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ORIGINAL ARTICLE

Investigate of Haemostatic and Fibrinolytic System Parameters Among Sickle Cell Anaemia Patients in the Khartoum State

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ABSTRACT

Introduction: A sickle cell anaemia one of a haemoglobinopathy, which constituted as a model for genetically inherited disorders, the course of the disease involves may crises, the investigation of hemostatic components as fibrinogen and fibrinolysis as D-dimer, reflect the overall hemostatic status in the sickle cell anaemia patients.

Aim: To investigates hemostatic and fibrinolytic system parameters among sickle cell anaemia patients in the Khartoum state.

Methods: The study was conducted in Khartoum state, in JafarIbn Auf Reference Hospital for children as descriptive case-control, a laboratory-based study from 2017-18, specimens were collected randomly of the study population with irrespective to age and gender, blood draw in tri-sodium citrate container, the ethical and consent were obtained.

The fibrinogen level was estimated by CA51 semi-automated coagulation analyzer optically based, and the D-dimer were assayed by MISPA-i2, a nephelometric based, the results for each parameter were recorded and using statistical package for the social sciences (SPSS) software for analysis by independent T-test and the statistical significance > 0.05.

Results: A 100 participants, 50 as study group HbSS sickle cell anemic Sudanese child clinically and laboratory-confirmed and 50 healthy as the control group, in comparing a mean of fibrinogen show statistically insignificant (P value 0.645) study group 291.1 ± 107.8 mg/dL and control group 283.4 ± 49.1 mg/dL, but there was a significant difference in comparing a mean of D-dimer in study group 0.56 ± 0.33 µg/mL and control group 0.33 ± 0.14 the P. value 0.00015.

Conclusion: The level of D-dimer may be used as a hypercoagulability biomarker in comparison to the level of fibrinogen level for sickle cell anaemia Sudanese child.

Keywords: D-dimer, Fibrinogen, Sickle cell anaemia, Sudanese child.

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INTRODUCTION

Sickle cell anaemia is a general classical form of genetically inherited diseases, form abnormalities of hemoglobin structurally, the sickle affecting the erythrocytes directly in which the clinical manifestations arise from classical theory for the tendency of hemoglobin to polymerize and lead to deforming the affected erythrocytes in crescent shape.[1-10] A single nucleotide change in the beta-globin chain gene leading to a substitution of valine for glutamic acid at position six of beta-globin chain gene, the homozygous present as HbSS and heterozygous as HbAS known as sickle cell trait, the hemoglobin polymerization is associated with different pathophysiological fashion, including; vascular crisis, bone crisis, and aplastic crisis, the hemoglobin

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polymerization was related to a reduction of iron and water content (cell dehydration), and increased erythrocytes density with persistent membrane damage, hemolysis and improved blood flow.[11-15]

The signs and symptoms of sickle cell anaemia, which vary from individual to another, and changed over time, include; anemic episodes, painful swelling of hands and feet, frequent infraction, delayed growth and visual problems[16-18] Sickle cell anaemia can lead to stroke: can occur if sickle cells blocking blood flow to .area of the brain. Acute chest syndrome, hyper pulmonary tension, organ damage, blindness and leg ulcer with gallstones and another symptom of sickle cell crisis or sickling crisis may be used to describe several independent acute conditions were occurring in sickle cell anaemia patients or in patients with sickle cell diseases.[19-22]

The vaso-occlusive crisis is caused by sickle shaped erythrocytes that obstruct capillaries and restrict blood flow to organ resulting in ischemia, pain, necrosis, and organ damage, and splenic sequestration crisis, because of its narrow vessels and function in clearing defective erythrocytes, the spleen is frequently affected. This spleen damage increases the risk of infection from encapsulated organisms, splenic sequestration crises are acute, painful enlargements of the spleen, caused by intrasplenic trapping of erythrocytes and resulting in a precipitous fall in hemoglobin level with the potential for hypovolemic shock), and a plastic crisis (are acute worsening of the patient's baseline anaemia, producing pale appearance, fast heart, and fatigue.[23-24] This crisis is normally triggered by parvovirus B19, which directly affects the production of erythrocytes by invading the erythrocyte precursors and multiplying in and destroying them and hemolytic crisis (acute accelerated drops in hemoglobin level), the erythrocytes break down at a faster rate. This is particularly common in patients with coexistent G6PD deficiency management is supportive, sometimes blood transfusion.[25]

