EVALUATION OF THE SEPTIC SCORE IN NICU AT AHMAD MAHER TEACHING HOSPITAL

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ABSTRACT

Background: *Neonatal sepsis is a life threatening yet treatable condition. Clinical features of sepsis are non-specific in neonates; a high index of suspicion is required for timely diagnosis. Non- infectious disorders may produce hematological changes similar to those seen with infections.*

The aim of the work: *was to evaluate the items of the hematological septic score used in Ahmed Maher Teaching Hospital to predict neonatal sepsis.*

Patient and Methods: *Data collected included; 1- history of predisposing factors. 2- Clinical criteria suggestive of sepsis 3- Hematological septic score from 0-7. 4- Blood culture results. The collecting data were analyzed. Significance of the clinical criteria was done by T-test, chi- square and Fischer`s exact test. Significance of each of individual hematological items was assessed by its sensitivity, specificity, positive predictive value and negative predicative value. Combination scores 2, 3, 4, 5 and 6 were also assessed in the same way.*

Results and discussion: *The study was completed with 548 cases. Clinical signs that were statistically significantly associated with culture positive (proven cases) of neonatal septicemia were seizures ($p = 0.0$), irritability, lethargy and poor feeding ($p<0.001$), hypo or hyperthermia ($p<0.02$), respiratory symptoms ($p<0.05$) and ($p<0.05$). So these clinical characteristics could be used as predictive signs of neonatal sepsis with poor diagnostic value. The only individual hematological score that could be used to predict neonatal sepsis was I/T ratio > 0.2 that had sensitivity 71% and negative predictive value 86%. All other tests had poor sensitivity. Combination scores 2, 3, 4 and 5 had also very poor sensitivity values (28.6%, 92.8%, 53.3% and 53.3%) respectively. Only combination score 6 had a sensitivity of 84.2%. So, it could be considered as a predictor for diagnosis of neonatal sepsis.*

Conclusion and Recommendation: *The hematological scoring system used in the neonatology department in Ahmad Maher Teaching Hospital was of limited value in early diagnosis of neonatal sepsis. New techniques should be included in the laboratory septic score used in Ahmad Maher Teaching Hospital.*

INTRODUCTION

Neonatal septicemia is a clinical syndrome of bacteremia characterized by systemic signs and symptoms in the first month of life. (1) It is estimated that in the developing countries 20% of all neonates develop sepsis (2), and it is responsible for 30-50% of total neonatal deaths. (3) Clinical features of sepsis are non-specific in neonates, and a high index of suspicious is required for timely diagnosis. (4) The gold standard for establishing a diagnosis of neonatal sepsis is through culture. However, several factors, including the small blood volumes obtained from neonates, the presence of low or intermittent bacteremia, as well as maternal intrapartum antimicrobial exposure, can make the confirmation of sepsis in a neonate a diagnostic challenge (1, 2). Given that the clinical diagnosis of infection in a neonate is unreliable (3) and that excessive, unnecessary empiric antimicrobial therapy for the treatment of suspected sepsis can promote antimicrobial resistance.(5)

A practical septic screen has been described and used in many units. Some suggestions for antibiotics use until results of culture and sensitivity are available should be included in the protocol of each unit. (6)

Aim of the work

The aim of this work was evaluation of items of the laboratory septic score used to predict neonatal sepsis in NICU in Ahmad Maher Teaching Hospital.

PATIENTS AND METHODS

Retrospective study was done at NICU in Ahmad Maher Teaching Hospital to all cases admitted to the unit in two years throughout the period from 1st January 2017 till 31st December 2018.

Data collected from each patient was as follows:

- Complete history including; predisposing factors for sepsis (premature rupture of membranes > 18hours, chorioamnionitis and intrapartum fever), place of delivery, mode of delivery and gestational age (GA).
- Clinical examination including weight, GA, and assessment of the clinical criteria suggestive of sepsis.
- Apnea, retraction, grunting, cyanosis.
- Bradycardia, tachycardia, hypotension, poor perfusion.
- Seizures.

