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ACUTE PHASE REACTANT PROTEINS PATTERN BY SPE IN SEPSIS PATIENT AND EVALUATION THE MOST COMMON MORTALITY MARKERS

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ABSTRACT

Introduction and aim: Septicemia, or sepsis, is the clinical name for blood poisoning by bacteria. It is the body's most extreme response to an infection. Sepsis that progresses to septic shock has a death rate as high as 50%, depending on the type of organism involved. sepsis can quickly lead to tissue damage, organ failure, and death. Several causes of infection, including parasites, bacteria, fungi. In this study include, One hundred (100) participants were enrolled in this study including three groups involved in this case-control study according to clinical diagnosis. The purpose of the present study is to find the effect some biomarker on sepsis patients like acute phase reactant proteins and HS.troponin and Pro BNP, albumin, prealbumin, α_1-acid glycoprotein ,C-reactive protein, α_1-antitrypsin, haptoglobin and fibrinogen, also to identified the common type of bacteria that occur in septic patient.This atudy conducted in the Imam Hussein hospital in Center ICU & Imam Zain Al-Abdeen hospital during the period from October 2022 to May 2023. **Materials and Methods:** A case-control study of patients with septicemia was conducted. In the Imam Hussein Center ICU/ Imam Zain alabdeen hospital during the period from October 2022 to May 2022.in Karbala city. **Results:** In this study found that (serum amyloid A) of the patient groups (A &B) for neonate and adult(mean ±SD) (33.91±17) (39.5± 27.76) (28.35±23.97) (27.76±20.62) significant higher than control groups (C) (mean ±SD) (5.38±5.12) (5.9±6.48) respectively at level P value (< 0.05),and there is no significant differences between adult and neonate in different groups. Show table(1). In this study found that (Fibrinogen) of the patient groups (A &B) for neonate and adult (mean ±SD) (413.5±98.42) (489±76.36) (434.35±168.11) (440.76±154.95) significant higher than control groups (C) (mean ±SD) (334.97±102.38) (306.31±136.99) respectively at level P value (< 0.05),and there is no significant differences between adult and neonate in different groups show table(2). In this study found that (HS-Troponin) of the patient groups (A &B) for neonate and adult(mean ±SD)(4.9±1.3)(7.6±1.4)(6.11±42.26) (5.20±38.67) significant higher than control groups (C) (mean ±SD) (0.95±0.3) (1.1±0.08) respectively at level P value (< 0.05),and there is no significant differences between adult and neonate in different groups show table (3). **Conclusion:** the routine hematological technique (CBC)and some of biomarker as (SAA _HS-Troponin _Fibrinogen) could use routinely to diagnosis of sepsis and this marker unreliable to assess the severity of disease, and gold stander for diagnosis is blood culture.

KEYWORDS: SAA-serum amyloid A; (A &B) (group A:patient with bacteria growth, group B: patient without bacteria.

INTRODUCTION

Sepsis is a serious medical condition that occurs in 30% of patients in intensive care units (ICUs). Early detection of sepsis is key to prevent its progression to severe sepsis and septic shock, which can cause organ failure and death.[1]

Sepsis is a life-threatening, dysregulated immune response that occurs, when the body's defensive reactions against infection damage its own tissues and organs.[2] In 2017, an estimated 48.9 million cases of sepsis were recorded worldwide with 11.0 million sepsis-related deaths, representing 19.7% of all global deaths.[3] Several types of organisms , such as bacteria, viruses, and fungi, are the cause for sepsis.[4] Increased breathing rate, fever, elevated heart rate, and confusion are a few

common signs and symptoms. Early diagnosis of sepsis is critical to halt progression to septic shock. Blood cultures are the gold standard for detecting microbial species in the body, however approximately 30–40% of patients with severe sepsis or septic shock have positive test findings.[5]

Sepsis is a clinically common disease in neonates, and the incidence is higher in premature and low birth weight neonates. Most neo-nates develop the disease 1 week after birth. Premature babies are infected through the respiratory system and full-term babies are infected through the skin and navel.[6]

