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Research Article,

Measurement of Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT), Fibrinogen Level, D-Dimer in Sudanese Infants and Children with Sepsis Khartoum State, 2022

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Abstracts:

Background: Sepsis is the most common worldwide cause of death in infants and children. It was Known that coagulative and inflammatory parameters were involved in the host's defense against sepsis resulted from severe infection and inflammation.

Materials and Methods: This was cross sectional study conducted at Albraa pediatric center, Khartoum, Sudan during the period from May 2022 to August 2022, to measure PT, APTT, fibrinogen level, D- dimer in Sudanese infants and children with sepsis. 50 patients were selected as a case group, and apparently healthy donors with no history of any coagulation problems or any chronic disease were selected as control group. 2.8 ml of venous blood samples were collected in Tri Sodium Citrate anticoagulant. The coagulation tests (PT, APTT, fibrinogen) were performed using semiautomatic device (coagulometer). I chroma was used for the D-dimer.

Results

When compared between case and control there was highly significant difference (p.value 0.000), in PT, APTT, fibrinogen and D- dimer. In addition, there was insignificant difference when the PT, APTT fibrinogen and D-dimer in cases compared with the gender, CRP and bacterial culture, and there was negative correlation between the parameters and the age except the D-dimer had appositive correlation. The most common types of isolated bacteria in sepsis patients is staphylococcus aureus.

Conclusion:

This study concluded that, PT, APTT, fibrinogen and D- dimer was significantly increased in patients with sepsis.

Keywords: sepsis, coagulation, PT, APTT, Fibrinogen and D-dimer.

Introduction:

Sepsis is a life-threatening situation that arises when the body's response to infection causes injury to its own tissues and organs, this initial phase is followed by suppression of the immune system. [1,2] Is initially characterized by excessive production of pro-inflammatory cytokines leukocyte activation and tissue damage, followed by release of anti-inflammatory cytokines and immunosuppression[3].

Sepsis remains one of the major causes of mortality in infants and toddlers worldwide.[4-6] in children peaks in the neonatal period symptoms may be

non- specific, while older children may show hyperthermia, tachycardia, tachypnea, hypotension and disorders in hemostasis up to the clinical picture of disseminated intravascular coagulation (DIC).[7] Infections causing sepsis are usually bacterial but may be fungal, parasitic or viral. [8] Risk factors include; young or old age, cancer, diabetes, major trauma, asthma, chronic pulmonary disease, multiple myeloma and burns.[9] Global epidemiologic data from systematic reviews revealed a variable prevalence of 13-300 per 100,000 people annually for sever sepsis. But, it is assumed to be higher in sub-Saharan Africa (SSA) where data are scarce. [10] This study was designed to measure PT, APTT, fibrinogen level, D- dimer in Sudanese infants and children with sepsis.

Materials and methods:

This was cross-sectional study, conducted at the laboratory of ALbraa pediatric center at Khartoum state during the period of May 2022 to august 2022. All patients attending ALbraa pediatric center and diagnosed with sepsis during the aforementioned period, also they have no history of bleeding, thrombi or under anticoagulant therapy were included as cases. In addition to that, apparently healthy children with no history of thrombi, bleeding or under coagulant therapy were selected as control group.

2.8 ml of blood samples were gathered in trisodium citrate anticoagulant container for PT, APTT, fibrinogen and D- dimer. The data was raisedusing pre-designed structural questionnaire; the demographic and clinical data concerning each participant was obtained from the registry data base office. The study was approved by the ethical committee of national university, faculty of medical laboratory, and the participants were fully informed about the advantages and disadvantages before participation in the research. SPSS version 23 statistical software (SPSS Inc., USA) was used for statistical analysis.

Procedure and Principle of Prothrombin time (PT) Test

Coagulometer was used for The PT and APTT. The principle of the test consists of the use of calcium thromboplastin to measure the clotting time of patient's plasma. The test measured as a whole. The activity of extrinsic coagulation factors: factor II (prothrombin), factor I (fibrinogen), factor V (proaccelerin), factor VII (proconvertin) and factor X (Stuart factor).

