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Original Article

The role of Hematological Scoring System (HSS) in early diagnosis of Neonatal Sepsis

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Abstract

Background: Timely diagnosis of neonatal sepsis is critical. Early diagnosis of neonatal sepsis is still a great challenge.

Objectives: To determine the significance of the hematological scoring system (HSS) for early detection of neonatal sepsis.

Study design: A case control study done at the neonatal ICU, Al-Azhar Assiut university Hospital. It included sixty newborn infants divided into three groups (20 newborn infant for each one), septic, probably septic and control groups. Perinatal history with emphasis on risk factors for neonatal sepsis, Neonatal physical examination and laboratory investigation, including complete blood picture with differential, blood film, HSS (hematological scoring system) and blood culture.

Results: HSS among septic group had a sensitivity (96%), specificity (90%), PPV (86.7%) and NPV (86%) and area under Receiver Operating Characteristic curve (ROC curve) with [95 % CI] was 0.76 (0.599 – 0.881). Immature/total WBCs ratio had a sensitivity (80.3%), specificity (78.2%), PPV (66.3%) and NPV (84.7%) in early detection of neonatal sepsis. Immature/mature WBCs ratio had a sensitivity (78.3%), specificity (66.5%), PPV (42%) and NPV (60%) in early detection of neonatal sepsis. Total leukocytic count in the septic group was statistically significantly increased compared with the corresponding values in the probable septic and control groups (P= 0.021*).

Conclusions: HSS is a useful test to distinguish the infected from non-infected infants. HSS is a simple, quick, readily available effective tool with high sensitivity and specificity in the early diagnosis of neonatal sepsis.

Key words: hematological scoring system (HSS), neonatal sepsis

Introduction

Sepsis is a life-threatening condition caused by uncontrolled, systemic, inflammatory response to bacterial, viral or fungal infection. Sepsis represents a substantial health burden. The incidence of sepsis and the number of sepsis related deaths are increasing [1]. The world health organization (WHO) estimates that 1 million deaths per year (10% of all under-five years' mortality) are due to neonatal sepsis and that 42% of these deaths occur in the first week of life [2]. The initial presentation of neonatal septicemia may be subtle and therefore, it is important not only to recognize the neonates with septicemia but also to identify the non-infected neonates. The primary objective of the clinician caring for infants at risk for neonatal infections is to identify all potential cases of bacterial diseases quickly and begin antibiotic therapy promptly. It is important, however, to determine which of these cases represent true infection and thus require a full course of antibiotic [3]. Early treatment of neonatal sepsis is vital to improve outcome. The condition has a gradual and subtle onset, with non-specific symptoms that may severely compromise the infant's clinical state if untreated, and may lead to life-threatening consequences [4]. Considering the high mortality and serious morbidity among neonates suffering from sepsis, a diagnostic marker with high sensitivity and specificity is desirable [5]. C-reactive protein (CRP) is an acute-phase reactant that synthesized by the liver within six hours after the onset of inflammation and tissue necrosis. Its rapid synthesis, short half-life and rapid decline with recovery, together with an association between greater increases and serious bacterial infections, have made the CRP test popular [6]. Blood culture is still gold standard for the diagnosis of sepsis but minimum 48 hours is required for the earliest result and it can be sterile in spite of clinical signs of sepsis [7]. Therefore, varieties of diagnostic infection markers

