القيمة التشخيصية للترفع الحروري في إنتان الدم عند حديث الولادة

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الملخص

خلفية البحث وهدفه: هدفنا من خلال هذا البحث تقييم نسبة انتشار الترفع الحروري في وحدة العناية المشددة لحديثي الولادة، ودراسة ترافقه مع إنتان الدم سواء الباكر أو المتأخر.

مواد البحث طرائقه: دراسة حشدية مقطعية أجريت في مشفى الأطفال الجامعي بدمشق خلال مدة 12 شهراً ابتداءً من شهر كانون الثاني عام 2013، وشملت حديثي الولادة كلّهم الذين راجعوا شعبة حديثي الولادة، وكانوا يعانون من ترفع حروري (<38º)

النتائج: من بين 5140 حديث ولادة راجعوا إسعاف حديثي الولادة خلال مدة الدراسة، عولج 2519 مريضاً من إنتان دم منهم 747 وليداً تظاهر بترفع حروري بنسبة 14.5% من مجمل المراجعين، اِسْتُبْعِدَ 126 وليداً، لوحظ إحصائياً انخفاض حساسية الترفع الحروري في سياق الإنتان، وخصوصاً عند الخدج التي بلغت الحساسية 14.21% مقابل 24.6% عند تمام الحمل، في حين ترتفع قيمة النوعية لتتجاوز ال 90% في كلتا المجموعتين (الخدج وتمام الحمل)، ومن جهة أخرى، فإن كلتا المجموعتين (الخدج – تمام الحمل) تمتلكان قيمة متوقعة إيجابية مرتفعة متقاربتين (74.4% - 72.6%) مقابل (42.3%-61.6%) من أجل القيمة المتوقعة السلبية. فيما يخص إنتان الدم الباكر فإنه يمتلك قيمة حساسية من أجل الترفع الحروري أقل من إنتان الدم المتأخر (20%-50%)، كما أن هناك تناسباً عكسياً بين حدوث الترفع الحروري وشدة إنتان الدمن وخصوصاً في إنتان الدم المتأخر، حيث كان هناك فارقٌ إحصائي مهم (p-value 0.00015 < 0.05).

الاستنتاج: الترفع الحروري عرض شائع نسبياً في شعبة حديثي الولادة بواقع 14.5%، وللترفع الحروري نوعية عالية لإنتان الدم عند الخدج وتمام الحمل مقارنة بقيمة الحساسية المنخفضة له. كما أن قيمة الحساسية ترتفع في إنتان الدم المتأخر مقارنة بالباكر، إن نسبة حدوث الترفع الحروري عند حديث الولادة يتناسب عكساً مع شدة إنتان الدم وخصوصاً الباكر.

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The Diagnostic Value of Hyperthermia In Neonatal Sepsis

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Abstract

Background and aim: In this study, we aimed to evaluate the prevalence of hyperthermia in the setting of a tertiary care neonatal intensive care unit (NICU) and to determine its relationship with early onset sepsis (EOS) and late onset sepsis (LOS) among newborns presenting with temperature symptoms.

Methods: In this cross-sectional study set in Pediatric Hospital Damascus Medical College, during 12 months (since Jan. 2013 till Dec. 2013); we included all newborns in the first 28 days after birth, hyperthermia (> 38 °C).

Results: Among 5140 newborns, 2519 newborns were treated for sepsis and 747(14.5% of all presented newborns) of them had hyperthermia, 126 of them were excluded. Statistically the fever had low sensitivity especially in preterm infants (14.21%) compared to (24.6%) in term infants, whereas the specificity was high and equal in both two groups (92.8%). On the other hand the Positive predictive values (PPV) were Similar (74.4% vs. 72.6%). Whereas the Negative predictive values (NPV) were (42.3% vs. 61.6%). Regarding the sepsis early onset sepsis (EOS). It had lower sensitivity than late onset sepsis (LOS) (20% vs. 50%), and the prevalence of the fever is inversely proportionate with the sepsis severity especially in EOS with p-value 0.00015 < 0.05.