Different laboratory investigations were screening, or confirmatory tests were coupled to determine the episodic characters for coming patients as newly diagnosed or follow-up coming, and different previous studies describe the hypercoagulability or thrombosis tendency by demonstrations of fibrinogen and D-dimer level in the sickle cell anaemia patients.[26-34]

MATERIALS AND METHODS

A study was descriptive case-control–laboratory-based study, was conducted in the Jaffar Ibn Auf Reference Hospital, the period of study during December 2017 to July 2018, a population of the study included 50 sickle cell anaemia child attending Jaffar Ibn Auf reference hospital as a study group, and 50 healthy children were irrespective to age and gender, specimens were collected 1.8 mL of venous blood randomly using a sterile disposable plastic syringe with tri-sodium vacationer through aseptic standard non-traumatic vein puncture technique then investigate blood parameters were done, the ethical consideration was obtained, and the statistical parameters by SPSS using independent t rest and statistical significance at p-value < 0.05.

Platelets' poor plasma was prepared for each participant, and the estimation of fibrinogen and d-dimer proceeded.

Measuring of D-dimer based nephelometric assay reagent used for in vitro quantitative determination of fibrin degradation product D-dimer level, using MISPA-i2 device, the MISPA-i2 device well controlled, and a test procedure was clear in the kit leaflet, the reference interval for D-dimer $> 0.5\mu g/mL$ most correctly reference range for childhood, and results were recorded and statistically analyzed.

Estimation of fibrinogen level was measured by semi-auto coagulation analyzer CA51, and was equipped with a precise pipette and test optically based, the device and reagents were well controlled a test procedure as clear in the kit leaflet, and a standard chart was established, the reference interval for fibrinogen 200-400mg/dL, results were recorded and statistically analyzed.

RESULTS

Our study was composed of hundred participants fifty as a control group and fifty as a study group as sickle cell anemic Sudanese child, clinically and laboratory-confirmed, in the Table 1 show independent t-test statistical parameter the population study for D-dimer and fibrinogen level. Figures 1 and 2 show the scatter mean plotted present statistically acceptable results.

DISCUSSION

The child with sickle cell anaemia surrounded by many risking events, if occur led to death, a study was established to measure the association of the D-dimer level as fibrin degradation product and the level of fibrinogen as one major hemostatic component, the sickle cell anaemia in Sudan as an African country with a high frequency of sickle cell gene in the different divers' ethnic groups and geographical area, this affected many children in our country.

Our study showed a significant association of the D-dimer level among sickle cell anaemia (HbSS), Sudanese child in compression of normal healthy, Sudanese child

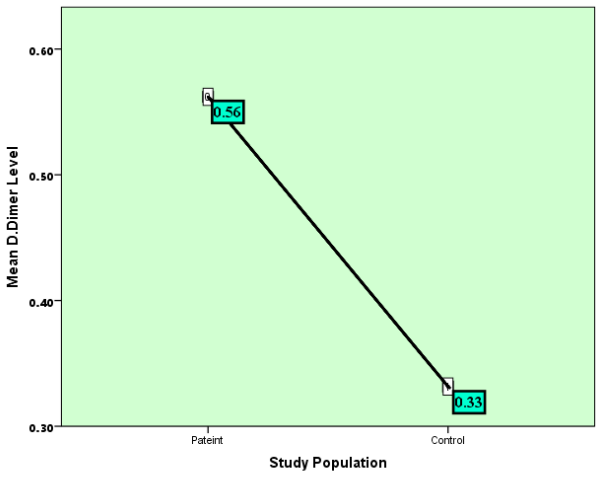

Figure 1: Shows the mean difference of D-dimer in patients and control groups. (p-value 0.00015)