studied in the last years. Delaying the treatment of a bacteremic infant leads to an increase in mortality while starting antibiotic therapy to every infant in the presence of clinical suspicion causes antibiotic overuse and nosocomial infections because of unnecessary hospitalization. Therefore, search for diagnostic markers of infection with high sensitivity and specificity is still required [8]. The early diagnosis of neonatal septicemia primarily based on clinical evaluation but laboratory diagnosis requires a microbiologic-clinical correlation. Many babies treated empirically with antibiotics for several days while waiting for bacteriologic culture for suspected infection because fatal infection reported in other study in the presence of negative blood culture [9]. The evaluation of tests for neonatal sepsis is important because the infection may present a very serious threat to the baby. Confirmation of the diagnosis may take time, and diagnostic test used to obtain a rapid indication of the infection status [10]. There is a need for an effective and accurate biochemical marker to support or exclude the diagnosis of infection. Hematological indices, acute phase reactants, protein markers, and cytokines, which extensively examined as adjunctive tests for diagnosis of sepsis [11]. None has shown sensitivity, specificity, positive predictive values (PPV), or negative predictive values (NPV) that can sufficiently guide clinical management [12]. Using of a variety of biomarkers with the potential to assist clinicians in the diagnosis of sepsis. Progressive advancement in biochemical and genetic research has led to the development of more sophisticated classes of biomarkers such as procalcitonin (PCT), interleukin 6 (IL-6), interleukin 8 (IL-8), interferon – gamma (IFN- γ), tumor necrosis factor – alpha (TNF-α), CD 64, soluble intercellular adhesion molecule (sICAM) 10 [13]. Increased mean platelet volume (>8.6fl) has been studied recently as a marker of EOS (early onset sepsis) and a

predictor for mortality especially in preterm neonates with a sensitivity of 97.14 % and a specificity of nearly100 % [14]. In addition, recent studies have shown that increase (20%) red blood distribution width within 6 hours after birth has been associated with EOS (early onset sepsis) and predicts a poor outcome [15]. There is a need for a rapid test for bacteremia, which is easy to perform and the reports of which can be available to the pediatricians quickly, a hematological Scoring System (HSS), is a simple, easy, cheap, and rapid adjunct for the diagnosis of clinically suspected cases of neonatal sepsis [16].

Methods

This is a case control study from (March 2017 to December 2017) and conducted on 60 neonates admitted to the Neonatal Intensive Care Unit. The study included three groups: Group1: 20 newborn infants with proved sepsis with either positive blood cultures or positive CRP or both. Group2: 20 newborn infants with probable sepsis with Strong clinical history but negative blood cultures. Group3: 20 normal newborn infants matched with other groups (post-natal age, sex and gestational age) without any evidence of sepsis or risk factors of N. sepsis. Inclusion criteria: Age (post-natal age before 28 days): newborns (1-4 weeks), terms and preterm, low and normal birth weight. Exclusion criteria: any newborn with major congenital anomalies, inborn error of metabolism (family history of previous neonatal deaths and early manifestations of poor feeding, vomiting and deterioration of level of consciousness after exclusion of common causes especially neonatal sepsis), severe jaundice due to ABO incompatibility, severe RDS due to surfactant deficiency, extreme low birth weight newborns and perinatal asphyxia (by excluding babies with poor Apgar Score). Methods: All infants subjected to full medical history taking (To detect risk factors for sepsis): Post-natal age, sex and gestational age. Obstetric history (circulage, obstructed labor,

oligohydramnios, placenta previa and placental separation) was reported. Prenatal history (diabetes mellitus, maternal fever >38°C, maternal UTI and other prenatal problems) was reported. Natal history (PROM, maternal fever, Type of delivery, Site of delivery) and postnatal history (low Apgar score at 1 and 5 minutes, aggressive resuscitation, respiratory distress, cyanosis, fever and other abnormalities in early minutes of life). Present history, which includes most common symptoms of sepsis and lastly resuscitation (Apgar score) [17].

Admission to NICU, clinical examination: general examination, general condition and activity. Vital signs (Color, heart rate, respiratory rate, temp. and capillary refill time). Estimation of gestational age using (New Ballard Score) was used [18]. Anthropometric measurements (Weight, Length, head, and abdominal circumferences) were recorded. Detection of clinical signs of sepsis: The infant is not doing well or going off, restlessness, lethargy, pallor and mottled skin. Temperature changes: hypothermia or hyperthermia, respiratory dysfunction (apnea, signs of respiratory distress), circulatory dysfunction (poor peripheral circulation, hypotension, prolonged capillary refill time), GIT dysfunction (abdominal distension, feeding intolerance, hepatomegaly and jaundice) and neurological dysfunction (irritability, hypotonia, lethargy) and hemorrhagic diathesis: petechiae or bleeding from puncture sites. Sclerema: this is a late feature of any serious illness especially in preterm neonates. Neonatal reflexes (Moro and Suckling). Colors, Skin, Umbilicus, Eyes and Napkin area were recorded. Systems examination: Chest: respiratory distress, air entry and adventitious sound. Abdomen: abdominal masses, distension, palpation of organs, auscultation of intestinal sounds, gastric Ryle passage and the potency of the anus. CVS: HR, perfusion, peripheral pulses, heart sounds and murmurs. CNS: Level of Conciseness,

