Some maternal and neonatal factors affecting early and late neonatal sepsis

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خلفية الدراسة: تسمم الدم يقسم الى قسمين هما النوع المبكر والنوع المتأخر.تسمم الدم المبكر لدى الاطفال حديثي الولادة يحدث في اول سبعة ايام ويكون بنسبة 85% في ال24 ساعة الاولى من الحياة.تسمم الدم المتأخر لدى الاطفال حديثي الولادة يحدث ما بعد الاسبوع الاول من الولادة ويكتسب عادة من المحيط الخارجي للطفل.

الغرض من الدراسة: الهدف من الدراسة هو لتوضيح بعض العوامل المتعلقة بالام والطفل على تسمم الدم المبكر والمتأخر مثل تمزق الغشاء الجنيني المبكر والولادة لدى القابلة والولادة المبكرة للطفل مع توضيح التغيرات للفحوصات الدموية مثل تأثير المضادات الحيوية على نتائج زرع الدم.

ألطرق قمنا بتحضير مجموعة اسئلة عن اسم المريض وعمره بالايام وجنسه مع توضيح تاريخ الحمل والولادة مع اخذ عينات دم لصورة الدم الكاملة وزرع الدم لتوضيح تاثير تسمم الدم على الفحوصات الدموية وتعيين المسبب الجرثومي عن طريق زرع الدم.

ألنتائج وجدنا ان الطفل حديث الولادة اكثر قابلية لتسمم الدم من النوع المبكر بالمقارنة مع النوع المتاخر كما وجدنا ان زرع الدم يتأثر بصورة كبيرة عند استخدام المضادات الحيوية قبل الزرع. ان حالة الوفيات هي الاكثر شيوعا في حالات تسمم الدم الولادي المبكر بالمقارنة مع النوع المتاخر.

ألاستنتاج وجدنا ان الطفل الخديج هو اكثر قابلية للإصابة بتسمم الدم الجرثومي من الذي مكتمل فترة الحمل مع ان تمزق الغشاء الجنيني يوثر اكثر على تسمم الدم من النوع المبكر بالمقارنة مع النوع المتأخر. كما وجد ان البروتين التفاعلي نوع (ج) والصفيحات الدموية خصوصا نقص الصفيحات الدموية تؤثر بصورة كبيرة على تشخيص تسمم الدم.

ألتوصيات: يوصي البحث بالعناية خلال الحمل خصوصا في الاشهر الثلاثة الاخيرة للحمل مع استخدام المضادات الحيوية بصورة وقائيه في حالات تمزق الغشاء الجنيني المبكر ومحاولة تجنب الولادة للطفل بصورة مبكرة لان الطفل ذو الولادة المبكرة اكثر قابلية للتسمم الجرثومي. تجنب استخدام المضادات الحيوية قبل زرع الدم لانه يوثر سلبا على نتائج زرع الدم.

Abstract

Background:

Neonatal sepsis categorized as early and late onset. Early neonatal sepsis (ENS) in the first 7 days of life with 85% occurs in the first 24 hours of life. Late neonatal sepsis (LNS)occurs after the first week of life and is acquired from care giving environment.

Aims of study:

To explain the effect of some maternal and neonatal factors on early and late neonatal sepsis, like premature rupture of membranes, midwife interference and prematurity. With change in blood investigations, like effect of antibiotics on the results of blood cultures.

Methods:

We prepared a questionnaire about the name ,age in days, gender with perinatal and maternal history and take blood samples for CBC and differential, blood culture, CRP and ESR to explain the effect of neonatal sepsis on the blood investigation results and identify the specific pathogen causing neonatal sepsis by blood culture.

Results:

We found that the neonate is more susceptible to ENS in comparison to LNS. Also we found that the blood culture result highly affecting by antibiotics used before culture. The mortality rate is more in ENS in comparison to late type.

