparum species compared with those infected with Vivax with a mean (825.9± 1029.78, 866.7 ±723.42 ng/ml) respectively, and (P; 0.00).

Table No (8): Correlation between d-dimer and Severity of malaria infection among case group.

Parasite density	N	Mean	Std. Deviation
< +1	5	200.0	173.21
+1	14	707.1	1021.66
+2	11	1272.7	1028.68

P-Value 0.000

There was a significant association between an increase in d dimer level and severity of malaria infection with a mean (200± 173.21, 707.1 ±1021.66, 1272.7± 1028.68 ng/ml) for <+1, +1 and +2 parasite density respectively (P; 0.00), result show gradually increase of d dimer level with an increase in parasite density.

5. DISCUSSION

This Prospective case control study was done in Al Tagana laboratory in Khartoum state, during the period from January to June 2017, to determine the d dimer level among Sudanese patient infected with malaria parasite. A total of 40 blood samples were included, 30 of these samples were collected from patient with malaria infection included as a case group and 10 samples were collected from apparently healthy individuals included as a control group. The samples were collected from different age and sex groups, child <14 year and adult (15 – 37) year, 32 males and 17 females. The study population divided into two group depend on the malaria parasite species, patient whose infected with P.*vivax* (3 patient), and remaining 27 patient infected with P.*falciparum*.

Present study showed a significant decrease of d dimer level associate with the age groups (P; 0.00), and was slightly decreased in a female group compared with male group with significant (P; 0.02), which indicate Adult and females with malarial infection has a susceptibility for thrombosis more radially than infected child and males respectively .This was agree with study done in Nigerian University of Ibadan by Oyugi O. Ben,[1] Yongo E. Arthy,[2] et al (2013).

The study also showed the difference of d-dimer level between patient whose affected with P.*vivax* and patient whose effected with P.*falciparum*, the d dimer elevated in P.*vivax* groups more than the other groups with statistical significant of (P; 0.00), reflect that patient infected with P. *falciparum* specie has susceptibility for thrombosis more radially than those infected with Vivax species. That refers to increase plasma levels of plasminogen activator inhibitor-1 (PAI-1) in P.

falciparum infected patient. Which agree with study done in India by S. Datta,[1] L.D. Roul,[2] et al. January (2011).

6. CONCLUSION

The present study concluded that Malaria patient have a hypercoagulable status, with increased risk of thrombosis which is more in female, adult and falciparum infected patient compare with males, child and vivax infected patient respectively.

ACKNOWLEDGEMENT

We would like to express deepest gratitude to Al Tagana laboratory in Khartoum state-Sudan.

REFERENCE

1. *"Malaria Fact sheet N°94". WHO. March 2014. Archived from the original on 3 September 2014. Retrieved 28 August 2014.*
2. Bidyut Prava Das, et al. *International Journal of Current Microbiology and Applied Sciences* .Hematological Changes in Severe *P. falciparum* Malaria, 2017; 6: 1733-1739.
3. *GBD 2015 Mortality and Causes of Death, Collaborators. (8 October 2016). "Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015". Lancet, 388(10053): 1459–1544.*
4. Miller LH, Wellems TE. Two worlds of malaria. N Engl J Med, 2003; 349: 1496.
5. *World Health Organization. "Malaria". The First Ten Years of the World Health Organization (PDF). World Health Organization, 1958; 172–87. Archived (PDF) from the original on 2011-07-08.*
6. World Health Organization, Communicable Diseases Cluster. Severe falciparum malaria. Trans R Soc Trop Med Hyg, 2000; 94(Suppl. 1): S1–S90.
7. Srichaikul T. Hemostatic alterations in malaria. Southeast Asian J Trop Med Public Health, 1993; 24: 86–91.
8. Srichaikul T, Archararit N, Siriasawakul T. Histamine changes in Plasmodium falciparum malaria. Trans R Soc Trop Med Hyg, 1976; 70: 36–8.
9. Clemens R, Pramoolsinsap C, Lorenz R, Pukrittayakamee S, Bock HL, White NJ. Activation of the coagulation cascade in severe falciparum malaria through the intrinsic pathway. Br J Haematol, 1994; 87: 100–5.
10. Pukrittayakamee S, White NJ, Clemens R, Chittamas S, Karges HE, Desakorn V, et al. Activation of the coagulation cascade in falciparum malaria. Trans R Soc Trop Med Hyg, 1989; 83: 762–6.
11. Mohanty D, Ghosh K, Nandwani SK, Shetty S, Phillips C, Rizvi S, et al. Fibrinolysis, inhibitors of blood coagulation, and monocyte derived coagulant activity in acute malaria. Am J Hematol, 1997; 54: 23–9.
12. L Rénia; S Wu Howland; C Claser ; G Charlotte; R Suwanarusk; T Hui Teo; B Russell; F Ng; Virulence, 2012; 3: 193.