anterior fontanels, tone and reflexes. Extremities and Genitalia to exclude congenital anomalies were done. Laboratory Investigation: Complete blood count was done at (DIRUI BCC-3600 three part differential Hematology analyzer, China) (this hematology analyzer adopts electrical impedance to test amount of red blood cell, white blood cell, platelets as well as volume distribution. Test hemoglobin concentration by colorimetric method, and based on this to calculate other parameters), and blood film [19]. C reactive protein [20]. CRP –latex reagent is a suspension of polystyrene particles sensitized with anti-Human C - reactive protein. When the reagent faced against the serum with C - reactive protein, an antigen-antibody reaction takes place being easily visualize because of the latex agglutination. Hematological Scoring System (HSS): this scoring system takes seven hematological parameters (Total WBC count, total polymorph-nuclear (PMN) count, immature PMN count, immature/total PMN ratio, immature/mature PMN ratio, platelet count and degenerative changes in neutrophils) into account and assigns a score of one to each of the seven hematological findings. There is one exception; an abnormal total polymorph nuclear (PMN) count assigned a score of two rather than one if fewer mature PMNs present in blood smear. The total score thus ranges from 0-8, and it has been suggested that if the total score is less than two, sepsis is very unlikely and if the score is more than 5 the likelihood of sepsis is very high.

Hematological scoring system (HSS), [7]

Variables	**Score**
• Increased of IT ratio of neutrophil > 0.2	1
• Increased (> 5,400/mm3) or decreased (< 1,800/mm3) of (PMN) count	1
• Increased of immature to mature neutrophil (IM) ratio ≥ 0.3	1
• Increased of immature PMN count > 500/mm3	1
• No neutrophils	2
• Decreased or increased of leukocyte count (≤ 5,000/mm3 or ≥ 30,000/mm3)	1
• Degenerative changes in PMN (vacuolization, toxic granule, and Dohle bodies)	1
• Decreased of thrombocyte count ≤ 150,000/mm3	1

Blood cultures: for cases with clinically diagnosed neonatal sepsis and infant at risk of neonatal sepsis only Blood samples collection: Under strict aseptic technique, we collect blood samples by:

a. Using pressure cuff, wearing sterile gloves.
b. Locate vein, disinfect vein puncture site.
c. Using sterile syringe and needle.
d. We should be sure that culture media is not contaminated.
e. Insert needle through rubber liver and inject blood into culture bottle.

Blood sample incubation:

a. Using fresh ethanol, ether we swap and wipe the top of each culture bottle.
b. We label each bottle with the name, number of patient date and time of collection.
c. Then we incubate the incubated media in BACTEC device.
d. Bottle was examined daily (up to 7 days) for antimicrobial growth which was shown at screen of bactec instrument which give +ve for +ve cultured bottles.

When growth was present, we did:

a. Subculture on blood agar and chocolate agar.
b. Incubate blood agar plates aerobically and Incubate chocolate agar in carbon dioxide atmosphere (anaerobic gas package).
c. Examine gram-stained smear of colonies depending on bacteria seen and then test the colonies further for coagulase, catalase, oxidase, urease and motility.
d. Antibiotic sensitivity disk.

Ethical considerations: Ethical approval: this study was approved from The Ethics Committee of Faculty of Medicine, Al-Azhar University, Assiut, and written informed consents were obtained from the parents and they informed about the nature and steps of the study.