During systemic infections, the liver regulates immune defenses via bacterial clearance, production of acute-phase proteins and cytokines, and metabolic adaptation to inflammation.[7]

Inflammation markers acute phase reactants (APR) that exhibit significant changes in serum concentration during inflammation. During acute and chronic inflammatory conditions, the liver also produces these important mediators, positive or negative can be classified Acute phase reactants, depending on their serum concentrations during inflammation. Positive acute phase reactants are upregulated, and their concentrations increase during inflammation. Negative acute phase reactants are downregulated, and their concentrations decrease during inflammation. Positive acute phase reactants include ferritin, fibrinogen procalcitonin, C-reactive protein, hepcidin, and serum amyloid A. and transferrin ,albumin, prealbumin, , retinol-binding protein, and antithrombin ,this is Negative acute phase reactants. (Gul R *et al.*, 2022). C-reactive protein, originally described as a molecule that was present in the circulation of patients with infections and that was capable of recognizing the C-type polysaccharides of *Streptococcus pneumoniae*.[8]

The appearance of higher acute-phase protein concentrations in bodily fluids like blood. is part of a more complex response to local or to systemic inflammation (sepsis) that has been referred to as the acute-phase response, which is characterized by decreased production of albumin by hepatocytes, reorientation of iron metabolism, and hormonal changes. These changes are also seen in the context of subclinical inflammation and chronic inflammatory diseases.[8]

MATERIALS AND METHODS

Study design and setting

This study case-control of patients with septicemia was conducted. In the Imam Hussein hospital in Center ICU/ Imam Zain Alabdeen hospital during the period from October 2022 to May 2022 in Karbala city. One hundred (100) participants were enrolled in this study including three groups involved in this case-control study according to clinical diagnosis, patients were suspected to be have septicemia by sign & symptom taken by physician which noted the information of patients file in the center, was taken [50 patients(8 neonatal , 42 adult)] from both sex[(14 female), (36 male)] and divided tow group :first group A includes patients with positive blood culture [23 (6 neonatal, 17adult)] the second group B includes patients with negative blood culture [27(2 neonatal ,25 adult)] and the third group includes healthy control [50 (10 neonatal, 40 adult)], [(11 female),(39 male)] People were picked from the general public and appeared to be in good health. in Medical staff and relatives free from sign and symptom. The neonates ages range (≤ 30 days), Adults (18_73 years).

Ethical consideration

The research followed the guidelines set forth by the Department of Clinical Laboratories at the University of Karbala's College of Applied Medical Sciences for dealing with biological substances and dangerous microorganisms. After acquiring the necessary authorization from the hospital administration and patients, The samples for this investigation were taken from patients at the Karbala Health Directorate's Imam Hussein Center ICU,and imam zian alabden hospital.

Statistical analysis

The quantitative data are expressed as mean ± standard deviation. The Student t-test was used to compare these data between discharged well patients and those required ICU admission. Binomial data were presented as frequency percentages and analyzed by Chi square test. Receiver operating characteristic (ROC) curve was used to evaluate the predictive value for all markers that had a significant variation between the two groups at admission in predicting ICU admission. All data were analyzed with SPSS for windows, v.25.0; IBM Corp, Armonk, New York, USA.

RESULTS

In this study found that (serum amyloid A) of the patient groups (A &B) for neonate and adult(mean ±SD) (33.91±17) (39.5± 27.76) (28.35±23.97) (27.76±20.62), significant higher than control groups (C) (mean ±SD) (5.38±5.12) (5.9±6.48) respectively at level P value (< 0.05), and there is no significant differences between adult and neonate in different groups. Show table (1)

Table 1: comparison between studied groups according to biochemicals parameters(serum amyloid A**) in neonatal and adult.**

Groups	Neonates (Mean ± SD)	Adults (Mean ± SD)	*P value*
A(Patient-with growth bacteria)	33.91 ± 17.00 [a]	28.35 ± 23.97 [a]	0.608 NS
B(patient-without growth bacteria)	39.5 ± 27.76 [a]	27.76 ± 20.62 [a]	0.488 NS
C(control group)	5.38 ± 5.12 [b]	5.9 ± 6.48 [b]	0.683 NS
P value	0.001*	0.001 *	Horizontal comparisons by t- test Vertical comparisons by Post Hoc NS: no significance * : significance

A: group with bacteria growth, (B): group without bacteria growth, (C): control group.

