Impact of bacterial sepsis on thrombocytes and mortality rate in Sudanese neonates

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Objectives: To find the effects of bacterial sepsis on thrombocytes, in correlation with causative bacteria and mortality rate.

Methodology: This study was performed on 50 Sudanese neonates presenting with septicemia, with an additional 50 neonates matched for age and weight as control group. The standard microbiological techniques, in addition to antimicrobial sensitivity testing, were used for the identification of microorganisms. Platelet (PLt) count was performed using a fully automated hematology analyzer.

Results: Thrombocytopenia was more severe in neonates with Gram-negative (Gm−ve) septicemia, (PLt=72.1x10^3/cmm), in comparison with those with Gram-positive (Gm +ve) septicemia, (PLt=83.1x10^3/cmm) (p<0.05). Most cases were with *Pseudomonas* infection (46%) with PLt count: 72.1 x 10^3/cmm and 6% mortality rate, followed by *Salmonella* (18%) and *Klebsiella* (14%) infection with Platelet count and mortality rate of (71.5 x 10^3/cmm, 6%) and (73.4 x 10^3/cmm and 2%) respectively. In contrast, cases with *Staphylococcus epidermidis* (72.1x10^3/cmm, 4%) and *E. coli* (71.2x10^3/cmm, 2%) infections had lower frequency (6% and 4%) and mortality rate (4% and 2%), respectively, irrespective of the fact that they also had low PLt count.

Conclusion: Thrombocytopenia is commonly caused by Gram-negative rather than Gram-positive bacteria. Therefore, treatment of thrombocytopenia must be of vital importance to alleviate complications of bacterial sepsis in neonates. (Rawal Med J 202;45:602-606).

Keywords: Thrombocytopenia, neonatal sepsis, Gm−ve septicemia, Gm +ve septicemia, Sudanese neonates.

INTRODUCTION

Platelets play an important role in the preservation of human life by assisting cessation of bleeding at the site of injury.[1,2] Low platelet count in children may be a life-threatening, as they might suffer from bleeding,[1] which may cause anemia. Certain types of diseases can cause low thrombocyte count, specifically some autoimmune diseases, e.g. systemic lupus erythematosus (SLE)[3] some hematological malignancies, e.g. acute leukemia[4] some anemias, e.g. megaloblastic anemia[5] hepatitis B[6] and bacterial sepsis.[7]

Bacterial sepsis among neonates increases the cost of medical care, causing severe morbidities by increasing length of stay in neonatal intensive care units (NICU).[8] Neonatal sepsis constitutes more than 50% of neonatal deaths.[9] Clinicians have been facing challenges in recognizing the consequences of neonatal sepsis.[10] It is prudent to manage the disease rapidly by administering correct antimicrobials to avoiding septic complications[11] and minimize mortality rate among neonates.[11,12]

In septic neonates, hemorrhagic diathesis emerges following disseminated intravascular coagulation (DIC) as a result of overconsumption of thrombocytes and coagulation factors.[13] Particularly in ill newborns, thrombocytopenia occurs predominantly among premature babies and neonates who are admitted in NICU.[14] This study aimed to deermine the effect of sepsis on circulating thrombocytes among Sudanese neonates with causative bacteria and mortality rate.

METHODOLOGY

The study included 50 septic neonates, comprising 26 female and 24 males. Control group had 27

females and 23 males. Ethical approval for the study protocol was obtained from the Alfajr College for Sciences Technology, Khartoum, Sudan and Informed consent from the parents was obtained for each patient and control neonate.

The patient specimens were collected from the Omdurman Teaching Hospital, Sudan. We collected 5 ml of venous blood from each neonate and processed for blood culture and platelet count. Approximately, 2.5 ml of blood samples were injected in each of the culture bottles containing 25 ml of Brain Heart Infusion Broth. The blood culture bottles were incubated at 37°C in an aerobic incubator. The bottles were observed for the indicators of growth such as turbidity, pellicle formation, hemolysis or gas production.

Blood, Chocolate and MacConkey's agar were used to subculture the bacteria from broth. The bacterial isolates were identified by the colony morphology, Gram's stain and biochemical characteristics. Antimicrobial susceptibility testing was performed by the Kirby Bauer Disc Diffusion method. Platelet count was done using a fully automated hematology analyzer.