Conclusion: hyperthermia was relatively a common symptom in our NICU with a prevalence of 14.5%. Fever had almost high identical specificity for both term and preterm infants compared to relatively low sensitivity value. With a higher sensitivity value in (LOS) than in (EOS). The incidence of fever is inversely proportionate with the sepsis severity especially in EOS.

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Introduction:

Neonatal Sepsis or Neonatal Septicemia or Sepsis Neonatorum is an infection in the blood that spreads throughout the body and occurs in a neonate. It is one of the commonest causes of Neonatal mortality and morbidity. It is estimated that 20% of all neonates develop sepsis [1], and it is responsible for 30-50% of total neonatal death in developing countries[2].Sepsis is an uncommon cause of fever; paradoxically, septic neonates more commonly present with hypothermia. However, sepsis is probably the most treatable life-threatening illness occurring in febrile newborn infants, especially those with temperature elevations exceeding 38° C to 39° C, who are more likely to have bacteremia, purulent meningitis, and pneumonia.[3]A thorough history and clinical exam are essential in the evaluation of febrile newborns. The most common etiologies of fever in neonates are: viral infection, dehydration, environmental hyperthermia (over heated, over wrapped, or in summer days), or a serious bacterial infection. Despite the fact that most fevers in infants arise from benign illness, we must be able to identify those infants at high risk for serious illness, to initiate empiric antibiotics in order to lessen the chances of serious adverse consequences, as these infants have fragile immune systems, and at high risk of sepsis (and septic shock) development.[4-7]The available criteria for identifying young febrile infants at low risk for sepsis are of limited reliability when applied to neonates.[5]The presenting symptoms are often subtle and may clinically be indistinguishable from those occurring in non-infectious conditions, including almost every sign of neonatal distress[6].The aim of this study was: (a) to evaluate the prevalence of fever in term and preterm newborns in the setting of a tertiary care neonatal intensive care unit (NICU) during the first 28 days of life;(b) to determine the fever as a risk factor for early onset sepsis (EOS) and Late onset sepsis (LOS) among newborns presenting with temperature symptoms.

Material and methods:

This was a cohort cross-sectional study carried out in the neonatal Emergency Room (NER) and tertiary-level neonatal intensive care unit (NICU) of the Pediatric Department, Damascus Medical College, during 12 months (since Jan. 2013 till Dec. 2013); our data are collected from neonates who attended NER and those who were admitted to the NICU, who had hyperthermia. These data include all laboratory results, perinatal data, and information on medication, and detailed results of all clinical examinations done in NER or at the admission (NICU). The clinical, perinatal and laboratory information were crosschecked to insure the accuracy. Inclusion criteria were: infant in the first 28 days after birth, hyperthermia (> 38 °C), and presence of medical letter, his mother or at least maternal grandmother.Temperature was measured rectally which is the most trustful method in our division, by using mercury thermometer the most available temperature measuring way in our hospital. The temperature was measured at the admission at NER or NICU. Hyperthermia was not regarded as being true if associated with well-known documented environmental causes. Depending on the onset of symptoms, the cohort was divided into two groups: a. within the first 72 hours of life (Early onset sepsis) [8-11], b. after 72 hours of age (Late onset sepsis) [8-9-10-11].The sepsis was defined as either a positive culture from blood cerebrospinal fluid (CSF), or urine; or as culture-negative clinical sepsis with three or more clinical signs: (i) respiratory symptoms (apnea, tachypnea >60/min, retractions, cyanosis, respiratory distress); (ii) cardiovascular symptoms (tachycardia >180/min or bradycardia <100/min, arterial hypotonia); (iii) neurological symptoms (lethargy, irritability, seizures); (iv) poor skin color or prolonged capillary refilling time >3 sec with either positive maternal risk factors (premature rupture of membranes >18 h, chorioamnionitis and fever during labor) or at least one abnormal laboratory marker.[12]And each group had been divided into two subgroups: term and preterm infants. The laboratory investigations included: white blood cells (WBCs) count and differential test, C - reactive protein (CRP), Blood culture, Blood gases, Lumbar Puncture (LP), and Urine analysis. In addition to Chest x- ray (CXR). Both clinical and laboratory data underwent a statistical analysis. The Statistical Package for Social Sciences (SPSS) version 16 (Chicago, IL, USA) was used for statistical analysis.