There was no significant difference in gender, maternal fever and antenatal care, between ENS and LNS groups. Prematurity was higher in ENS group compared to LNS group (44.7%, vs. 29%) respectively; and the difference was significant (p = 0.042). Mode of delivery showed no effect in ENS group (NVD = C/S = 50%); while it seems to be more effective in LNS group as (74.2% vs 25.8%) of patients are C/S, (p = 0.003).Only (13.2%) of ENS subjects were home

delivery , while (25.8%) of LNS subjects were home delivery, (p = 0.048). Midwife interference was more effective in LNS subjects than ENS subjects, (35.5%, vs. 18.4%) respectively, (p = 0.019).Premature rupture of membrane was significantly more frequent in ENS subjects than LNS subjects (31.6% vs. 16.1%) respectively, (p = 0.028).Death was more frequent in ENS subjects than LNS subjects; (18.4%, vs. 3.2%) respectively .

Conclusion and Recommendation:

We found that the premature neonate more susceptible for neonatal sepsis than full term with premature rapture of membrane more frequently affecting ENS in comparison to late type. we found also that the C-reactive protien and platelets count had high sensitivity to the diagnosis of neonatal sepsis.We recommend antenatal care especially in the third trimester and use of antibiotic prophylaxis if there is a history of leaking liquor and avoid prematurity because premature neonates are more prone to early neonatal sepsis. Antibiotics should be avoided before blood culture aspiration to avoid false negative results.

Introduction

Neonatal sepsis may be categorized as early or late onset. Eighty-five percent of newborns with early-onset infection present within the first 24 hours, 5% present at 24-48 hours, and a smaller percentage of patients present between 48 hours and 6 days of life [1]. Onset is most rapid in premature neonates. Early-onset sepsis syndrome is associated with acquisition of microorganisms from the mother [2]. Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize in the mother's genitourinary tract, with acquisition of the microbe by passage through a colonized birth canal at delivery[3]. The microorganisms most commonly associated with early-onset infection include group B Streptococcus (GBS), Escherichia coli and Listeria monocytogenes [4].

Late-onset sepsis syndrome occurs at 7-90 days of life and is acquired from the caregiving environment. Organisms that have been implicated in causing late-onset sepsis syndrome include coagulase-negative staphylococci, Staphylococcus aureus, E. coli, Klebsiella, Pseudomonas, Enterobacter, Candida, GBS, Serratia, Acinetobacter, and anaerobes[4]. The infant's skin, respiratory tract, conjunctivae, gastrointestinal tract, and umbilicus may become colonized from the environment, leading to the possibility of late-onset sepsis from invasive microorganisms. Vectors for such colonization may include vascular or urinary catheters, other indwelling lines, or contact from caregivers with bacterial colonization [1].

Pneumonia is more common in early-onset sepsis, whereas meningitis and bacteremia are more common in late-onset sepsis. Premature and ill infants have an increased susceptibility to sepsis and subtle nonspecific initial presentations; therefore, they require much vigilance so that sepsis can be identified and treated effectively [5].

The fetal immune system develops in a sterile and protected environment, and therefore lacks antigenic experience. It must also be modulated in order to co-exist with the mother's immune system. Soon after birth, the newborn is exposed to the "hostile world" of bacteria, viruses, fungi, and parasites, and must immediately defend itself. [6].

The T cell-mediated immunity: T cell-mediated immunity is not transferred from mother to fetus, in contrast to humoral immunity. Thus, young infants rely exclusively on their own T cells plus elements of the innate immune system to fight infections caused by intracellular pathogens, respond to vaccination, and reject foreign tissue. Viral infections: Although it is reasonable to speculate that infants might be more susceptible than adults to viral infections, most infants overcome viral infections with little difficulty. Nevertheless,

certain specific impairments can be demonstrated. The cytotoxic CD8+ T cell response to CMV is similar in neonates and adults, although the CD4+ T cell response is reduced [7, 8]. Both CD8+ and CD4+ T cells responses to HIV infection appear lower than in adults, probably explaining the rapid progression of the disease in neonates in the absence of anti-retroviral therapy [9, 10]. The neonatal response to HSV infection is characterized by delayed INFgamma production compared to adult cells, possibly accounting for the occasional fulminant infection [11]. In contrast, neonatal NK cells produce the same amount of INFgamma when exposed to HSV as adult NK cells [12].