Principl of Activated partial thromboplastin time (APTT)

The test involved the calcification of plasma in the presence of a standardized amount of platelet substitute and a specific activator. This procedure minimizes test variables by standardized the contact activation and optimizes the concentration of platelet like phospholipids. The APTT explores the intrinsic coagulation pathway (factors X11, X1, 1X, V111, X, V, 11, 1).

Principle of Fibrinogen Test

The test was done by BioMed-Fibrinogen kite, for quantitative determination of Fibrinogen in plasma. The principle of this kite is addition of thrombin coagulates fresh citrated plasma; the coagulation time is proportional to the fibrinogen concentration. This allows the estimation of plasma fibrinogen by functional clotting assay.

Principle of D- Dimer test

Ichroma™ D-dimer is fluorescence Immunoassay (FIA) for the quantitative determination of D-Dimer in human whole blood / plasma. The test will be used a sandwich immune detection method; the detector antibody in buffer binds to antigen in sample, forming antigen antibody complexes and migrates onto nitrocellulose matrix to be captured by the other immobilized-antibody on test strip. The more antigen in sample forms the more antigen-antibody complex and leads to stronger intensity of fluorescence signal on detector antibody, which is processed by instrument for ichroma™ tests to show D- dimer concentration in sample.

Results:

Socio- demographic data

In the present study 50 children affected by sepsis were selected as cases and apparently healthy 50 children were selected as control group. In the control group; the mean of age was (8.6± 3.6), 56% were female and 44% were male. In the case group; the mean of age was (5.5 ± 3.4), 60% were female and 40% were male, CRP was done only for 42% and the culture was done for 60%. Regarding the isolated bacteria; 46.7% was staph aureus, 33.3 % was S.pneumoniae, 16.7 % M.tuberculosis and

3.3% was N.meningitis. (Tables 1, 2, 3, 4) (figures 1,2,3,4,5) .

Table (1): Distribution of age in study population

Case	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	50	1	12	5.5	3.4
Control	**N**	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Age	50	1	13	8.6	3.6

Table (2): Distribution of gender in study population

	Gender	Frequency	Percent
Case	Male	20	40.0
	Female	30	60.0
	Total	50	100.0
Control	Male	22	44.0
	Female	28	56.0
	Total	50	100.0

Table (3): Distribution of assessment of infection

Assessment of infection		Frequency	Percent
CRP	Yes	21	42.0
	No	29	58.0
	Total	50	100.0
Culture	Yes	30	60.0
	No	20	40.0
	Total	50	100.0

Table (4): Distribution of isolated bacteria

Isolated bacteria	Frequency	Percent
S.aureus	14	46.7
S.pneumoniae	10	33.3
N.meningitis	1	3.3
M.tuberculosis	5	16.7
Total	30	100.0

