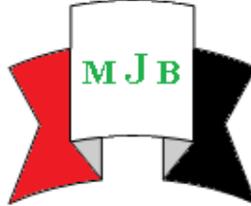


The Role of C-Reactive Protein in Diagnosis of Neonatal Sepsis

Sabah Hassan Alatwani

College of Medicine , Misan University

E-mail: dralatwani@yahoo.com



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Abstract

Across-sectional study was conducted in Amara city hospitals during a period from March 2013 till February 2014. The study sample includes 88 neonates (43 with clinical features of septicemia and 45 neonates who were normal). Blood culture and C-reactive protein tests were done for all neonates. In comparison with the result of blood culture, the C-reactive protein test was found that 42 out of 45 neonates as true negatives, the remaining 3 neonates showing sepsis and were considered as false negative. While 32 out of 43 neonates were considered as true positive. Finally the study showed that the sensitivity of C-reactive protein examination was 74.4%, specificity was 93% , positive predictive value was 91% and negative predictive value was 79%, so the C-reactive protein had important role in detection of the neonatal sepsis and consider an supportive tool to gold standard (blood culture) test for diagnosis of septicemia.

Key words: Blood culture , C-reactive protein, neonatal sepsis

دور سي بروتين التفاعلي في تشخيص الانتان الوليدي

الخلاصة

دراسة مقطعية اجريت في مستشفيات مدينة العمارة خلال المدة من اذار ٢٠١٣ ولغاية شباط ٢٠١٤. شملت الدراسة ٨٨ وليداً (٤٣ منهم لهم الميزات السريرية للانتان و٤٥ وليداً سويًا). اجري فحص زرع الدم الجرثومي وسي بروتين التفاعلي للجميع. اظهرت نتائج اختبار سي بروتين التفاعلي بالمقارنة مع الزرع الجرثومي للدم بأن ٤٢ وليداً من اصل ٤٥ وليداً ظهرت بأنها موجبه كاذبه (والحالات الثلاث الباقية اظهرت انتانا وعدت كاذبة سالبه. بينما اظهرت ٣٢ حالة من مجموع ٤٣ حالة موجبه للزرع الجرثومي الدموي وعدت انتانا باستخدام اختبار سي بروتين التفاعلي. واعتبرت موجبة حقيقية. وفي النهاية أظهر اختبار سي بروتين التفاعلي حساسية بلغت ٧٤.٤% وخصوصية ٩٣% والقيمة التخمينية الموجبة ٩١% والقيمة التخمينية السالبة ٦٩%. ولتلك الاسباب فإن اختبار (سي بروتين التفاعلي له دور هام في تحديد) اكتشاف) الانتان لدى حديثي الولادة ويعد اختبار ساند للزرع الجرثومي للدم (الذي يعد بدوره اختباراً مثالياً رئيساً لتشخيص الانتان).

Introduction

Neonatal Sepsis can be defined as any systemic bacterial infection confirmed by a positive blood culture in the first month of life .Up to 10% of infants have infections in the first

month of life, resulting in 30-50% of total neonatal deaths in developing countries (1). These neonatal deaths are attributed principally to infection, birth asphyxia and consequences of premature birth and low birth weight (2).

The diagnosis of neonatal sepsis on the basis of the clinical symptoms is not possible (3). Although isolation of the causative microorganisms by using blood culture has been the golden standard method for its diagnosis (4). The clinical manifestations of newborn infections vary and include subclinical infection, mild to severe manifestations of focal or systemic infection, and, rarely, congenital syndromes resulting from in utero infection(5).

C-reactive protein is an acute phase reactant synthesized by the liver which opsonizes invading pathogens. Levels of CRP increase within 6 hours of an inflammatory stimulus and may rise up to 1000-fold. Measurement of CRP provides a direct index of acute inflammation and, because the plasma half-life of CRP is 19 hours, levels fall promptly once the stimulus is removed (6). CRP levels in healthy full-term and preterm infants may range from 2 to 5 mg/L during the first few days of life. During the neonatal period, an established upper normal CRP level of 10 mg/L has been identified in many studies.(7)

Aim of the study

To determine the diagnostic performance of CRP as early diagnostic markers for the detection of neonatal sepsis in the intensive neonatal care unit in comparison to that of blood culture.

Patients & Methods

Across-sectional study was conducted in Amara hospitals (Al-Sader and Al-Zahrawy Hospitals), during the period

from march 2013 till February 2014, Including neonates who had been admitted to the neonatal intensive care unit in both hospitals.

The newborns whose have sepsis divided into early neonatal sepsis (from birth to 7days of life) and late neonatal sepsis (from 8 to 30 days of life). Data was collected using a special forum, constructed by the researcher and based on the standard criteria, including demographic information (age, sex, mode of delivery, type of feeding). The results of C-reactive protein and blood culture tests. The analysis of data was carried out using statistical packages for social science, version 16.0(SPSS-16.0). Data were presented in form of table of numbers and percentages. Chi-square test (χ^2 -test) was used for testing the significance of association between variables under study. Statistical significance was considered whenever the P-value was equal or less than 0.05.