Ptients & methods

Study design:

This prospective study has been carried out in the neonatal care unit at the Children Welfare teaching Hospital and Baghdad Teaching Hospital / medical city /Baghdad /Iraq ;during the time period from 1st of August 2007 through 1st or 31 March 2008.

Subjects:

A total number of 138 sample subject (neonate) were randomly selected(hospitalized) to full fill the criteria of the study, being neonate (less than 28 days age) with clinical features suggestive of sepsis such as feeding intolerance, apnea, cyanotic spells, respiratory distress , perinatal history of infection , Moro reflex and all other feature suggest the neonatal sepsis [25]. Later on, neonates were divided according to age into two groups:

1- Early neonatal sepsis group (ENS) of age range from(0 to 7 days), with a mean age of 3.3 days and total number of 76 (55.1%) of total.
2- Late Neonatal Sepsis group (LNS) of age range from 8 to 28 days, with a mean age of 17 days and total number of 62 (44.9%) of total.

Data collection:

Information were recorded by prepared a special questionnaire which included subject code, name, age in days, gender, gestational age (preterm or full term)date and cause of admission, perinatal history, maternal history of fever, history of prolonged rupture of membrane, whether antibiotics used or not before investigations and other information regarding results of blood tests. Data analysis was computer aided. An expert statistical advice was sought for. Statistical analyses were done using SPSS version 13 computer software (Statistical Package for Social Sciences).

Results

There was no significant difference in gender, maternal fever and antenatal care, between ENS and LNS groups, (p value > 0.05) this is not significant .Prematurity was higher in ENS group compared to LNS group (44.7%, vs. 29%) respectively; and the difference was significant (p = 0.042).

Mode of delivery showed no effect in ENS group (NVD = C/S = 50%); while it seems to be more effective in LNS group as (74.2% vs 25.8%) of patients are C/S, (p = 0.003).Only (13.2%) of ENS subjects were home delivery , while (25.8%) of LNS subjects were home delivery, (p = 0.048). Midwife interference was more effective in LNS subjects than ENS subjects, (35.5%, vs. 18.4%) respectively, (p = 0.019).Premature rupture of membrane was significantly more frequent in ENS subjects than LNS subjects (31.6% vs. 16.1%) respectively, (p = 0.028).Death was more frequent in ENS subjects than LNS subjects; (18.4%, vs. 3.2%) respectively, (p = 0.004) . There was a significant difference in the type of causative organism between the two groups, the most common organism in ENS subjects was the Enterobacter (28.9%) while the least common in the same group was the E-coli species. In comparison, the most common organism in the LNS group was the Staph epidermis species (19.4%), (p = 0.007) .(figure 1.1).

Table1.1: Frequency distribution of possible risk factors and the outcome of ENS & LNS of gender, prematurity, mode of delivery, place of delivery, midwife interference, premature rupture of membrane, maternal fever, antenatal care, feeding history and outcome in early neonatal sepsis and late neonatal sepsis groups.

Characteristics	Values	Early neonatal Sepsis Number (percent)	Late neonatal Sepsis Number (percent)	P Value
Gender	Male	46 (60.5%)	34 (54.8%)	0.308
	Female	30 (39.5%)	28 (45.2%)	
Prematurity	Premature	34 (44.7%)	18 (29.0%)	0.042
	Mature	42 (55.3%)	44 (71.0%)	
Mode of delivery	NVD	38 (50.0%)	46 (74.2%)	0.003
	C/S	38 (50.0%)	16 (25.8%)	
Place of delivery	Hospital	66 (86.8%)	46 (74.2%)	0.048
	Home	10 (13.2%)	16 (25.8%)	
Midwife interference	Yes	14 (18.4%)	22 (35.5%)	0.019
	No	62 (81.6%)	40 (64.5%)	
Premature rupture of membrane	Yes	24 (31.6%)	10 (16.1%)	0.028
	No	52 (68.4%)	52 (83.9%)	
Maternal fever	Yes	18 (23.7%)	16 (25.8%)	0.463
	No	58 (76.3%)	46 (74.2%)	
Antenatal care	Good	18 (23.7%)	8 (12.9%)	0.192
	Poor	32 (42.1%)	34 (54.8%)	
	None	26 (34.2%)	20 (32.3%)	
Feeding history	Breast	36 (47.4%)	24 (38.7%)	0.005
	Bottle	14 (18.4%)	12 (19.4%)	
	Mixed	10 (13.2%)	22 (35.5%)	
	Not yet	16 (21.1%)	4 (6.5%)	
	Discharged well	62 (81.6%)	60 (96.8%)	

