



Determination of Prothrombin Time, Activated Partial Thromboplastin Time and D-Dimer Levels among Malaria Infected Patients in Sinnar State, Sudan

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Abstract

Malaria is one of the major causes of disease for people living in tropical and subtropical areas. Blood coagulation activation is frequently found in patients with malaria. The aim of the current study is to assess prothrombin time, activated partial thromboplastin time and D-dimer in patient suffering from malaria. This study includes 50 patients who have malaria parasite and 50 persons as control. Sandwich chemiluminescence immunoassay uses ABEI to label an anti-D-dimer monoclonal antibody and uses another D-dimer monoclonal antibody to coat magnetic microbeads. Prothrombin Time (PT) and Partial Thromboplastin Time (PTT) were measured for all case and control and SPSS software was used to evaluate the correlation. Results of D-dimer in all patient in mean were 1.92 ± 1.09 ng/ml; the D-dimer level was significantly higher among patients (p value = 0.00) compared to control (0.41 ± 0.10 ng/ml). PT in patient in mean was 16.34 ± 2.67 seconds and the mean of PT result in control was 14.29 ± 0.92 seconds; the mean of INR results in patients was 1.22 and the mean of INR results in control was 1.19. The results of PTT in patients in mean were (30.40 ± 4.73 second) and the mean of PTT results in control were (27.82 ± 1.49 seconds). Also, our result shows no statistically significant in PT, APTT and D-dimer between male and female. In conclusion, our study revealed higher D-dimer levels, PT and APTT among patient with Malaria, while the gender showed no effect on the level of D-dimer levels, PT and APTT.

Subject Areas

Infectious Diseases

Keywords

Malaria, D-Dimer Level, PT, PTT

1. Introduction

Malaria is one of the major causes of disease for people living in tropical and subtropical areas. Despite intensive control efforts during the twentieth century, approximately 40% of the world's population still remains at risk of infection. Malaria disease is parasitic infection caused by plasmodium species specially falciparum & vivax, malariae, and ovale [1]. Most morbidity and mortality are caused by plasmodium falciparum and the greatest disease burden is in African population. Many factors influence the severity of malaria. Malaria is rarely associated with bleeding; disseminated intravascular coagulation occurs in about 5% of patient with severe malaria [2]. Coagulation is a complex network of interaction involving vessels, platelets and factors. The ability to form and to remove a clot is truly a system depending on a system of checks and balances between thrombosis and hemorrhage that includes both procoagulants and anti-coagulants. Coagulation divided into two major system primary and secondary systems of hemostasis [3]. Coagulation cascade has two pathways: contact activation pathway and tissue factor pathway which lead to fibrin formation after joint to common pathway. The pathway is a series of reaction in which a zymogene of serine protease and its glycoprotein cofactor are activated to catalyze the next reaction in the cascade; the coagulation factors generally indicated Roman numbers with a lower case [4], with exception of fibrinogen which is fibrin clot subunit. The coagulation factors are enzyme precursors or cofactors [5]. D-dimer, the final product of plasma in-mediated degradation of fibrin-rich thrombi, has emerged as a simple blood test that can be used in diagnostic algorithms for the exclusion of venous thromboembolism. D-dimer levels have certain advantages over other measures of thrombin generation, because it is resistant to *ex vivo* activation, and relatively stable, and has a long half-life [6]. The coagulation system is increasingly recognized to play an important role in malaria. Obstruction of small vessels and binding of parasitized red blood cells to endothelial cells are crucial events in the pathogenesis of severe malaria, and endothelial cell activation and activation of the coagulation cascade are proposed to be involved in this process [7].

2. Material and Methods

This was a hospital based, analytic, descriptive cross-sectional study, conducted in Sudan-Sinnar hospital from September 2019 to October 2019. The subjects were selected from the coming patients to outpatients of emergency units. After informed consent, PT, APTT, D-dimer of all subjects was done. 50 persons (with different age and sex).The inclusion criteria for the selection of cases were diag-

nosis of malaria (with deferent stages). The exclusion criteria: Patients with disorder in which the proteins that control blood clotting become over active (disseminated intravascular coagulation), Patients with liver disease and Patients with Warfarin (Coumadin) use. Three ml of blood samples were drawn from each individual of study population, using standard venipuncture techniques. Sample was collected and then centrifuged at 3000 rpm for 15 minutes to obtain platelet poor plasma (PPP) and transparent plasma [8]. The separated plasma was analyzed to do PT, APTT and D-dimer or stored at 2 - 80 c if not tested immediately. PPP were estimated using MAGLUM800 (Snibe diagnostic). The normal ranges of PT 10 - 15 sec, APTT 28 - 40 sec and D-dimer less than 0.5 µg/ml fibrinogen-equivalent units (FEU). These values were used to confirm abnormal cases and then to find Correlation of PT, APTT and D-dimer with positive cases of Malaria. Statistical analysis was performed using SPSS (SPSS, version 16), data were expressed as mean and standard deviation ($M \pm SD$), the means were compared using independent T. test and Pearson's correlation analysis was used for correlation of parameters measured, p-value < 0.05 was considered as statistically significant. This study was approved by faculty of medical laboratory sciences, Alneelain University, Khartoum, Sudan, and ethical clearance was obtained from ministry of health. All participant patients have signed an informed consent before samples collection.