RESULTS

Platelet count was significantly lower in all patients with sepsis, 81.3×10^3 as compared to the control group 238.2×10^3, (p<0.01) as shown in Fig. 1. Patient groups were classified based on the Gram's stain typing of the causative bacterial agent into Gram-negative, 82% (n=41) and Gram-positive, 18% (n=9). The former showed that the PLt count was significantly lower, at 72.1×10^3/cmm compared to the latter, 83.1×10^3/cmm, (p<0.01) as shown in Fig. 2.

Table 1. Platelet count by causative and its mortality in the patient group.

| Type of bacteria	PLt count X 10³/cmm (±SD)	Frequency % (Number)	Mortality % (Number)
Pseudomonas (Gram – ve)	72.1 (5.2)	46 (23)	6 (3)
Salmonella (Gram – ve)	71.5 (4.5)	18 (9)	6 (3)
Klebsiella (Gram – ve)	73.4 (6.2)	14 (7)	2 (one patient)
Staph. epidermidis(Gram +ve)	72.1 (4.5)	6 (3)	4 (2)
Strep. Faecalis (Gram +ve)	82.6 (4.2)	6 (3)	-
E. coli (Gram – ve)	71.2 (5.8)	4 (2)	2 (one patient)
Staph. aureus (Gram +ve)	88.7 (6.8)	4 (2)	-
Streptococci (Non group B) (Gram +ve)	89.1 (4.6)	2 (1)	-

Table 2. Hemostatic tests in each group of study population.

| Parameter	Platelets count x 10³/cmm (±SD)
Control	238.2 (61.1)
Patient	81.3 (8.4) (a)
Recovered patients	83.6 (14.5) (a)
Dead patients	54.3 (12.1) [a]
Early onset sepsis	72.3 (16.2) [a]
Late onset sepsis	53.9(15.5) [a]
Gram negative	72.1 (5.4) (a)
Gram positive	83.1(5.4) [a]

Significance determined by comparison of each group with controls indices. (a) = P<0.01; (b) = p < 0.05; (c) = p >0.05. *Statistical significance shown in parenthesis.

Fig. 1. Platelets count in a patient group versus a control group.
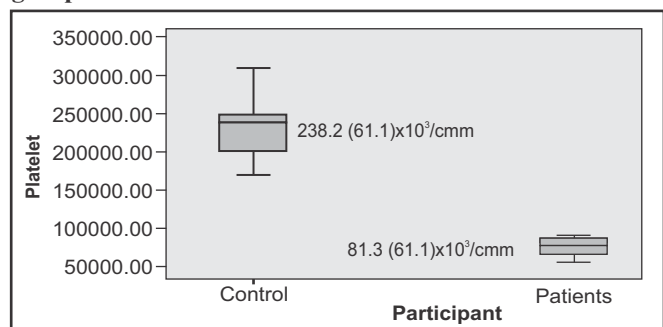
Key: Significance determined by comparison of each group with controls indices. (a) = P<0.01; (b) = p <0.05; (c) = p >0.05. *Statistical significance shown in parenthesis.

Fig. 2. Platelet count in the patients with Gram negative against patients with Gram positive bacteria
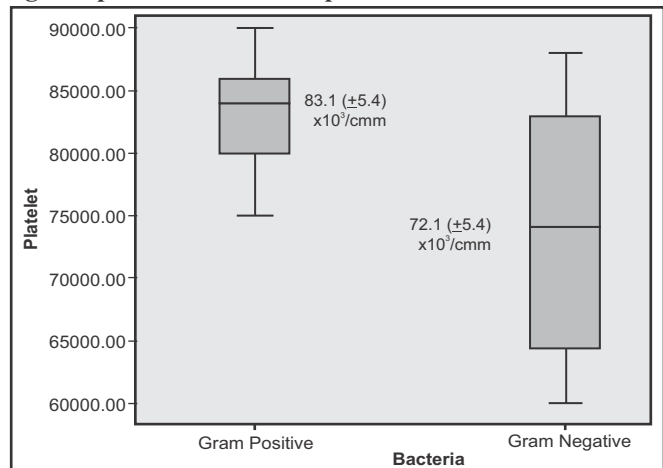
Key: *Significance determined by comparison of each group with controls indices (a) = P<0.01; (b) = p <0.05; (c) = p value >0.05. *Statistical significance shown in parenthesis.*