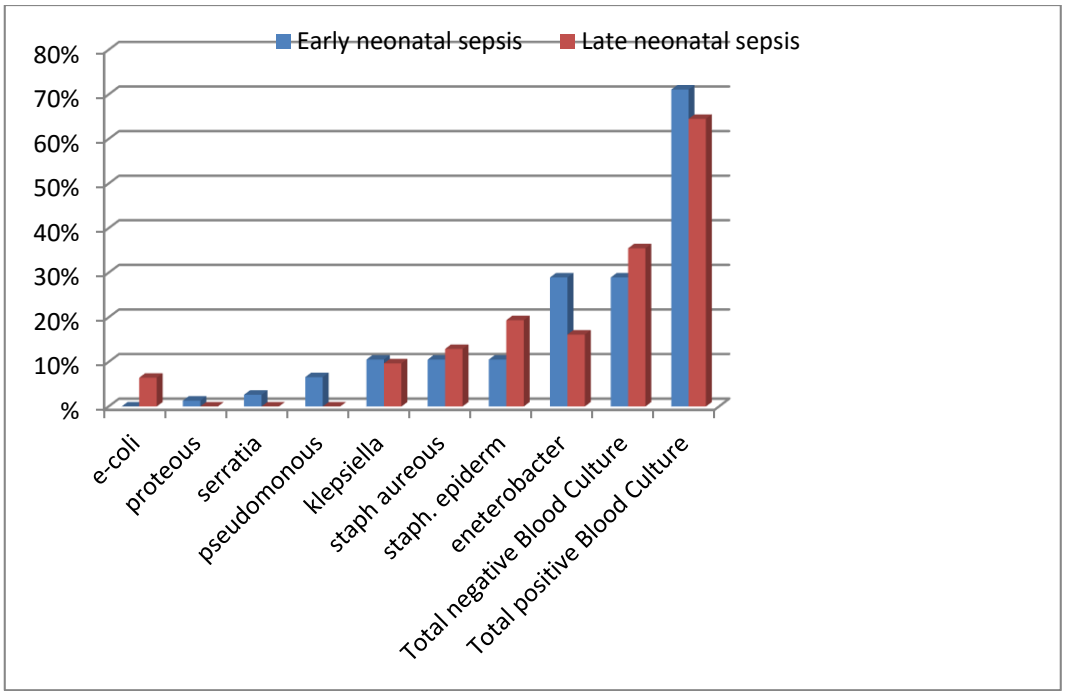

Figure 1.1: Frequency distribution of type of organisms in early and late neonatal sepsis subjects.

Discussion

During the six months period of study, 138 newborns admitted with suspected sepsis. Early neonatal sepsis group of age range from 0 to 7 days, with a mean age of 3.3 days and total number of 76; (55.1% of total) and Late Neonatal Sepsis group of age range from 8 to 30 days, with a mean age of 17 days and total number of 62; (44.9% of total).

Prematurity is higher in early neonatal sepsis group compared to late neonatal sepsis group (44.7% vs. 29%) in this study, while Stoll BJ Hansen study 2002 [13] had (23% vs. 22%), this is due to premature infant documented immune dysfunction, also this due to vertical transmission from maternal genital tract. Premature infant often require prolonged intravenous access, endotrachial intubation or other invasion procedure make him more susceptible to infection [14]

In this study,(71.1%) of early neonatal sepsis group and(64.5%) of late neonatal sepsis group were positive blood culture. While Najla IM (2004) has documented (75%) blood culture positive cases [15].

Anwar et al (2000) has documented (42%) blood culture positive of neonatal sepsis [16]. Also Nahlah Al Gabban et al, (1997) has reported (42.8%) blood culture positive cases of neonatal sepsis[17]. While Aurong Zeb et al, (2003) has reported (55%) culture positive of NS [18]. This variation in blood culture positivity may depend on the criteria of studied groups, volume of sample, sampling site and antibiotic used prior to the sample.