Results

Among 5140 newborns who presented to neonatal emergency department (during 12 months), 2519 newborns were treated for sepsis and 747(14.5% of all presented newborns) of them had hyperthermia, 126 of them were excluded (lack in information). A total of 621 newborns (366 [59%] males and 255 [41%] females) entered the study. They were divided into two groups, the full term group including 445 patients of which 283 (63.5%) patients were male and 165 (36.5%) female (male : female ratio 1.74:1) with a mean age of 9.67+2.7 days. The preterm group consisted of 176 premature infant, 94 (53.4%) patients were male and 82 (46.6%) were female (male: female ratio 1.15:1), with a mean age of 5.39±1.9 days, and a

median gestational age of 35w+2days. Table 1 shows the baseline characteristics of the 621neonates analyzed.

TABLE 1 Baseline characteristics of neonates

	Preterm infants	Full term
Total n (%)	176 (28.3%)	445 (71.7%)
Gender, Male n (%)	94 (53.4%)	366 (59%)
Gestational age median (week)	35w+2days	39w+1day
Birth weight, median (g)	1986	3753
PROM* (n)	53	96
Maternal fever (n)	36	42
Hospital birth n (%)	156 (88.6)	309(69.4)
5-min APGAR score	8 (6–10)	9 (6-10)
Temperature at admission (C°)	38.7 ± 0.5	38.9 ± 0.8
Required inotropic support, n (%)	115 (65.3	104 (23.3)
PH (mean)	7.12 (6.98- 7.34)	7.17 (6.91-7.41)
Seizures n (%)	5 (2.8)	42 (9.1)
Needed ventilation n (%)	17 (9.6)	37 (8.4)
Positive CRP** n (%)	85 (48.3)	179 (40.2)
Intrapartum antibiotic prophylaxis(complete course)	0	0

*Premature rupture of membranes

**C-Reactive Protein

A total of 176 preterms presented with hyperthermia (28.3%): 45 infants (25.6%) had no noticeable signs of infection either clinically or laboratory, they had environmental causes (table 2).

Table 2

Non-infectious cause	n (%)
Over-wrapped	23(51.1)
Over-heated room	12(26.7)
Non-infectious dehydration	8(17.8)
Direct exposure to Radiant	2(4.4)

Laboratory-proven sepsis (preterm infants)was diagnosed in 131/176(74.4%) with pneumonia (49.6%) being the most frequently etiology, in 89 preterms (67.9%) the sepsis diagnosis was made by laboratory data, where 42 preterms (32.1%) the diagnosis was made by clinical data, and the infected preterms are divided into two subgroups: EOS (93 /131) and LOS (38/131) .

In regards to full term infants, it was found that 323 of 445 infants (72.5%) had sepsis diagnosis, by means of clinical or laboratory data, in 36.3% and 63.7% respectively, also this group was divided into two subgroups: EOS (89/323) and LOS (134/323).(table 3).