- Abdominal distention, pre-feeding residual.
- Irritability, lethargy, poor feeding.
- Hepatomegaly or splenomegaly.
- Hyperthermia or hypothermia.
- Complete blood picture and assessment of hematological septic score from 0-7.

1. Total leukocytic count:

   < 5000/mm3

   or > 25000/mm3 at birth

   or > 21000/mm3 at 72 hrs.

   1. Total polymorphonuclear leukocytic count < 1750/mm3 or > 7500/mm3.
   2. Immature PMNL >400/mm3
   3. Immature/Total ratio (I/T) > 0.2.
   4. Immature / mature ratio > 0.3.
   5. Toxic granulations.
   6. Platelet count < 150000 in full term or < 100000 in preterm.

Rodwell et al., 1988 (13)

This score is the one used in NICU in Ahmed Maher Teaching Hospital for its applicability in our hospital

Hematological septic score was repeated every three days all over the stay. All patients suspected of neonatal sepsis (presence of predisposing factor or clinical criteria suggestive of sepsis or hematological septic score 3/7 or more) at admission or at any time during the stay were subjected to blood culture immediately.

Exclusion criteria:

1. Cases not suspicious of sepsis

2. Any patient who did not complete his laboratory works either the complete blood picture or the blood culture.

Statistical Analysis:

The collected data were analyzed. In evaluating the significance of the clinical characteristics in diagnosis of neonatal sepsis, parametric tests were used for comparison (t-test for variable with normal distribution), as well as non-parametric tests (when the variable showed no normal distribution). Chi-square test and Fisher`s exact test. (When necessary) with significant set at 95%.

In the evaluating the items of hematological score, we measured the sensitivity, specificity, positive predictive value and negative predictive value for each of the seven items.

Thus we calculated the sensitivity, specificity, positive predictive value, and negative predictive value of combination scores 2,3,4,5 and 6 (average of all possible combination of each score).

RESULTS

- Total number of admissions during the period from 1/1/2017– 31/12/2018 were 734 cases.
- 276 cases were excluded from the study; 231 were not suspicious of sepsis, 45 did not complete their laboratory investigations (33 died within few hours of admission before taking blood culture from them and in 12 cases blood culture bottles were not available)
- So the study was completed with 458 cases who are clinically suspected as neonatal sepsis.
- Positive blood culture was documented in 48 cases representing an isolation rate of 10.5%
- 73 cases died during the study representing a mortality rate of 16%

Table (1): Demographic characteristic of studied cases

	Number (458)	Percent
Gestational age (weeks)		
>37w	209	45.4
<37w	249	54.6
Sex		
Male	271	59.2
Female	187	40.8
Mode of delivery		
Vaginal	190	41.5
Cesarean section	268	58.5
Place of delivery		
Hospital	385	84.1
Private clinic	50	10.9
Home	23	5
Type of suspected sepsis		
Early onset	264	57.6
Late onset	194	42.4
Rate of isolation		
Full term (>37w)	27	56
Preterm (<37w)	21	44

Predisposing factor		
PROM	171	37.4
chorioamoninitis	22	4.8
intra-partum fever	11	2.4
No apparent risk factor	254	55.4

This Table shows that Sepsis was more common in male then female. Cesarean section was the main mode of delivery at hospital; Early onset sepsis was the main type of sepsis.

Table (2): Correlation between the clinical findings and the result of blood cultures in studied cases

	Number	**Blood culture results**		**p-value**
		+ve	**-ve**	
a-Respiratory symptoms; respiratory distress	304	26	278	0.05
b- Bradycardia, hypotension, poor perfusion	46	3	43	0.26
c- Seizures	68	22	46	0.000
d- Abdominal distension, pre-fed residual	160	19	147	0.6
e- Irritability, lethargy, poor feeding	234	12	222	0.001
F- Hepatomegaly, splenomegaly	35	7	28	0.05
G- Hyper or hypothermia	77	10	67	0.02

This table shows that the signs and symptoms that were statistically highly significantly associated with culture positive (proven cases) of neonatal septicemia were seizures, irritability, lethargy and poor feeding, hypo- hyperthermia.