In this study found that (HS-Troponin) of the patient groups (A &B) for neonate and adult(mean ±SD)(4.9±1.3)(7.6±1.4)(6.11±42.26) (5.20±38.67) significant higher than control groups (C) (mean ±SD) (0.95±0.3) (1.1±0.08) respectively at level P value (< 0.05),and there is no significant differences between adult and neonate in different groups. Show table(4-12).

Table (4-12): Comparison Between Studied Groups According To Biochemicals Parameters(Hs-Troponin) In Neonatal and Adult.

Groups	Neonates (Mean ± SD)	Adults (Mean ± SD)	*P value*
A (patient with growth bacteria)	4.9±1.3	6.11±42.26[a]	**0.445 NS**
B (patient with growth bacteria)	7.6±1.4	5.20±38.67[a]	**0.094 NS**
C (control group)	0.95±0.3	1.1±0.08[b]	**0.671 NS**
P value	**0.007**	**0.003**	Horizontal comparisons by t- test Vertical comparisons by Post Hoc NS: no significance * : significance
LSD	**S**	**S**	

A: group with bacteria growth, (B): group without bacteria growth, (C): control group.

In this study found that (Fibrinogen) of the patient groups (A &B) for neonate and adult (mean ±SD) (413.5±98.42) (489±76.36) (434.35±168.11) (440.76±154.95) significant higher than control groups (C) (mean ±SD) (334.97±102.38) (306.31±136.99) respectively at level P value (< 0.05),and there is no significant differences between adult and neonate in different groups show table(4-14).

Table 4-14: Comparison Between Studied Groups According To Biochemicals Parameters(Fibrinogen) In Neonatal and Adult.

Groups	Neonates (Mean ± SD)	Adults (Mean ± SD)	*P value*
A	413.50 ± 98.42 [ab]	434.35 ± 168.11	**0.779 NS**
B	489.00 ± 76.36 [a]	440.76 ± 154.95	**0.671 NS**
C	334.97 ± 102.38[b]	306.31 ± 136.99	**0.203 NS**
P value	**0.043 ***	**0.015**	Horizontal comparisons by t- test Vertical comparisons by Post Hoc NS: no significance * : significance
LSD	**S**	**S**	

A: patient group with bacteria growth, (B): patient group without bacteria growth, (C): control group.

DISCUSSION

Inflammation markers acute phase reactants (APR) that exhibit significant changes in serum concentration during inflammation. During acute and chronic inflammatory conditions[9] and Sepsis had been defined using criteria. If the SIRS criteria are negative, it is extremely improbable that the individual has sepsis; if they are positive, there is only a slight chance that they do. There were various degrees of sepsis, sepsis, severe sepsis, and septic shock, according to SIRS.[10] Biomarkers of sepsic patients on admission could reflect not only the severity but also the accumulated influences from the day of disease onset because the day of admission of patients with sepsis is not always the onset day of injury, such as that caused by trauma, burns, or cardiac arrest.[11]

Biomarkers can have an important place in this process because they can indicate the presence or absence or severity of sepsis[12]

In This study examined the Mean levels of Serum Amyloid A in septic patient the results found that (all group Patients in neonate and adults **)** were significantly higher than control group, the current study was similar to.[13] suggests that SAA gradually rises and peaks 3–4 days after infection in patients with respiratory virus infections. Clinical symptoms typically appear 36–48 hours after infection. other suggests that patients with virus have a large amount of IL-1β, IFN-γ, IP-10, and MCP released, causing the activation of SAA. These inflammatory factors can be used as indicators to reflect the body's response to infection.[14]

And according to other studies, those who had severe acute respiratory syndrome had much higher levels of SAA, indicating that SAA could be utilized as a biomarker to track the development of respiratory disorders.[13] Even at very low concentrations, SAA can cause chemotaxis and activate chemokines to stimulate an inflammatory response.[15]

[16]Found that serum amyloid A gradually increases after virus infection. It increases earlier than CRP, and the increase is obvious, reaching a peak on the 3–4 days after infection.