Statistical analysis

Data collected, coded, revised and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The data presented as number and percentages for the qualitative data. Mean standard deviations and ranges for the quantitative data with parametric distribution. Median with inter quartile range (IQR) for the quantitative data with non-parametric distribution, Chi-square test was used in the comparison between two groups with qualitative data and Fisher exact test was used instead of the Chi-square test when the expected count in any cell found less than 5. The comparison between more than two groups with qualitative data and parametric distribution done by using One Way Analysis of Variance (ANOVA) test and Kruskall-Wallis test was used in the comparison between more than two groups with quantitative data and non-parametric distribution. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value considered significant as the following: $P > 0.05$: Non-significant (NS)

$P < 0.05$: Significant (S)

$P < 0.01$: Highly significant (HS)

Sensitivity and specificity: the sensitivity of a diagnostic test is the proportion of patients for whom the outcome is positive that correctly identified by the test. The specificity is the proportion of patients for whom the outcome is negative and correctly identified by the test. Positive predictive value (PPV): probability that the disease is present when the test is positive (expressed as a percentage) = a (true +ve) / a (true +ve) + c (false –ve). Negative predictive value (NPV): probability that the disease is not present when the test is negative (expressed as a percentage) = d (true –ve) / d (true –ve) + b (false +ve).

ROC: Receiver Operating Characteristic was calculated using the statistical program SPSS to obtain area under the curve, specificity and sensitivity. An ROC curve is a graphical representation

of the trade-offs between sensitivity and specificity. Plotting sensitivity (on the y-axis) versus the specificity (on the x-axis). This graphical approach of ROC analysis makes it relatively easy to grasp the inter relationships between sensitivity and specificity of a particular measurement. In addition, calculations of the area under the ROC curve provide a summary measure of the accuracy of the diagnostic test. The larger the area under the curve, the better the diagnostic test. The principal use of ROC in medicine involves assessing performance of diagnostic tests.

Results

This study included 60 newborns divided into 3 groups, 20 newborn infants for each: group 1 (septic group), group 2 (probable septic group) and group 3 (control group).

Klebsiella is the most frequent organism isolated from the septic infants (30 %), followed by Escherichia coli (20%) and GBS (15 %), (table 1 and figure 1).

There are a statistically significant differences between all groups as regard Mean + SD of HSS parameters (p value < 0.01); (count of total WBC, PMN, immature WBCs, platelets number and I/T, and I/M ratios), (table 2).

There are a statistically significant differences between all groups as regard HSS scores (p value < 0.001). Eighty-five % of Score 0 - 2 is present among control group, Forty % of Score 3- 4 is present among probable septic group and 75 % of score ≥ 5 is present among septic group, (table 3 and figure 3).

The sensitivity, specificity, PPV and NPP of HSS is: 96 %, 90 %, 86.7 % and 86 % respectively (table 4 and figure 2).

The most sensitive HSS parameter is I/T ratio (80.3%) with NPV 84.7%, (table 5).

The most specific HSS are: Platelets number (90 % and PPV 88.2 %), followed by Total WBC count (78.3%) and I/T ratio (78.2%), (table 5).

Discussion

Hematologic scoring system (HSS) can improve the diagnostic accuracy of

complete blood count. It can be used as a screening test for diagnosing sepsis. However, it is important to simplify and standardize the interpretation of this global test. HSS can be a useful test to distinguish the infected from the non-infected infants. It has high sensitivity and specificity, the certainty of sepsis being present with higher scores [16]. There were non-statistically significant differences between studied groups as regards gender, gestational age, mode and site of delivery. In our study klebsiella was the most common organism isolated in septic group (30%). E.coli represents (20%) and Group B streptococci (GBS) represent (15%) then CONS and Enterobacter (10% for each), finally Staphylococcus aureus, strept.pneumonia and candida albican represent (5% for each) were the most next organisms. Stoll and Hansen (2011), isolates Klebsiella spp. 25%, E coli 17.5%, Staphylococcus aureus18%, Group B Streptococci 7% and Acinetobacter spp. and Pseudomonas spp. were 12% for each [21]. Jacob, et al., 2018, isolates Staphylococcus aureus 22.5%, Klebsiella spp. 18.6%, Acinetobacter species 12.8, Pseudomonas aeruginosa 8.1 % and Escherichia coli (7%) [22]. From the variable results obtained from different studies, it is evident that the causative organisms causing neonatal septicemia vary from nursery to nursery, between different geographical areas and in the same catchment area with time. This variation may be due to differences in the environment, the microbial etiology of sepsis and supportive care practice between centers [23]. Our study showed that HSS has a sensitivity of (96%), specificity of (90%), PPV of (86.7%) and NPV of (86%), and area under the curve (AUC) (95% CI) is 0.76 au (0.599 – 0.881). Jacob, et al., 2018 states that a HSS score of 3 and above had the highest sensitivity of 87% and specificity of 85% (area under the curve (AUC) = 0.9 au) [22]. Munazza Saleem, et al., (2014) found that the HSS was having a