Table 3

	Total	sepsis	fever	Fever+ sepsis+	Fever – sepsis +	Fever + sepsis -	Fever - sepsis -
Preterm	1443	967	176	131	791	45	580
Full term	2697	1552	445	323	989	122	1587

The statistical study of table (3) is illustrated in table (4).

table 4

Parameter	Preterm	Full term
Sensitivity	14.21%	24.62%
Specificity	92.8%	92.8%
Positive predictive value(PPV)	74.4%	72.6%
Negative predictive value (NPV)	42.3%	61.6%

Table (4).In regards to EOS and LOS, a total of 182 neonates presented with EOS, and 172 with LOS, and the prevalence of hyperthermia showed in table (5)

Table 5

	Total	Fever +	Fever –	Sensitivity
EOS	182	37	145	20%
LOS	172	86	86	50%

The prevalence of severe infections in febrile neonates presenting to the emergency department regarding EOS and LOS is detailed in tables (6) + (7) Table (7)

Table 6

	With fever	Without fever
Mild to moderate sepsis	87	115
Severe sepsis	36	116

Table 7

	With fever	Without fever
Mild to moderate sepsis	87	115
Severe sepsis	36	116

Chi-square statistic is 14.3753, the p-value is .00015 < 0.05

Discussion:

The clinical problem of interpreting fever in the newborn is that it might be the only clinical sign for neonatal bacterial infection[13]. Febrile and hypothermic newborns are evaluated by pediatricians or neonatologists and the decision to perform septic work-up and/or to start antibiotic therapy depends on the newborn's appearance, its perinatal history and the laboratory results. In our study we found that term newborns were described as being more likely to react to a bacterial infection with fever than preterm newborns did. The temperature symptoms were a common symptom in our NICU with a prevalence of 14.5%, Voora et al. reported on a prevalence of fever

of 1% in term newborns with 10% of these febrile newborns having sepsis.[14]

There was a remarkable difference regarding the sensitivity, where it was founded in preterm and full term newborns, 14.2% and 24.6% respectively, Even though they both have low sensitivity value, the term infants has higher sensitivity, it means that term newborns were more likely to react to a bacterial infection with fever than preterm newborns did. Also we found comparable results regarding (NPV) between the preterm and full term infants, 42.3% and 61.6% respectively. Unlike the two previous statistical markers, specificity and (PPV) did not have any remarkable difference between the two groups of infants, and both have high specificity.

On the other hand it has been found that the hyperthermia has a higher sensitivity in (LOS) than in (EOS) (50% vs. 20%) this is because the reaction to the acute phase proteins and the cytokines becomes more mature as the infants become older.

For table (7) which demonstrated the relationship between the fever and the sepsis severity we found that the chi-square statistic is 14.3753, the p-value is .00015, which means that the prevalence of the fever is inversely proportional with the sepsis severity especially in EOS.

Schwartz et al. described a decrease of the prevalence of severe infections in febrile neonates presenting to the emergency department with increasing postnatal age declining from 22% (3–7 days of life) to 12% (22–28 days of life)[7].

Nora H. et al [15] found that the sensitivity of fever for infection was inversely proportional with the gestational age , without any deference in specificity except for NPV which were higher in full term infants , table (8), the previous results were compatible with ours.

Table 8

Parameter	<28 weeks	28-37 weeks	Full term
Sensitivity	9	19	27
Specificity	94	96	96
(PPV)	25	19	33
(NPV)	82	96	95

Also they found that Temperature symptoms were rarely observed in EOS-negative newborns (8%) but despite low sensitivity, were highly specific for bacterial infection in preterm and term newborns.

In conclusion, hyperthermia symptom was relatively a common symptom in our NICU with a prevalence of 14.5%. Fever had almost high identical specificity and positive predictive value for both term and preterm infants compared to relatively low sensitivity value, with a higher sensitivity value in (LOS) than in (EOS). Despite its low sensitivity, temperature symptoms were highly specific for bacterial infection in preterm and term newborns, the prevalence of the fever is inversely proportional with the sepsis severity especially in EOS.

So we recommend to consider (hyperthermia) as an important and considerable infectious sign especially in term infants , after the first 72 hours of life or very ill newborn, and we must do the full infectious screening and scrutinize the history in front of any febrile neonate.

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