In this study ,(31.6%) mothers of neonates had premature rapture of membrane in early neonatal sepsis while (16.1%) in the late neonatal sepsis. This result differs from Goldenberg RL. Et al study who reported (50.6%) for early neonatal sepsis & (25.85%) for the late neonatal sepsis [19]. Brodie SB, et al report (42.3%) for early neonatal sepsis and (18.8%), for the late neonatal sepsis [20].This difference is explained by direct exposure of neonate to vertical transmission of microorganism from genital tract during the

labour process especially for early neonatal sepsis.

The attack rate of neonatal infection increase in presence of maternal fever in which (23.7%) in early neonatal sepsis & (25.85%) in late neonatal sepsis.

Goldenberg (2000) showed (88.2%) association with maternal fever in ENS and (10.4%) in late neonatal sepsis [21]. while Brodie [20] explains that only (44.1%) in early neonatal sepsis and (19.7%) in the late neonatal sepsis. This difference depends on the type of microorganism, duration of fever, gestational age and duration of membrane rapture.

Antenatal care also had affect on the health of the neonates in which there is (23.7%) of those with irregular antenatal care and (34.25%) of those with no antenatal care in this study.Gensen HB, et al explained that there is (40.7%) association with poor antenatal care and (66.4%) of those with no antenatal care [22]. This depends on the education of the mother and community and regularity of antenatal care and the methods applicable for good antenatal care.

In this study the mortality rate reported (18.4%) for early neonatal sepsis, and (3.2%) for late neonatal sepsis. Adams-Chapman I, et al (2002) reported (10%) mortality rate of neonatal sepsis and this is depend on the hygiene and sterilization technique for each centre and availability of facilities of early diagnosis and treatment of sepsis [23].

Although it is not specific for neonatal sepsis, CRP has high sensitivity for neonatal sepsis (24).

In this study, CRP (C-reactive protein) are positive in (63.2%)of neonates in early neonatal sepsis and (61.3%) in late neonatal sepsis. These results differ from that of Tariq Ghafoor, et al. (2005), who observed (35.5%) positive CRP for proven sepsis by blood culture (24). Shabbir et al, (1994), found positive CRP in (74%)..The discrepancy in the result of CRP may be due to different methods of estimation and/or variation in criteria of positivity of the test.

Platelet count has a moderate sensitivity (p=0.01). For those with early neonatal sepsis in comparison to the results of WBC and ANC (p=0.152) and (0.429) respectively. These findings differ from Tariq Ghafoor et al,(2005), who reported ANC(absolute neutrophil count) , platelet and WBC with early neonatal sepsis of (71.4%),(64.3%) and (39.3%) respectively for proven sepsis [23].This depend on severity of infection, age of neonate and criteria of studied group as the thrombocytopenia is generally observed in the neonatal sepsis and they were normal when the neonatal sepsis has been diagnosed.In this study, ESR had lowest sensitivity (p=0.121) that makes the ESR poor predictor of sepsis..

Conclusions:

1. Premature neonates were more susceptible for neonatal sepsis than the full term babies.
2. Antibiotics used before blood culture aspirate highly affect the culture results.
3. Premature rapture of membrane more frequently affecting the early neonatal sepsis in comparison to the late neonatal sepsis.
4. We found that the CRP (C–reactive protein) and platelet count especially thrombocytopenia had high sensitivity to the diagnosis of neonatal sepsis. Also they guide us not to miss any case of sepsis if blood culture was falsely negative.

Recommendations:

1- We recommend good antenatal care especially in the third trimester and education to the mother if there is to use antibiotics prophylaxis if there is leaking liquor more than 18 before the onset of labour.

2- Antibiotics should be avoided as soon as possible before blood culture aspirate to avoid false negative blood culture.

3 –Prevention of premature delivery because premature neonate are more prone to early neonatal sepsis.

4_Further studies are required to show the benefit of other investigations like; C-reactive protein and platelets count in case of false negative blood culture or to follow up patients with neonatal sepsis after proven blood culture.

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