Neonatal bacterial sepsis: risk factors, clinical features And short term outcome

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Summary:

Background: Neonatal infections are afrequent and important causes of neonatal morbidity and mortality especially in the developing countries.

Objective: The aim of the study is to determine the clinical picture, risk factors associated with neonatal sepsis and to estimate short term outcome from neonatal sepsis and its relation to birth weight, gestational age, onset of sepsis and type of bacteria.

Patients and Methods: A prospective study was conducted on 80 neonates presented with sepsis who had been admitted to intensive care unit in Children Welfare Teaching hospitals in Baghdad over six months period between (15th of January 2008 to 15th of June 2008).A thorough history and physical examination were carried out, and samples of blood were taken for blood culture and sensitivity.

Results: Eighty neonates were studied, sepsis was confirmed by clinical and laboratory measures. Fifty five (68.7%) neonates were males and 25(31.2%) were females. Fifty four (67.5%) were preterm and 26 (32.5%) were full term. Fifty nine (73.25%) neonates were still alive during period of hospitalization and discharged home, while 21 (26.25%) neonates died. Early onset sepsis was detected in 26 (32.5%) neonates while late onset sepsis was detected in 54 (67.5%) neonates, However, the death rate was higher in early onset sepsis (57.7%) compared to late onset sepsis (18.5%). The death rate was higher in neonates with maternal history of prolonged rupture of membrane >18 hours (54.8%), also it was increased when there was fever or infection during pregnancy.

Conclusions: The study showed that the most common neonatal risk factors that increase the incidence of mortality were early neonatal sepsis, home delivery, prolonged rupture of membrane more than 18 hours and maternal fever or infection, and the most common features were lethargy, absence or weak moro reflex and reluctant to feed, The most common bacteria isolated from blood cultures was *E. coli.*

Keywords: Neonatal sepsis, risk factors, clinical features and mortality

Introduction

Infections are a frequent and important cause of neonatal morbidity and mortality (1).It was found that neonatal deaths account for a third of global child mortality and that infections are a major cause of neonatal mortality(2). The incidence of sepsis varies from one center to another, but it ranges from 1-4 in 1000 live birth in most centers (3), but the incidence of bacterial septicemia in developing countries reaches 10-50 per 1000 live births (4). The mortality of neonatal septicemia varies between 13-45%, Infection accounts for 10-20% of infant mortality (5). Moreover most babies who die from sepsis die within the first 14 days of life, this may be due to increasing number of premature or LBW babies (6). Good outcome depend on early diagnosis, and effective strategies to prevent nosocomial sepsis must be included like judicious antibiotics initiation, programs to increase emphasis on hand-washing compliance; cautious insertion and handling of central venous catheters; minimizing central venous catheter duration (7,8). Maternal factors increase risk of infection 3-4 fold, while prematurity and LBW increase the risk 20-fold (6). Most centers

reports group B streptococci (GBS) as the most common, followed by gram negative enteric organisms especially *E.coli*. other pathogens include *Listeria monocytogenes, Staphylococcus,* other *Streptococci,* anaerobes and *Haemophilus influenza* (2). The most common organisms causing the early onset infection are GBS, *E.coli*, other Streptococci, and *H. influenza* (6). While the organisms causing late onset infection are GBS, *Listeria monocytogenes* and *Salmonella* (1). The initial diagnosis of sepsis is usually by a clinical suspicion because it is imperative to begin treatment before the results of cultures are available depending on the following: - temperature irregularity, change in the behavior, skin changes, feeding or cardiopulmonary or metabolic problems (2). The sign & symptoms of sepsis according to their frequency are as follow: -
The reluctance to feed, lethargy, fever, Jaundice, tachypnea, chest retraction, hypothermia, septic umbilicus, pallor, diarrhea, seizure, cyanosis & abdominal distension (9). No single laboratory test has been found to have enough specificity and sensitivity and therefore laboratory confirmation must be used in conjunction with risk factors and clinical signs (6). These tests include culture of blood, urine and cerebrospinal fluid, leukocyte

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profile, platelet count, acute phase reactants (ESR, C-reactive protein), latex agglutination tests, or counter immune electrophoreses, and polymerase chain reaction (PCR) (1,10,11,12). Treatment is most often begun before a definite causative agent is identified. It consists of a penicillin (usually ampicillin) plus an aminoglycoside such as gentamycin (2,13,14). And therapy for most of blood stream infections should be continued for a total of 7 -10 days or for at least 5-7 days after a clinical response had occurred (1). Mortality from neonatal sepsis ranges between 10 and 40% (mean 20%) and has not fallen for many years, serious morbidity can also result and long term sequelae like deafness, developmental delay and seizure disorders are seen in 40-80% of survivors following neonatal meningitis (6,15).