Table (3): Evaluation of sensitivity and specificity of hematological items in neonates with proven sepsis by positive blood culture

item	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy
a-Total leukocytic count	5	54	11	85	81
b-Total polymorpho-nuclear leukocytic count	24.1	85.2	22	89.6	90
c- Immature polymorpho-nuclear leukocyte	27	67.2	11.2	85.8	61.8
d- Immature/Total ratio	71	87.2	78	86	76.5
e- Immature/Mature ratio	5	95.3	14	86.7	83.3
f- Toxic granulations	13.4	81.5	10	86	72.5
g- Platelet count	18.4	92.5	27.4	88.1	82.6

This table shows that alteration in the total leukocytic count was of poor value in early diagnosis of neonatal sepsis. The immature/total ratio of neutrophils is accepted for early diagnosis of neonatal sepsis

Table (4): Evaluation of hematological scoring system in neonates with proven sepsis by positive blood culture

Hematological score (out of 7)	Sensitivity (%)	Specificity (%)	Positive Predictive value (%)	Negative predictive value (%)
2	28.6	67.8	13.8	86.6
3	42.8	55.2	12.3	86.5
4	53.3	46.8	12.9	81.9
5	53.3	54.8	38.5	75.1
6	84.2	25.1	13.3	86.2

This table shows that the presence of six abnormal parameters had a statistically significant role in early diagnosis of neonatal sepsis.

DISCUSSION

Early diagnosis and treatment of neonatal sepsis is essential to prevent severe life threatening complications. In this era of multi-drug resistance, it is mandatory to avoid unnecessary use of antibiotics. Thus rapid diagnostic test(s) that differentiate infected from non- infected infants, have the potential to make a significant impact on neonatal care. (7)

Unfortunately, clinical signs are non-specific and often manifest themselves in the absence of positive culture. Positive cultures ranged from 8%-73% in the diagnosis of potential neonatal sepsis. An additional drawback of cultured- based diagnosis is the 24-48 hours assay time. (8)

In our study, the clinical signs and symptoms that were statistically highly significantly associated with culture positive (proven cases) of neonatal septicemia were seizures (p= 0.0), irritability, lethargy and poor feeding (p<0.001), hypo-hyperthermia (p value<0.02). Also the presence of respiratory signs or hepatomegaly or splenomegaly where significantly associated with culture positive (proven cases) of neonatal septicemia where p-value in both cases were <0.05.

Fanaroff et al., 1988 in their study of 395 patients with positive blood culture (proven sepsis) reported that the presenting features of neonatal septicemia were increasing apnea (55%), feeding intolerance, abdominal distention or guaiac positive stool (43%), increasing respiratory effort (29%), lethargy and hypothermia (23%). (9)

However, other studies **Luciano et al., 2011** and **Weber et al., 2003** when they studied the significance of these clinical characteristics in early diagnosis of neonatal sepsis they found that none of the clinical characteristics used in our study showed precision to distinguish between the two studied groups (proven sepsis and suspected sepsis) where p value was > 0.05 in studying each of these characteristics. (10) and (11).

So, the clinical characteristics could be described as predictive signs with low diagnostic value for neonatal sepsis, needing other associated diagnostic proof to confirm the diagnosis.

Beside the laboratory alterations for the diagnosis of neonatal sepsis, the patient clinical situation should be valued as the risk of bacterial infection in asymptomatic infants is very low. (12).