sensitivity of 90%, specificity of 74.5%, PPV was 65.9% and NPV was 93.2% [24]. In contrast to our study Khair, et al., (2010); reported that a moderate sensitivity and specificity of HSS respectively (71%) and (73%) with a PPV (24%), and high NPV (95%) [25]. Pramana, et al., 2016, states that the HSS sensitivity, specificity, PPV and NPV were 80.9%, 92.7%, 85%, and 90.5% respectively [7]. Our results showed the HSS score of ≥ 5 is present in 75 % of septic group and in 35% of probable septic group. We found that the higher the score the greater the certainty that sepsis was present. Majority of neonates with sepsis had score ≥ 5 and sensitivity =80% and specificity =90%. Therefore, score of 5 is more specific and increases the likelihood of sepsis. A score < 2 suggests that sepsis was unlikely [3]. In our study, we demonstrate that low sensitivity (46%), moderate specificity (78.3%), with (PPV: 33.42%) and (NPV: 46.9%) of the total leukocyte count for detecting neonatal sepsis. These results were similar to the results reported by (Zaki and El Sayed, 2009), in which the total leukocyte count sensitivity was (48%) and specificity was (77%) [26]. These results were also similar to the results reported by Ottolini, et al., 2003 [27]. In contrast to our study, the study done by Khurshid and Mustafa, (2000) which showed that abnormal leukocyte count is the most specific test with better positive and negative predictive value than I/T ratio [28]. In our study, we demonstrate that low sensitivity (49.6%), specificity (66.5 %) with PPV (42.5%) and NPV (63.3%) of total PMNs leucocytes count. In contrast to our study, Zaki and El Sayed (2009) reported that there was moderate sensitivity (77.8%) and high NPV (84.93%) of total PMNs leucocytes count [26]. Our study showed that I/M PMN count is a moderate sensitive test (78.0%), low specificity test (66.5%), PPV (42%) and NPV (60%). Our study is supported by Khurshid and Mustafa (2000) found that I/M ratio has sensitivity (71%) [28]. In

contrast to our study Ghosh, et al., (2001) reported that there was high sensitivity of I/M ratio (93%), specificity (81%), PPV (32%) and NPV (99%) [29]. Also Khair, et al., (2010) reported that I/M ratio of PMN count is a highly specific test (specificity 92.85%) [25]. In our study, we demonstrate that sensitivity (80.3%), specificity (78.2%), PPV (66.3%) and NPV (84.7%) of I/T ratio of the total leukocyte count for detecting neonatal sepsis. These results were nearly similar to the results by Buch, et al., (2011) reported that sensitivity and specificity of I/T ratio were (92%) and (88.57%) respectively [30]. In contrast to our study Walliullah, et al., (2009) who reported that there was decrease of both sensitivity and specificity of I/T ratio, (70%) and (56%) respectively [31]. Asitava Debroy, et al., 2016 states that, among definite septic neonates the I:T PMN ratio was 90 % (was highly sensitive) followed by immature PMN count (20%). Also, I:T PMN ratio (96.6%) was highly specific followed by I:M PMN ratio. Positive predictive value was highest for I:T PMN ratio (100%) which was helpful in identifying neonates who really had sepsis. Negative predictive value was highest with I:T PMN ratio(96.6%) which indicated that the neonates did not have the evidence of sepsis [3]. Bhalodia, et al., 2017, reported that, HSS had the highest sensitivity (93.7%) and identified >90% of neonates with clinical suspicion of sepsis. Furthermore, total leukocyte count showed high specificity but least sensitivity, immature to total ratio and immature to mature ratio showed high specificity and high sensitivity, and platelet count showed high negative predictive value and least positive predictive value [16]. Neonates with sepsis develop thrombocytopenia, may be due to disseminated intravascular coagulation (DIC) and the damaging effects of endotoxin on platelets. Thrombocytopenia is frequently associated with sepsis and indicated a poor prognosis. This thought to be due to