Patients and Methods:
This study was done prospectively on 80 neonates with features of sepsis and had positive blood culture, admitted to neonatal department of Children Welfare Teaching hospital, during the period between 15th of January 2008 to 15th of June 2008. A special questionnaire was designed for the purpose of the study (after excluding neonates with obvious congenital anomalies and those with prior antibiotic therapy). The following information were taken:- name, age, sex, gestational age, present body weight ،place of delivery (Hospital or home) ,mode of delivery(NVD or C/S) ,history of maternal fever or infection during pregnancy, premature rupture of membrane ،congenital anomalies ،clinical pictures (Reluctant to feed   ،absence or weak moro reflex ، jaundice ،convulsion ، sclerema lethargy , respiratory   distress bulging fontanelle, bleeding tendency, temperature and presence of diarrhea), investigations (Blood culture and sensitivity) and outcome of each neonate was recorded on discharge from neonatal nursery unit, and neonates with sepsis were grouped into those who survived and those who died. A sample of at least 2ml of blood per set was taken from peripheral vein from disinfected skin using iodine solution that left to dry and then wipped off with (70%) alcohol, samples were taken before antibiotic administration, and cultured aerobically and anaerobically.
Statistical analysis: Statistical analysis was done using Fisher's exact and Chi-square test for comparison of proportion, P-value of less than 0.05 was considered as statistically significant. P-value < 0.01 as highly significant and P-value <0.001 as extremely significant.

Results:
Among eighty neonates with signs and symptoms of septicemia were included in the study. Regarding the clinical presentation in neonatal sepsis ,it was found that there was statistical significance of lethargy , absence or weak moro reflex and jaundice (P< 0.05), the   presence   of   diarrhea   was   highly

significant(P<0.01),   and   the   occurrence   of convulsion, sclerema and bleeding tendency were associated with extremely statistical significance (P<0.001). At the same time we found that reluctance to feed , respiratory problems, bulging fontanelle and change of body temperature were not significant statistically. (*Table-1*)
Fifty nine (73.75%) neonates were discharged home after improvement and twenty one (26.25%) died during the period of hospitalization. The *outcome of neonates with sepsis in relation to different neonatal variables* are illustrated in *(Table-2)*. The presence of fever or infection during pregnancy was found to be extremely significant (P<0.001). Death of neonate with early onset sepsis was more than in neonate with late onset sepsis (52.4%) versus(47.6%)(P<0.05), also the delivery at home and early rupture of membrane were associated with increment in death rate(P<0.05). This table also reveals that mode of delivery, gestational age, birth weight and sex of the neonate were not significant statistically.
It was found that *E. coli* was the most common bacteria isolated in 19(23.7%), followed by *Klebsiella pneumoniae*16(20%), and *Enterobacter 15* (18.8%). Other bacteria were *Staph aureus* in 13(16.3%), group B *streptococc*i 9(11.2%), *Staphylococcus   aureus*   and   *Pseudomonas aeruginosa 5(6.2%) , Salmonella 2(2.5%) and Staph albus* in 1(1.3%).*(Table-3)*

Table (1) :- Outcome of neonates with sepsis in relation to different neonatal variables

Total number of patients		Outcome		P-value
		Alive No. (59) (73.75%)	Died No. (21) (26.25%)	
Age (days)	<7 days	15(42.3%)	11(57.7%)	< 0.05
	7-28 days	44(81.5%)	10(18.5%)	
Sex	Male 55(68.75%)	39(71%)	16(29%)	> 0.05
	Female 25(31.25%)	20(80%)	5(20%)	
Site of delivery	Hospital	52(78.8%)	14(21.2%)	< 0.05
	Home	7(50%)	7(50%)	
Mode of delivery	NVD	41(78.8%)	11((21.2%)	> 0.05
	C/S	18(64.3%)	10(35.7%)	
Body weight	<1.5 kg	6(60%)	4(40%)	> 0.05
	1.5-2.49 kg	25((69.5%)	11(30.5%)	
	>2.5 kg	28(82.4%)	6(17.6%)	
Gestational age	<37 weeks	41(75.93%)	13(24.07%)	> 0.05
	>37 weeks	18(69.3%)	8(30.7%)	
Rupture of membrane > 18 h	Yes	14(45.2%)	17(54.8%)	< 0.05
	No	45(91.8%)	4(8.2%)	
Fever or infection During pregnancy	Yes	25(58.1%)	18(41.9%)	< 0.0001
	No	34(91.9%)	3(8.1%)	