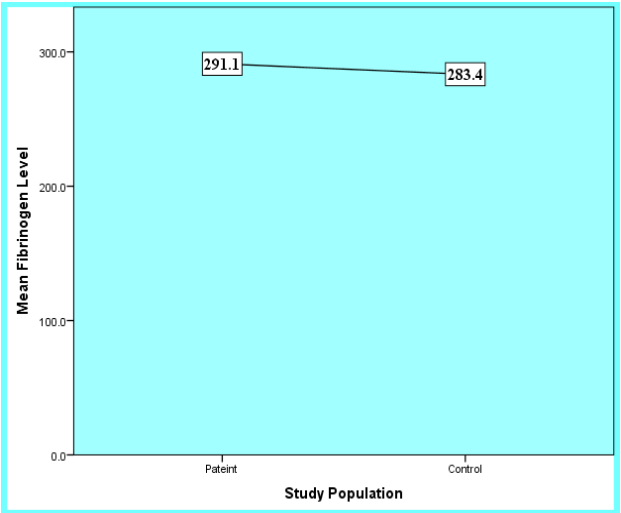

Figure 2: Shows the mean difference in fibrinogen levels in patients and control groups. (p-value 0.645)

Table 1: Shows the description of the mean value of the estimated D-dimer and fibrinogen

Study population / *Tested parameter*	*Patient* *mean ± SD*	*Control* *mean ± SD*	*P. value*
Fibrinogen level	291.11 ± 107.77	283.37 ± 49.05	0.64500
D-dimer level	0.56 ± 0.33	0.32 ±0.14	0.00015

HbAA. The mean of D-dimer level show (study group 0.56 ± 0.33 µg/mL and control group 0.33 ± 0.14), the p-value = 0.00015. This was agreed with a study done in Sudan by Mahdi *et al*. that shows the significant elevation in the mean level of D-dimer in the sickle cell anaemia patient (1847.47 ± 2004.92 ng/mL) as compared to control group (238.0 ± 166.0 ng/mL).[28] Our finding with a similar trend of the previous study done in different populations that reported the higher level of D-dimer amongst sickle cell patients as a fibrinolytic marker for hypercoagulability.[28]

Our finding of mean of D-dimer was conflicted with a study done in Nigeria by Ekwere, *et al*. that shows there was no elevation in the level of D-dimer as the mean difference between case and control,[34] the confliction may due to the unmatched geographical and environmental state.

Our study showed an insignificant association of the fibrinogen level among sickle cell anaemia (HbSS) Sudanese child in compression of normal healthy Sudanese child (HbAA), the mean of Fibrinogen level show (study group 291.1 ± 107.8 mg/dL and control group 283.4±49.1 mg/dL), the p-value 0.645, this was agree with study done by Ekwere *et al* that conclude there was insignificance difference of sickle cell case and normal group.[34]

Our finding was conflicted with Nilesh, *et al*. that perform the measuring of fibrinogen level in the Indian sickle cell population the mean of fibrinogen level showed significant higher for Hb SS patient (mean 522.24 mg/dL) as compared to normal Hb AA control (mean 275.26 mg/dL).[35] Our findings disagreed with a study done by Buseri *et al*. in Nigeria for measuring fibrinogen level among sickle cell anaemia patients that show a significant raising in fibrinogen level of sickle cell anaemia patients than the control group.[26] The evidence of confliction in an increase of fibrinogen level may due to the fibrinogen indicate as inflammatory markers.

The study limitations were restricted with many factors like the sample size and the acceptance of subjects to participate in the study; other limitations may due to the reagent supplying and the cost-effectiveness.

CONCLUSION

This study concluded the confirmed hypercoagulable status in the sickle cell anaemia with higher D-dimer levels among the Sudanese child sickle cell anaemia population in comparison with healthy control child groups. And the study was concluded the normal level of fibrinogen in Sudanese child sickle cell anaemia population.

Our recommendation to an overcalling program that covers the thrombotic tendency in the sickle cell anaemia patients as preventative as possible of pulmonary embolism

and more advanced sophisticated molecular genetics study established to decrease mortality and motility in the Sudanese sickle cell anaemia child.

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CONTRIBUTION OF AUTHORS

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this the authors have equally contributed to this study.

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