increased platelet destruction, sequestration secondary to infections, failure in platelet production due to reduced megakaryocytes, [32]. In our study, thrombocytopenia showed sensitivity of (75%), specificity of (90%) and PPV (88.2%), NPV (78.3%). These results were nearly similar to the results reported by Khair, et al., (2010) and Haider, et al., (2010) who found that thrombocytopenia has sensitivity of 64%, specificity 81.45%, PPV 71.11% and NPV 76% [25] and [33].

Limitations: 1- VLBW and preterm infants less than 28 weeks gestation were not included in this study, due to many problems other than sepsis can change the parameters of HSS.

2- Comparison of HSS with other sepsis markers not included in this study due to small sample size.

Conclusions

Hematological Scoring System (HSS) is a useful test to distinguish the infected from non-infected infants. HSS is a simple, quick, readily available effective tool with high sensitivity and specificity in the early diagnosis of neonatal sepsis.

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Author's contributions

AAH, YTK and MSE equally contributed in the study concept, design, supervision, methodology, statistical analysis and data collection. AMH performed the investigations and laboratory workup and wrote the first draft of the manuscript.

Conflict of interest

Authors declare they have no conflict of interest

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Table (1): Blood culture among septic group

Blood culture organism	Septic group (No=20)	
	No	**%**
Candida albican	1	5
CONS	2	10
E.coli	4	20
Enterobacter	2	10
GBS	3	15
Klebsiella	6	30
Staphylococcus aureus	1	5
Strept. pneumonia	1	5

E. Coli: Escherichia Coli, GBS: Group B-Streprococci

Table (2): Hematological Scoring System (HSS) parameters (Mean ± SD) of studied groups

Parameters	Sepsis (N=20)	Probable sepsis (N=20)	Controls (N=20)	P value
Total WBC count	20.04±11.2	15.5±9.38	12.2±3.03	0.001**
Total PMN count	9283±3802	6641±466	5529±958	0.035*
Immature count	2099±376	800±395	200±145	0.001**
I/T ratio	0.22±0.09	0.12±0.84	0.03±0.15	0.001**
I/M ratio	0.7±0.90	0.87±0.15	0.96±0.84	0.016*
Degeneration	25.3±0.82	19±0.11	0.0±0.0	0.001**
Platelet count x10^{x3}	112.5±30.7	174.9±100	249±71	0.001**

*Statistically significant **Highly significant

WBC: White blood cells, PMN= polymorphnuclear cells – I/T= Immature/total – I/M=Immature/mature

Table (3): Hematological Scoring System (HSS) scores in studied groups.

Scores	Sepsis (N=20)		Probable sepsis (N=20)		Controls (N=25)		P1	P2	P3
	N	%	N	%	N	%			
Score 0–2	0	0.0	5	25.0	17	85.0			
Score 3–4	5	25.0	8	40.0	2	10.0	<0.01*	<0.001*	<0.001*
Score ≥5	15	75.0	7	35.0	1	5.0			

*Statistically significant ** highly significant

P value < 0.05: statistically significant – P value ≤ 0.01: statistically highly significant, P1: between septic and probable septic groups – P2: between septic group and controls, P3: between probable septic group and controls

Table (4): Receiver operating characteristic (ROC) curve for differentiation of early diagnosis of neonatal sepsis according to HSS findings.