Table (2): Clinical features and outcome of neonatal sepsis

Clinical features		Outcome		P-value
		Alive (59)	Died (21)	
Reluctance to feed	+	32	16	>0.05
	-	27	5	
lethargy	+	43	17	<0.05
	-	16	4	
Absent or weak moro reflex	+	38	19	<0.05
	-	21	2	
Respiratory distress	+	28	11	>0.05
	-	31	10	
Jaundice	+	30	17	<0.05
	-	29	4	
Bulging fontanelle	+	5	2	>0.05
	-	54	19	
Convulsion	+	11	17	<0.001
	-	48	4	
Bleeding tendency	+	9	18	<0.001
	-	50	3	
Sclerema	+	8	14	<0.001
	-	51	7	
Temperature	Hyperthermia	7	3	>0.05
	Normothermia	39	11	
	Hypothermia	13	7	
Diarrhea	+	7	6	<0.01
	-	52	23	

Table (3): The relationship between the causative organisms and the outcome of patients

Bacteria	Total number of patients	Alive 59 (%)	Died 21 (%)
E. coli	19(23.7)	13(68.4)	6(31.6)
Klebsiella pneumoniae.	16(20)	5(31.3)	11(68.7)
Enterobacter species	15(18.8)	11(73.3)	4(26.7)
Staphylococcus aureus	13(16.3)	4(30.8)	9(69.2)
Group B-Streptococcus.	9(11.2)	8(88.9)	1(11.1)
Pseudomonas aeruginosa	5(6.2)	1(20)	4(80)
Salmonella species	2(2.5)	2(100)	0(0.0)
Staphylococcus albus	1(1.3)	1(100)	0(0.0)

Discussion:
In this study, the high mortality rate reported (26.25%) , was the same or approximate to the result of Stoll B. in USA (28%)[(16).Dawodu A et al, in Al-Dammam (Saudi Arabia)(28%) (17),and by Koutouby A et al, in UAE (26%) (18),while higher mortality were reported by Duha Sabeeh Jumah et al in al Basrah(44.16%) (19).
These differences in mortality rate in neonatal sepsis among different countries may be explained by many factors e.g. socioeconomic, geographical and racial factors, use of ventilators, different strains microorganisms and use of different antibiotics. The

percentage of mortality in early onset sepsis was (52.4%) and it was slightly higher than in late onset sepsis (47.6%), a higher early onset mortality rate found in other studies (19,20,21). While other studies showed that the mortality rate is higher in late onset sepsis (17,22).The early onset sepsis is mainly related to maternal genito-urinary tract infection while late onset sepsis is mainly related to longer hospital stays with nosocomial infections and the use of invasive devices(13, 14). There was no statistically significant difference in the frequency of death between both sexes, a similar result was obtained by Koutouby A in Dubai (18),Rodriguez M et al, in Mexico (20),although other studies reported a higher percent of death among males with sepsis[(18,23),suggesting the possibility of sex linked factors in host susceptibility.
In this study there was significant association between home delivery and increment in neonatal death (50%) in comparison with hospital delivery, a similar result was extracted by Duha Sabeeh Jumah et al in al Basrah (19),Wax JR,et al in USA (24),Susan Mayor in London (25).The difference may be caused by a lower rate of medical intervention and access to neonatal resuscitation. This study illustrated that low birth weight LBW were risk factors for death in neonates with sepsis, a result similar to many previous studies carried in different countries whether developing or developed world (17,19,20),which may be explained by the fact that these neonates need prolonged hospitalization which increases risk of nosocomial infection or related to inherent immunological deficiency. Prolonged rupture of membrane (>18hr), fever. or infection during pregnancy all were associated with significant increment of death ,a result similar to previous study in Dubai and Saudi Arabia (17,18). Among the clinical presentation:- Lethargy, Absent or weak moro reflex, Jaundice, convulsion , bleeding tendency, Sclerema and diarrhea all of them were associated with significant rise of neonatal death and it is relatively similar to previous study of Al-Zwaini in Iraq (26). The mortality was higher in neonates whose blood culture were positive for *P.aeruginosa* (80%), *Staphylococcus aureus* (69.2%) followed by *klebsiella* (68.7%) & *E.coli* (31.6%). Similar results were obtained by many studies in Saudi Arabia (27), Dubai (18), and Mexico (20). All these studies showed a higher incidence of gram negative micro-organisms among neonates with sepsis who died compared to those who survived.

Conclusion:
The most common neonatal risk factors that increase the incidence of sepsis were age of patients ,home delivery, early rupture of membrane and fever or infection during pregnancy. Early onset sepsis was more common than late onset one. The most common features were lethargy, absent or weak moro reflex and reluctance to feed .The most

common organism isolated from Blood cultures was Gram negative microorganism & mainly *E.coli*.

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