# *Bacteriological neonatal sepsis and outcome in kirkuk city 2021*

**Dr. HUSSEIN IBRAHIM MAHDI*,Dr. JAMEEL IBRAHIM AZEEZ*,Dr. ALI QAIS ABDULKAFI**.**

***Pediatrics department , Azadi teaching hospital, Kirkuk, Iraq.**

****** Pediatric department , Nasr hospital, Kirkuk, Iraq.**

**Abstract**

***Background***

Sepsis is the commonest cause of neonatal mortality ,and its responsible for about (30 - 50% ) of the neonatal deaths every years in developing countries. Neonatal sepsis is bacteremia characterized by, many signs and symptoms of infections in the first month of life.

***Objectives:***

1.To detect the prevalent pathogenic agents in neonatal sepsis in neonates admitted to special care baby unit(SCBU), the difference in spectrum of microorganisms in early onset , late onset in neonatal sepsis and to determine the risk factors that are associated with increase incidence of neonatal sepsis.

4.To determine the case fatality of different pathogenic agents.

***Patient and methods***

A prospective study done to detect the risk factors ,pathogenic agents and outcome of septicemia in neonates admitted to special care baby unit (SCBU) in pediatric hospitals in Kirkuk city , during 6 months from 1st January 2021 to 1st june 2021.

***Results***

Two hundred neonates were studied , sepsis was confirmed in 175 neonates (87.5%) by positive blood culture. Preterm neonates in this study were118 (59%), Prolonged rupture of amniotic membranes( > 18-hrs) , was reported in 123 (61.5%), history of maternal fever was reported in 130 (65%) . incidence in male was 120 (60%) while in female was 80 (40%). Early onset disease (0-7 days) had occurred in 69 (34.5%) , while 131 (65.5%) was the percentage of late onset disease(8-30 days) . most of the late onset disease was nosocomial infections 60 (53.57%). The predominant isolates in both early and late onset diseases were Gram negative bacteria 138 (78.8%) . the common organism in early onset sepsis was E.coli 31 (49.20%), while the common organism in the late onset sepsis was Klebsiella 50 (44.64%). The total mortality rate was 82 (41%) , in the early neonatal onset was 26 (42.02%) and while in the late neonatal onset disease was 56 (42.7%) was . Candida albicans and Pseudomonas aeroginosa have the high mortality (100%), but there is no death was recorded in pneumococcal sepsis .

***Conclusion*** Neonatal septicemia generally is present in developing countries more common than developed countries.

Prematurity , prolonged rupture of membranes and maternal fever during pregnancy are an important risk factors of neonatal sepsis .

Keywords: neonatal ,sepsis,bacterial, kirkuk.

## *INTRODUCTION:*

Sepsis represents a major contribute to the global morbidity and mortality and has been declared as a priority by the WHO.[1] The high septicemia incidence across all age groups is found in neonates affect an estimated 3 million babies worldwide (22 per 1000 live births) with a mortality of 11–19% and un quantified long-term neurological defects.[2]

International data are difficult to standardize in the absence of criteria for neonatal septicemia. Recently in adults the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3-) have defined sepsis as a life-threatening organ dysfunction that caused by a response to infection.[3]

The Sequential Organ Failure Assessment Score (S.O.F.A.) reflects changes in organ function altering from baseline. The pediatric S.O.F.A. has been proposed and was found to be a reliable predictor of in hospital mortality in children.[4] The recently described neonatal S.O.F.A. (n SOFA), predicted mortality on Very Low Birth Weight (V.L.B.W.) infants with late onset sepsis.[5]

Neonates differ substantially to adults and older children due to altered immune function and potential intrauterine exposure to infection.[6]

Neonatal immunology is not clearly delineated and has been extrapolated from research in umbilical cord blood that although easily accessible for study is more immunotolerant and doesnt entirely reflect postnatal immune responses.[7] A recent meta-analysis and systematic review, demonstrated that use of the neonatal E.O.S. calculator is associated with a major reduction in the use of empirical antibiotics for suspected early onset sepsis( E.O.S.)[8]

Procalcitonin and C.R.P.(C- reactive protein) demonstrates that biomarkers can be used to shorten antibiotic treatment in patients who improve rapidly after treatment and have negative blood cultures.[9]

Confirmation of chorioamnionitis histologically may or may not be helpful for diagnosis of neonatal sepsis.[10]

The lack of an internationally accepted consensus definition of neonatal sepsis, there are no definitions associated with long-term outcomes. This lack hinders, ongoing collaborative research and benchmarking. Core outcomes are required, to standardize clinical trials, of sepsis and allow comparison between trials. In addition prioritizing research goals with families is essential.[11,12]

**The Aims :**

1. To detect the prevalent pathogenic agents in neonatal sepsis in neonates admitted to SCBU.
2. To point out the difference in spectrum of microorganisms in early onset , late onset neonatal sepsis.
3. Determine, the risk factors that are associated with increase incidence of neonatal sepsis.