Considering the high morbidity and mortality associated with neonatal sepsis, tests with high sensitivity and high negative predictive value are most desirable because all infants with sepsis have to be identified. (13)

In our study, alterations in the total leukocytic count had a sensitivity 5%, specificity 54%, positive predictive value 11% and negative predictive value 85%, so these parameters was of poor value in early diagnosis of neonatal sepsis. Similar data were reported by **Rodwell et al., 1988** (14) and **Kuruvilla, 1998** (15). However, **Khair et al 2010** found that alterations in the total leukocytic count had a sensitivity 50%, specificity 91%, positive predictive value 43% and negative predictive value 93%, (16), thus he reported that alteration in the total leukocytic count acts as a good parameter for confirmation of sepsis.

In our study, alterations in the absolute neutophilic count (neutropenia or neutophilia) had a sensitivity 24.1%, specificity 85.2%, positive predicative value 22% and negative predictive value 89.6%, so this parameter was not statistically significant for the early diagnosis of neonatal sepsis. This coincides with the data found by **Khair et al., 2010** (17).

In our study, increase in the immature neutrophil count had a sensitivity 27%, specificity 67.2%, positive predictive value 11.2%, and negative predictive value 85.8%. Nearly similar results were reported by **Khair et al., 2010**. So, this parameter could not be used alone for early diagnosis of neonatal sepsis.

The immature/total ratio of neutrophils (I/T ratio) had a sensitivity 71%, specificity 87.2%, positive predictive value 78% and negative predictive value 86%. So, this parameter was the only accepted one statistically in our study for early diagnosis of neonatal sepsis due to its relatively high sensitivity and negative predictive value. More evident data for this parameter were found by **Rodwell et al., 1988** who found that alteration in the I/T ratio had sensitivity 96%, and negative predictive value 99%, and **Khair et al., 2010** who reported that I/T ratio > 0.2 had a sensitivity 100%, and negative predictive value 100%.

In our study, alteration in the immature/mature ratio of neutrophils (I/M ratio) showed very poor value in diagnosis of neonatal sepsis as sensitivity was only 5%, specificity 95.3% positive predictive value 14% and negative predictive value 86.7%.

However, different data were found by **Ghosh et al., 2001** who found that this parameter had a sensitivity 93%, specificity 81%, positive predictive value 32%, and negative predictive value 99%. (16) **Khair et al, 2010** who reported that I/M ratio > 0.3 had a sensitivity 100%, specificity71%, positive predictive value 11%, and negative predictive value 100%. These studies reported that this parameter could be used as a predictor for infection.

In our study, thrombocytopenia had a sensitivity 18.4%, specificity 92.5%, positive predicative value 27.4%, and negative predictive value 88.1%. So thrombocytopenia could not be used as a specific marker for early diagnosis sepsis. Similar conclusion was reported by other study by **Shirin et al 2005**, (18)

In our study, the presence of toxic granulations was not statistically significant in diagnosis of neonatal sepsis as it had sensitivity 13.4%, specificity 81.5%, positive predictive value 10%, and negative predictive value 86%.

As no single individual hematological parameter had a very high sensitivity and negative predictive value to be a reliable single test for early diagnosis of neonatal sepsis, combination of these parameters in the form of hematological septic score had been recommended.

In our study, combination score 2 had a sensitivity 28.6%, specificity 67.8%, positive predictive value 13.8%, negative predictive value 86.6%. Combination scores 3, 4, 5 had a better sensitivity value of 42.8%. 53.3% and 53.3% respectively. However, these scores had a poor statistically significant value for early diagnosis of neonatal sepsis.

However, in the study done by **khair et al ., 2010**, the combination score 3 had a sensitivity of 100%, specificity 21% , positive predictive value 15%, and negative predictive value 100%, while the combination score 4 had also 100% sensitivity and 100% negative predictive value, but with higher specificity 60 %, and positive predictive value 26%. So this study concluded that both combination scores 3 and 4 could be used as a screening test for early diagnosis of neonatal sepsis. However, score 4 is more reliable.

In our study, combination score 6 had a sensitivity 84.2%, specificity 25.1%, positive predictive value 13.3%,and negative predictive value 86.2%. This meant that the presence of six abnormal parameters had a

statistically significant role in early diagnosis of neonatal sepsis.