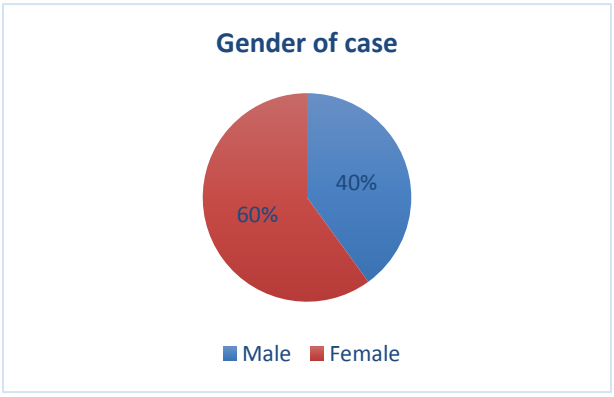

Figure (1): Distribution of gender of case

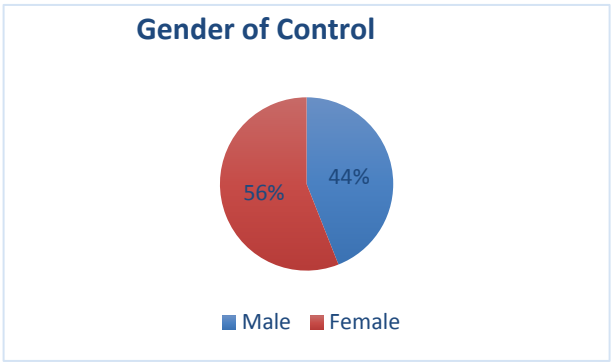

Figure (2): Distribution of gender of control

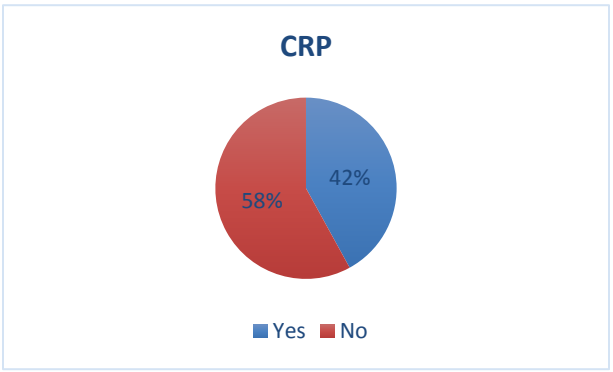

Figure (3): Distribution of CRP

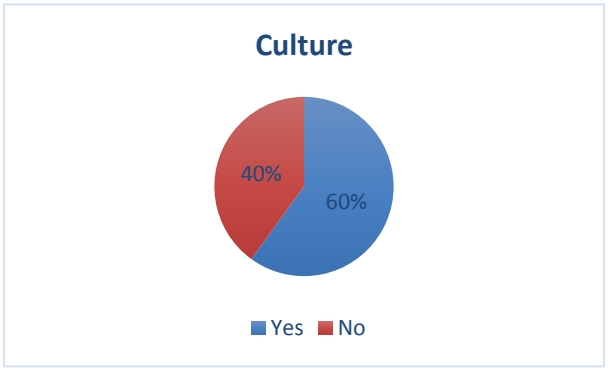

Figure (4): Distribution of culture

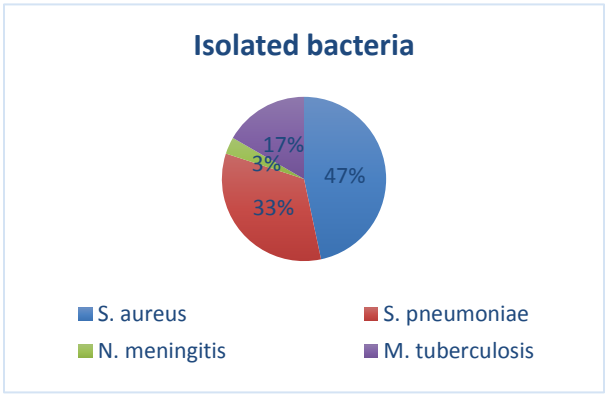

Figure (5): Distribution of isolated bacteria

Hematological Results

For the PT, APTT, fibrinogen and D-dimer when compared between case and control group there was highly significant differences (p. v= 0.000) (table 6). While there was an insignificant difference when the parameters in cases compared with the gender, CRP, and culture, in addition there was a negative correlation between the parameters and the age (P. V≥0.05) except the D-dimer had appositive correlation (table 7,8,9, 10).

Discussion:

Sepsis is the vaital causes of mortality in infants and toddlers worldwide; however the number of deaths by sepsis has considerably reduced in the last couple of decades. This was a cross sectional; hospital base study carried out at ALbraa pediatric center- Khartoum state, for the measurement of prothrombin time (PT) and activated partial thromboplastin time (APTT), fibrinogen level and D- dimer in Sudanese infants and children with sepsis... The results revealed that; the mean of age in the case group was (8.6± 3.6) , 56% were female and 44% were male, this finding disagree with Scott Watson etal which reported; Incidence of sepsis was the highest in infants , fell dramatically in older children (10 to 14 year olds), and was 15% higher in boys than in girls. [11]