Marker	AUC (95% CI)	Significance	Sensitivity	Specificity	PPV	NPV
HSS	0.76 (0.599–0.881)	0.001 S	96%	90%	86.7%	86%

AUC: Area under curve, HSS: Hematological Scoring System, PPV: Positive predictive value, NPV: Negative predictive value

Table (5): Performance of individual hematologic findings in early diagnosis of neonatal sepsis

Item	Sensitivity (%)	Specificity (%)	PPV	NPV
Total WBC count	46%	78.3%	33.42%	46.9%
Total PMN count	49.6%	66.5%	42.5%	63.3%
I/T ratio	80.3%	78.2%	66.3%	84.7%
I/M ratio	78.3%	66.5%	42%	60%
Platelets	75%	90%	88.2%	78.3%

*Statistically significant **Highly significant

WBC: White blood cells, PMN: Polymorph nuclear, PPV: Positive predictive value, NPV: Negative predictive value, I/T= Immature/total – I/M=Immature/mature

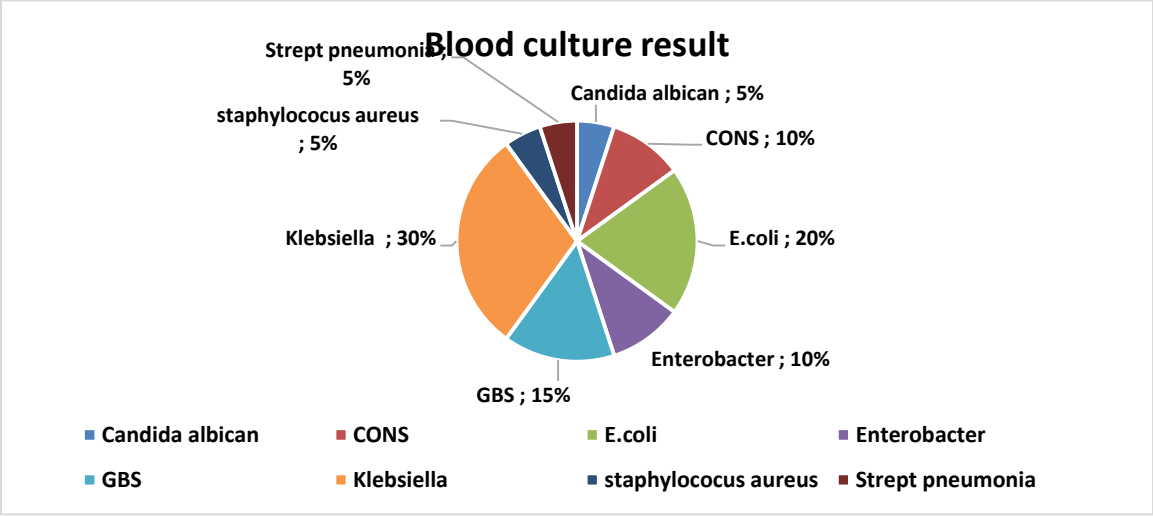

Fig. (1): Causative organism in septic group
CONS: coagulase negative staphylococci - E.coli: Escherichia coli – GBS: group B streptococci