In our study, combination scores 2, 3, 4, 5 and 6, had specificity values ranging from 25.1% to 67.8 these values are lower than the specificity of each of the seven individual parameters that ranged from 54% to 95.3%. So these combination score had no role even in the confirmation of the presence of neonatal sepsis.

CONCLUSION

- Presence of any of these clinical signs suggestive of neonatal sepsis (seizures, irritability, lethargy, poor feeding, hypo or hyperthermia, respiratory symptoms or organomegaly) could be a predictive sign with low diagnostic value for early diagnosis of neonatal sepsis.
- Increase I/T ratio > 0.2 was the only individual hematological parameter that could be useful for early diagnosis of neonatal sepsis but with limited sensitivity value.
- Presence of six abnormal hematological parameters (combined score 6) was the only scoring system that had statistically significant value in early diagnosis of neonatal sepsis.

We concluded that hematological scoring system used in the neonatology unit in Ahmad Maher Teaching Hospital was of limited value in early diagnosis of neonatal sepsis.

RECOMMENDATION

1. Consider other diagnostic test such as erythrocyte sedimentation rate, C - reactive protein, pre-calcitonin, CD 64, and polymerase chain reaction for diagnosis of neonatal septicemia.
2. The hematological scoring system used in the neonatology department in Ahmad Maher Teaching Hospital should be updated and re-evaluated.

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تقييم العلامات الاكلينكيه والفحوصات المعملية التى تستخدم لتشخيص مرض تسمم الدم بقسم الأطفال حديثى الولادة بمستشفى أحمد ماهر التعليمى

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مرض تسمم الدم من الأمراض التى تهدد حياة الأطفال المولودين خلال الأربعة أسابيع الأولى من العمر ، وقد اثبتت الدراسات المتعددة أن التشخيص السريع للمريض هو أهم العوامل التى تساعد على شفاء الطفل المصاب بنسبه كبيرة . تأتى صعوبة تشخيص المرض فى كون الأعراض المصاحبة للمريض، وكثير من الفحوصات المعملية لتشخيصه تتشارك مع كثير من الأمراض التى تصيب المواليد فى هذا العمر ، ومن هنا كانت الحاجة الماسة لوجود آليات لتشخيص المرض تجمع بين الدقة الشديدة وسرعة النتائج المرجوة

الغرض من هذا البحث هو عمل تقييم للعلامات الاكلينكيه والفحوصات المعملية التى تستخدم لتشخيص المرض بقسم الأطفال حديثى الولادة بمستشفى أحمد ماهر التعليمى.

تم عمل دراسة مسبقة لجميع الحالات التى تم دخولها للقسم على مدى عامين خلال الفترة من 2009/1/1 – 2010/12/31 . تم دراسة الأتي فى كل مريض:

1. التاريخ المرضى للطفل شاملاً أى مسببات ساعدت على حصول المريض فى فترات الحمل – الولادة – بعد الولادة

2. فحص اكلينيكى شامل للطفل.

3. صورة دم كاملة مع عدد كرات الدم البيضاء الكلى والنوعى (خلايا ناضجة – غير ناضجة) وعدد الصفائح الدموية مع إعطاء تقييم معملي من صفر – 7.

أى طفل به عامل مسبب للمرض أو حصل على تقييم اكلينيكى أو معملي 7/3 أو أكثر عند الدخول أو أى وقت خلال وجودة بالقسم تم عمل مزرعة وحساسية للدم لتشخيص المرض بصورة قاطعه.

أى مريض لم يستكمل أى من الأبحاث السابقة تم استبعاده من البحث. تم تجميع نتائج البحث وعمل دراسة احصائيه للنتائج لبيان أى من العلامات الاكلينيكيه أو الفحوصات المعملية التى تستخدم فى القسم كانت له أهميه احصائيه فى التشخيص السريع للمرض.