In the present study CRP was done only for 42%, the blood culture was done for 60% and the isolated bacteria; 46.7% was staph aureus, 33.3 % was S.pneumoniae, 16.7 % M.tuberculosis and 3.3% was N.meningitis. While; Weidhase et al said; CRP is a well-known parameter for diagnosis of sepsis or assessment of predictor of successful antibiotic therapy.[12] one of study done by Cui et al revealed ; serum CRP has good clinical prognostic value for patients with sepsis and septic shock, on the second , thired, and fifith days, serum CRP level was increased in the no survivor group than in the survivor group. [13] But Xiaomeng Tang etal found, there was no significant difference in aspect of CRP level on PICU admission between non survivors and survivors' patient [14]

Regarding the kinds of isolated bacteria Abhimanyu Sharma etal reported; in 10 cases positive based on culture (nine on blood culture, one on culture of pleural fluid), Staphylococcus aureus and Klebsiella pneumoniae were identified in six and four patients, respectively. Similar finding was mention by Martin M Meremikwu eta al which shown that S. aureus and gram-negative rods (Pseudomonas spp and coliform) are the leading causes of septicaemia in children in South-east Nigeria, a pattern similar to that of other low income countries.[15,16]

For the PT and APTT our results revealed; there was clearly prolongation in the PT and APTT with highly significant differences when compared between case and control group. In spite there was an insignificant difference when the PT and APTT in cases compared with the age, gender, CRP and culture, this finding was similar to Christian Niederwanger et al result which reported; Survivors sepsis patients showed significantly higher PT levels and aPTT. Also said; Prolongation leads to poorer outcome. A long aPTT might reflect the most severe cases of sepsis due to consumption of coagulation factors or high dose heparin therapy, but may also be caused by a FXII deficiency. In septic patients, FXII deficiency can be protective via attenuation of the FXII-dependent bradykinin generation, complement activation and further contact pathway activation.[17] Other study showed; the levels of of PT and APTT were significantly associated with hospital mortality in septic patients. [14]

In this study the fibrinogen level results showed; there was clearly increasing in fibrinogen with highly significant differences when compared between case and control group. In spite there was an insignificant difference when the fibrinogen level in cases compared with the age, gender, CRP and culture, this finding was similar to Abhimanyu Sharmaet et al result which reported; Plasma fibrinogen was significantly (P<0.01) higher in patients compared with controls (mean ± SD of 317.4 ±79.5 mg/dL) (reference range: 150-400 mg/ dL). The difference was statistically significant. Plasma fibrinogen increased in eight (16%) and decreased in three (6%) patients; and was normal in all controls.[17] a study done by Xiaomeng Tang et al showed that the fibrinogen levels were significantly lower in no survivors than survivors. Multivariate logistic regression analysis showed significant associations between fibrinogen, lactate level, and hospital mortality. Also said; Fibrinogen is a valuable prognostic biomarker for pediatric

sepsis. The level of fibrinogen lower than 2 g/L on PICU admission is closely related to the greater risk of hospital death in pediatric sepsis. [18]

the D-dimer results showed; When compared the D- dimer between cases and control group there was significant increase of D- dimer with (P = 0.000).Also, in the case group there was an insignificant difference between D- dimer and the gender, CRP, and culture, in addition there was a positive correlation between the D- dimer and the age (P. V≥0.05), this finding was similar to study done by Al-Biltagi M, et al found that the D-dimer was significantly higher in septic cases group [19]. Another study done by Abhimanyu Sharma, et al. showed that D-dimer was positive in 36 (72%) patients and negative in all controls. The difference was statistically significant (P<0.01). They stated that though none of the current study patients developed overt disseminated intravascular coagulation, the high positivity for D-dimer suggested that it should be measured in children with sepsis for early identification of DIC. This can aid better management as additional coagulation-based therapy such as recombinant anti-thrombin and thrombomodulin may help to improve prognosis.[17]

Conclusion:

This study concluded that, PT, APTT, fibrinogen and D- dimer was significantly increased in patients with sepsis, and an insignificant difference when the parameters in cases compared with the gender, CRP, and culture; in addition there was a negative correlation between the parameters (PT, APTT and fibrinogen) and the age, appositive correlation between D-dime and the age.

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