3. Result

The studied of total Malaria patients Sinnar state—Sudan were 50 and 50 as control groups. They have been categorized into different ages whose frequencies are (16 - 26 years) about 30%, (27 - 37 years), and >37 years about 22%, the most affected categories were 27 - 37 years which was 47% shown in **Table 1**. The results of D-dimer in all patients in mean were 1.92 ± 1.09 ng/ml; the D-dimer level was significantly higher among patients (p value = 0.00) compared to control (0.41 ± 0.10 ng/ml). PT in patient in mean was 16.34 ± 2.67 seconds and the mean of PT result in control was 14.29 ± 0.92 seconds; the mean of INR results in patients was 1.22 and the mean of INR results in control was 1.19. The results of PTT in patients in mean were 30.40 ± 4.73 seconds and the mean of PTT results in control was 27.82 ± 1.49 seconds (**Table 2**). Also, our result shows not statistically significant in PT, APTT and D-dimer between male and female in (**Table 3**).

Table 1. Age distributions of patients.

Age group	Frequency	Percentage (%)
16 - 26 Years	15	30.0
27 - 37 Years	24	48.0
>37 Years	11	22.0
Total	50	100.0

Table 2. Assessment of PT, APTT and D-dimer between case and control in Sinnar state-Sudan.

Parameters	Case (mean \pm SD)	Control (mean \pm SD)	p-value
PT	16.34 \pm 2.67	14.29 \pm 0.92	0.000
APTT	30.40 \pm 4.73	27.82 \pm 1.49	0.000
D-dimer	1.92 \pm 1.09	0.41 \pm 0.10	0.000

Table 3. Assessment of PT, APTT and D-dimer between male and female in Sinnar state-Sudan.

Parameters	Male (mean \pm SD)	Female (mean \pm SD)	p-value
PT	16.15 \pm 1.92	16.45 \pm 3.14	0.684
APTT	30.16 \pm 3.92	30.58 \pm 5.29	0.759
D-dimer	1.41 \pm 1.62	2.28 \pm 2.34	0.149

4. Discussion

In severe malaria, there is increased turnover of the coagulation cascade that results in consumptive coagulopathy, which may lead to development of DIC. The exact mechanism is not known; however, it has been hypothesized that infected erythrocytes possess pro-coagulant activity because of changes in the lipid distribution across the inner and outer surfaces of the infected erythrocyte membrane [9]. Numerous studies conducted in the Sudan to determine the effects of coagulation among heart disease patients, pregnancy complication, liver disease and thrombophilic patients, but there are not enough studies conducted in Sudan in open literature, to our knowledge about evaluation of coagulation among patients with malaria infection [10] [11] [12].

In this study we found high levels of plasma D-dimer ($p = 0.00$), PT ($p = 0.00$) and PTT ($p = 0.00$) were found among patients with malaria, this finding was consistent with several studies have shown altered levels of coagulation parameters in malaria patients [9] [13] [14]. Also, Riedl *et al.* find that the plasma thrombin generation potential began to change during parasitic infection [7]. Also Das *et al.*, find prolonged PT, prolonged APTT in 80%, 70% out of 40 cases ($p < 0.05$ in both parameters) [15]. Our result shows no statistically significant in PT, APTT and D-dimer between male and female, this finding agrees with study conducted by Agab Eldour *et al.* and they concluded gender had no effect on the level of fibrinogen [16]. Also our finding disagrees with other study and finds that gender is significant factor affecting blood coagulation system [17]. Other study conducted by Sarah *et al.*, showed no significant differences in PT and APTT values between genders and concluded gender and age do not play any role in affecting the mechanisms by which malaria changes the normal coagulation cascade [18]. Our study has some limitations, such as the relatively small number of subjects. Our finding on these results must be determined in further large controlled studies. Also we do not consider the other disorder than malaria

parasite like liver disease and other diseases that can change blood coagulation, because there is strong association between hemostatic changes and liver disease because hemostasis and most coagulation factors are synthesized by liver [19]. Also another limitation in our study should including other bio-markers, such as interleukins or Thrombin generation assays.

5. Conclusion

In conclusion, our study revealed higher D-dimer levels, PT and APTT among patient with Malaria, while the gender showed no effect on the level of D-dimer levels, PT and APTT

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Conflicts of Interest

There is no conflict of interests between authors.

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