Results

The study sample includes 88 neonates who were admitted to neonatal intensive care unit in Amara hospitals. Blood culture examination had yield sepsis in 43 neonates .The mean age of neonates was 11.5 ±7.3 day and the range was (birth-28)days . Forty five neonates were male from whom 51% were having sepsis, while the females represented 43 neonates (46%) were having sepsis, with no statistical significant association between sepsis and gender, as shown in table 1.

Table 1: Distribution of neonatal sepsis according to gender

Gender	Neonate						
	Sepsis		normal		Total		P value
	N	%	N	%	N	%	
Male	23	51	22	49	45	100	0.66

Female	20	46.5	23	53.5	43	100	
Total	43	48.8	45	51.2	88	100	

Regarding feeding pattern, the study showed that 53 neonates were on breast feeding from whom 21 (39.6%) were having sepsis while neonate on bottle

feeding was 35 from which 22 (62.8%) was sepsis, and it shows statistical significant association between sepsis and feeding pattern , as shown in table 2.

Table 2: Distribution of neonatal sepsis according to feeding pattern

Type of feeding	Neonate						P value
	sepsis		normal		Total		
	N	%	N	%	N	%	
Breast	21	39.6	32	60.4	53	100	0.03
Bottle	22	62.8	13	37.2	35	100	
Total	43	48.8	45	51.2	88	100	

About 71% of neonates who were delivered by C/S had sepsis while 33.9 % of neonate with normal vaginal

delivery had sepsis, with a significant association according to the mode of delivery as shown in table 3.

Table 3: Distribution of neonatal sepsis according to mode of delivery

Type of delivery	Neonate						P value
	sepsis		normal		Total		
	N	%	N	%	N	%	
NVD	18	33.9	35	66.1	53	100	0.005
C/S	25	71	10	29	35	100	
Total	43	48.8	45	51.2	88	100	

NVD: normal vaginal delivery, C/S: cesarean section

Regarding onset of sepsis, 65.1% of sepsis occur in early life of neonate)

while the remaining sepsis occur in late life of neonate, as showing in table 4.

Table 4: Distribution of neonatal sepsis according to onset

Onset of sepsis	N	%
Early	28	65.1
Late	15	34.9
Total	43	100

Investigation by C-Reactive Protein for those neonates, we found that 35(39.7%) of neonates had sepsis. In comparison with the results of blood culture, the CRP results were found to be within normal range in 42 out of 45 neonates with negative results of blood culture and were considered as true negatives, the remaining

3 neonates were considered as false negative. Thirty two out of 43 neonates with positive blood culture were found to have positive results and were considered as true positive. The remaining 11 neonates were considered as false positive. As shown in table 5.

Table 5: Comparison of blood culture results with C. Reactive protein results.

RESULT OF BLOOD CULTURE	C. REACTIVE PROTIEIN		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE BLOOD CULTURE (SEPSIS)	32	11	43
NEGATIVE BLOOD CULTURE (NORMAL)	3	42	45
TOTAL	35	53	88

Finally our study showed that the sensitivity of CRP examination was 74.4%, specificity was 93% , positive predictive value was 91% and negative predictive value was 79%.

Discussion

Diagnosis of neonatal sepsis is difficult to be established and remains a challenge for neonatal health care providers .The gold standard for detecting bacterial sepsis is blood culture. However, as pathogens in blood cultures are only detected in approximately 25% of patients, the

sensitivity of neonate's blood culture is expected to be low (8).

In our study, the prevalence of neonatal sepsis was 48.7%. In male was higher than in female (51%, 46% respectively), there is no statistical significance according to the gender of neonates. This result is similar to the result of study conducted in Babylon-Iraq 2013(9).

Regarding the feeding pattern, this study shows that the prevalence of sepsis among bottle- fed neonates was higher than that in neonate on breast feeding (62.8% VS. 39.6%) with a statistical significance

difference. This result is in agreement with result of study conducted in Pakistan (10).

In the same manner the study found that the prevalence of neonatal sepsis among neonates who were delivered by C/S was higher (71%) than those delivered by NVD 33.9 % with a statistical significant difference and it is similar to result of study carried out in Iraq and Pakistan (9, 10).

Regarding onset of sepsis, 65.1% of sepsis occur in early life of neonate while the remaining sepsis occur in late life of neonates .The results indicated that the prevalence of early onset of sepsis (EOS) were common compared with late onset sepsis (LOS), which is in consistence with the reports from other developing countries e.g. in Iran (77.5% vs. 22.5%) (12) and Bangladesh (70.7% vs. 29.3%)(11). However, an increased LOS compared with EOS has been reported in Saudi Arabia (39% vs. 61%) (11) and Libya (31% vs. 69%) (12). The possible explanation for low frequency of LOS in this study might be attributed to the early discharge policy in the Iraqi hospitals since the newly delivered mother is discharged from hospital within 3 hrs. for normal vaginal delivery and after 24 hr. for cesarean section.

Lastly, in comparison with blood culture our study showed that the sensitivity, specificity, positive predictive value and negative predictive value of CRP examination was 74.4%, 93%, 91% and 79% respectively, which was in agreement with other study result that have been done in Egypt (8).

Conclusions

C-Reactive Protein has an important role in detection of the neonatal sepsis and is considered a supportive tool to gold slandered [blood culture] test for diagnosis of septicemia. Sensitivity, specificity, positive predictive value and negative predictive value of CRP test was 74.4%, 93%, 91% and 79% respectively.

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