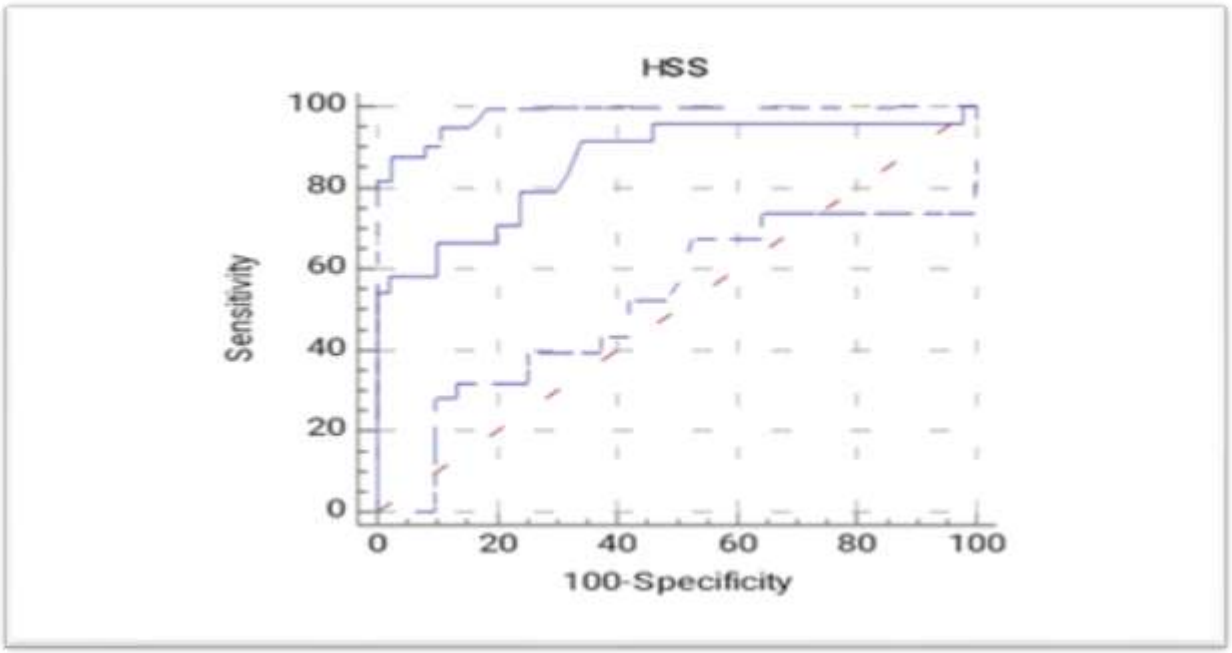

Fig. (2): ROC curve for differentiation of early diagnosis of neonatal sepsis according to HSS findings

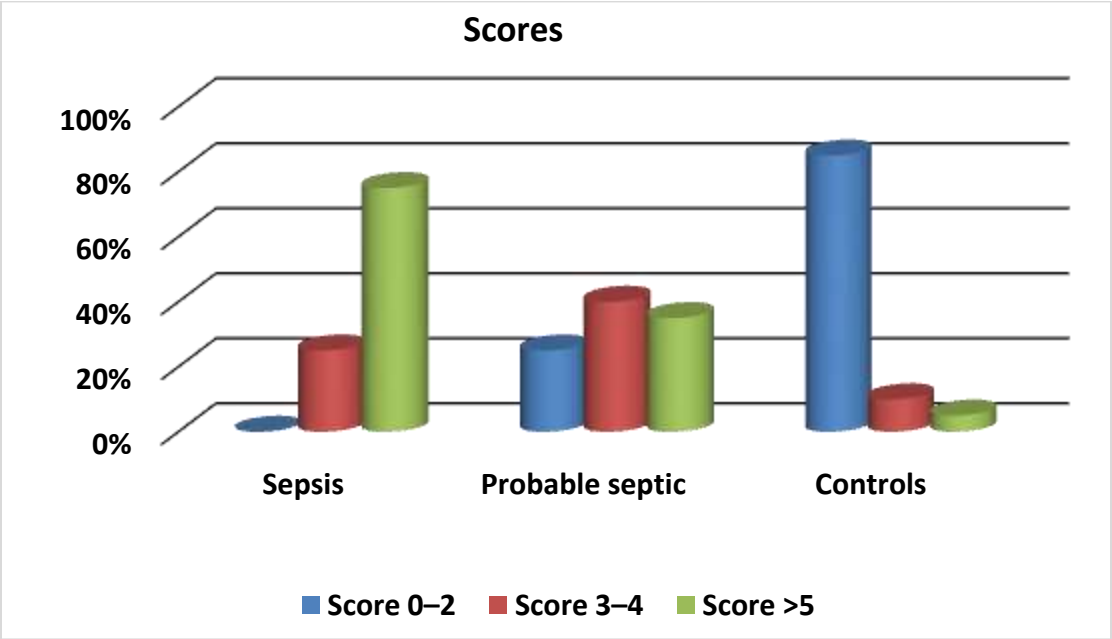

Fig. (3): Scores of HSS among different groups

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