In other study The potential role of SAA1 in host defense against virus[17] found SAA1 has been reported to directly activate neutrophils and to recruit them to the lung during infectious and inflammatory processes. Neutrophils are the most abundant cell recruited to the lung in the early phase of IAV infection. There are different forms and preparations of SAA1 that have found to have different effects on phagocyte responses, through various receptor, suggest that Serum amyloid A can be significantly increased in both bacterial and viral infections, Using serum amyloid A combined with other indicators, bacterial and viral infections can be distinguished.

and other study on Patients less than 28 weeks found The high sensitivity, specificity, positive predictive value and negative predictive value of SAA protein could help the clinicians for early diagnosis of neonatal sepsis.[18]

[19]suggest HS. Troponin may be released during sepsis because of direct myocardial injury from inflammation or infection. a higher serum troponin level is a prognostic indicator of high mortality in sepsis cases. Its impact has had inconsistent reports because of differences in troponin types (troponin I or troponin T), disease severity, cutoff values, and the time to measurement.[20]

Wilhelm et al.2014 reported that non-survivors of septic patients had higher sensitivity troponin on admission compared with survivors.[21]

[22]Suggest Elevated troponin identifies a subset of patients with sepsis at higher risk of death.

Troponin elevation is probably multifactorial and a common finding among critically ill patients with sepsis. It might be that myocardial dysfunction accounts for troponin elevation and could potentially explain the troponin's association with mortality. Alternatively, raised troponin may indicate a more fulminant disease process. There is no guideline on the appropriate approach and management of septic critically ill patients with elevated troponin.[23] However, vigilance for objective evidence of acute coronary syndrome, prompt management of sepsis and optimisation of myocardial oxygen demand/supply balance are of paramount importance. of cardiac troponins as a sepsis screening tool and addition of troponin to sepsis bundles could be helpful in prognostically stratifying critically ill patients with sepsis, so that early evaluation (by echocardiography or angiography) and management is appropriately initiated. It would stand to reason that septic patients with high pre-test probability of coronary artery disease and very high troponin levels (above 10% of the co-efficient variance) undergo cardiac investigations during their ICU stay. However, we believe that cardiac troponins form one part of a much larger diagnostic, prognostic and therapeutic puzzle.[23]

A useful predictive biomarker for pediatric sepsis is fibrinogen. This is consistent with earlier research, which found that neonates and adult who died had lower plasma fibrinogen levels. Plasma fibrinogen was also found to be a useful tool for evaluating neonatal outcomes, showing that inflammation-induced increased coagulant activity and decreased fibrinolysis result in fibrin deposition in the microcirculation, which causes organ dysfunction.[24]

Iskandar et al 2013 reported that adult patients with sepsis had decreased plasma fibrinogen in 23.5% of cases and elevated plasma fibrinogen in 43.5% of patients Acute phase reactant fibrinogen may be increased in the initial stages of sepsis.[25] Another study The reduced fibrinogen in patients with acute infection may possibly indicate activation of coagulation leading to its consumption.[26]

CONCLUSION

the routine hematological technique (CBC)and some of biomarker as (SAA- fibrinogen- troponin) could use routinely to diagnosis of sepsis and thes marker unreliable to assess the severity of disease, and gold stander for diagnosis is blood culture, the biomarker such as troponin could use to assess the severity of disease, used of non-lab parameter Temp ,RP,PR,BP and lab test such as CBC,CRP and SAA several of all patient in word many behave septicemia and then used the gold stander for the diagnosis of sepsis which is blood culture.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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