Table 1 listed by platelet count, in the patient group stratified by causative agent and mortality rate. Stratified in this way, only the *Pseudomonas* stand out (46%) with 6% mortality rate and low PLt count 72.1×10^3/cmm, followed by *Salmonella* and *Klebsiella* (at ~18% and 14%, respectively) with PLt count, 71.5×10^3/cmm and 73.4×10^3/cmm, respectively. In contrast, cases with *Staphylococcus epidermidis* and *E. coli* had lower frequency and mortality rate without having low PLt count. The mortality rate in patients with *Enterococcus faecalis*, *Staphylococcus aureus* and *Streptococci* (Non-group B) was 0%, although they also had thrombocytopenia. Mortality figures are shown in Table 2.

DISCUSSION

Approximately 1% of women at term gestation have positive cultures from amniotic fluid,[15] but the rate of microbial invasion of the amniotic cavity is approximately 32% in those women with preterm labor.[16] A study reported that the rate of microbial invasion in preterm premature rupture of membranes was as high as 75%[17], and another study found that the neonatal sepsis was accounted for in 30-50% out of the total deaths in the third world countries.[18] Therefore, it would be useful to detect and alleviate the complications of sepsis to reduce its mortality rate.

Our findings revealed that the neonatal sepsis in Sudan might be a cause of premature labor, as 66% of septic neonates were preterm and history of leaking membranes was taken. Our result was significantly higher, (p<0.01) in comparison with healthy neonates, who matched in age and gender without sepsis, attending the same hospital. The healthy neonates were initially suspected for bacterial sepsis but later on clinical diagnosis revealed them to be healthy. This finding is in agreement with similar studies in other ethnic groups.[15,19] Therefore, it has become imperative to know the main complications with an effective treatment for neonates with sepsis such as thrombocytopenia.

In this study, severe thrombocytopenia was noticed with sepsis, especially premature ones, as their platelets count was significantly low compared to the control group, (p<0.001) (Table 1). Our finding is similar to other studies in other ethnic groups as they reported that thrombocytopenia was prevalent in patients with severe sepsis,[1] which can be an early predictor of septicemia[20] and a very common finding in sepsis.[21]

We found that thrombocytopenia was more severe in patients with gram negative (Gm −ve) septicemia rather than patients with gram positive (Gm +ve) septicemia. In the patient group, 10 (20%) died as a result of neonatal sepsis with severe thrombocytopenia (54.3×10^3/cmm) compared to the recovered neonates (83.6×10^3/cmm), as shown in Table 2. This indicates that the illness of septic neonates might rapidly develop and in some instances become life threatening, as a result of thrombocytopenia which was found as one of the main neonatal sepsis complications beside others such as acute organ dysfunction, hypotension and ischemia. Therefore, neonates with confirmed or suspected early-onset bacterial sepsis must be managed quickly by giving platelet transfusion, when its range of $10 - 50 \times 10^9$/L based on clinical situations[22] for avoiding morbidity and reducing the mortality rate among the preterm neonates.

In this study, severe thrombocytopenia was found to be common in the septic neonates, especially premature newborns. This reflects that bleeding might occur in most Sudanese neonates with sepsis who are admitted at Maternal Teaching Hospital, Khartoum. This finding is in line with Ahmed et al,[23] who reported that thrombocytopenia was a common complication of neonatal sepsis.

Limitation of this study includes the small sample size. More studies on neonatal sepsis are needed with larger sample size to clarify more precisely the relationship between bacterial sepsis and thrombocytopenia.

CONCLUSION

The commonest cause of bacterial sepsis in neonates resulting in severe thrombocytopenia was because of Pseudomonas, Salmonella and Klebsiella infection. Therefore, the earliest diagnosis and treatment of these bacteria in neonates with suspected early and late-onset sepsis are crucial to alleviate the complications of sepsis such as thrombocytopenia before it may lead to severe hemolysis.

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