عدد الحالات التى استكملت البحث 548 حالة . عدد حالات مزارع الدم الايجابية 48 حالة بنسبه 10.5% من الحالات المشتبه بها . تم تقسيم الحالات الى حالات تأكد

إصـــابتها بمـــرض التســـمم الـــدموى (مزرعـــة دم ايجابيـــة) وحـــالات مشـــتبه اصـــابتها بمـــرض التســـمم الـــدموى (مزرعـــه دم ســـلبيه) العلامـــات الاكلينيكيـــة التـــى كانـــت لهـــا أهميـــة احصـــائيه فـــى تشـــخيص المـــرض كانـــت كـــالآتي . وجـــود تشـــنجات عصـــبية ($p=0.0$)، اضـــطراب عصـــبى أو خمـــول أو صـــعوبة فـــى الرضـــاعة , ($p<0.001$) هبـــوط أو ارتفـــاع بدرجـــه حـــرارة الجســـم ($p<0.02$) ، صـــعوبة فـــى التـــنفس ($p<0.5$) ، تضـــخم بالكبـــد أو الطحـــال . ($p<0.5$) أوجـــد البحـــث أن وجـــود أى مـــن العلامـــات الاكلينيكيـــة الســـابقة أدى الـــى احتمـــال الأصـــابه بمـــرض تســـمم الأطفـــال عنـــد الاطفـــال حـــديثى الـــولادة وأن هـــذه الاحتمـــال الاكلينيكـــى لابـــد مـــن تدعيمـــه بفحوصـــات معمليـــة لتأكيـــد التشـــخيص . الفحـــص المعملـــى الوحيـــد الـــذى كـــان لـــه أهميـــة احصـــائيه فـــى تشـــخيص المـــرض كـــان) نســـبه عـــدد كـــرات الـــدم البيضـــاء الغيـــر ناضـــجة الـــى عـــدد كـــرات الـــدم البيضـــاء النيوتروفيـــل (حيـــث بلـــغ نسبة حساسيتة 71% وقيمة التنبؤ السلبى له 86%.

تـــم عمـــل تجميـــع للفحوصـــات المعمليـــة المختلفـــة ، ودراســـة امكانيـــة تحســـن نســـبة حساســـية تشـــخيص المـــرض بأســـتخدام هـــذه التجميعـــات . أوجـــدت الدراســـة أن تجميـــع عـــدد أثنـــين أو ثلاثـــة أو أربعـــه أو خمســـة مـــن هـــذه الفحوصـــات المعمليـــة اذا كانـــت إيجابيـــه لـــم تســـاعد علـــى تحســـين نســـبة حساســـية تشـــخيص المـــرض حيـــث بلغـــت نســـب حساســـيه تشـــخيص المـــرض لهـــذه التجمعـــات كـــالآتى (28.6 % ، 42.8% ، 53.3% ، 53.3%) بالترتيـــــــب بينمـــــــا وجـــدنا أن تجميـــع عـــدد ســـته مـــن هـــذه الفحوصـــات الاكلينيكيـــة اذا

كانت ايجابيه رفع حساسية تشخيص المرض الى 84.2% وقيمة التنبؤ السلبى له 86.2. %.

استنتجت الدراسة أن الفحوصات المعملية التى استخدمت للتشخيص المبكر لمرض تسمم الاطفال حديثى الولادة بمستشفى أحمد ماهر التعليمى لم تكن لها أهمية احصائية فى تشخيص المرض بأستثناء نسبه عدد كرات الدم البيضاء الغير ناضجه الى عدد كرات الدم البيضاء النيوتروبيل (بنسبه حساسية متوسطة) وكذلك تجميع عدد سته نقاط ايجابية من الفحوصات المعملية المستخدمة ، ولكن التطبيق العملى لاستخدام هذا العامل سيحد كثيراً من الاستفادة به.

أوصت الدراسه ضرورة اضافه فحوصات معملية جديدة تساعد على دقة وسرعة تشخيص مرض تسمم الدم للأطفال حديثي الولادة بمستشفى أحمد ماهر التعليمى.