4.To determine the case fatality of different pathogenic agents

**Patients & Methods**

The prospective study has been done to outline pattern of the pathogenic organisms causing neonatal sepsis that admitted to (SCBU) in pediatric hospitals From 1st of January 2021 till 1st of june 2021, 200 neonates were studied to determine the pathogenic agent of their sepsis symptoms. .

Neonate with clinical features suggestive of sepsis such as reluctance to feed, apnea, cyanosis, dyspnea, or has history of infection in perinatal period were included in the study. Data include age, sex , date of admission, indication of admission, age of onset of the symptoms, history of prior hospitalization, the

results of blood culture, and these neonates were followed in the ward to identify the progress of their illness and their outcome. All septic neonates receiving antibiotic therapy prior to admission to the ward were excluded from the study. Neonates were classified into two groups according to age of onset of the symptoms, the early onset disease, when the symptoms of sepsis appear (0 -7 days) of life, and the late onset disease, when the feature of sepsis occur after about (8 - 30 days) of life.

From 1st of January 2021 till 1st of june 2021, 200 neonates were studied to determine the pathogenic agent of their sepsis symptoms. 2ml of blood is taken from peripheral vein from 2 sites and cleaned by alcohol and the sample was taken before giving antibiotics and each mixed separately with brain- heart infusion broth then incubated at 37Ċ for 7 days and cultured aerobically .

Another 3rd blood sample taken from neonates at risk of anaerobic infection (early onset sepsis, omphalitis and necrotizing enterocolitis), such sample were mixed with thioglycolate broth and cultured unaerobically. Subculture from conventional bottle after (6_12) hours incubation on the blood and MacConkey agar, after 48 hours, a 2nd subculture performed, bottles were examined macroscopically daily for 7 days and when appear visible growth , the bottle was opened aseptically, a little amount of broth was taken away with a sterilized loop and 3rd subculture done. Bacterial isolate were identified and characterized by conventional procedure by Baily and Scott diagnostic microbiology .

Gram positive streptococci were identified on blood agar surrounded by a well defined zone of complete hemolysis. Bacitracin tests were used to exclude group A streptococci. Listeria monocytogenes were identified as Gram positive rodes with its specific motility character and catalase test. Candida albicans were identified by colony morphology and germ tube methods.

**Statistical analysis**

All data are analyzed by using z- test , the percentage , mean ,chi-square and P value ( not significant if > 0.05 , significant < 0.05 and highly significant < 0.001 ) .

## Results

During the six months period of the study 200 neonates with clinical features of septicemia were including in this study ( those with prior to antibiotics treatment were excluded ). The causing agents were isolated by blood culture in 175 (87.5%) of neonates . As shown in table(1) Preterm patients were 118 (59%) while full term patients were 82 (41%).

| Variable | No. | percentage |
|---|---|---|
| **Full term** | 82 | 41 |
| **Preterm** | 118 | 59 |
| **Total** | 200 | |

**Table 1:** classification of 200 cases of neonatal sepsis according to gestational age .

**P value > 0.06 ( not significant )**

As shown in table(2) , among the total number of patients , 120 babies were male (60%) .while 80 babies were female (40%).

**Table 2**: sex distribution of neonatal sepsis

| Variable | No. | Percentage |
|---|---|---|

| | | |
|---|---|---|
| **Male** | 120 | 60 |
| **Female** | 80 | 40 |
| **Total** | 200 | |

**P value > 0.08 ( not significant )**

As shown in table(3) Prolonged rupture of amniotic fluid membranes(more than 18 hours) , was reported in 123/200 (61.5%) .

**Table 3:** Effect of prolonged rupture of amniotic membranes on neonatal sepsis

| Variable | No. | Percentage |
|---|---|---|
| **More than 18 hours** | 123 | 61.5 |
| **Less than 18 hours** | 77 | 38.5 |

**P value < 0.04 ( significant )**

As shown in table(4) maternal fever at time of delivery was reported in 130/200 (65%) , while 70/200 (35%) was presented without history of maternal fever before delivery.

**Table 4**: Association between maternal fever and neonatal sepsis.

| Maternal fever | No. | percentage |
|---|---|---|
| **Yes** | 130 | 65 |
| **No** | 70 | 35 |
| **Total** | 200 | |

**P value < 0.001 ( highly significant )**

As shown in table (5) Patients have early onset disease were 69 (34.5%) and 131 (65.5%) have late onset . culture positive cases accounted for 63 (36%) of early disease compared to 112 (64%) in late onset disease .

**Table 5**: classification of 200 patients with neonatal sepsis accord to early and late onset of disease.

| Patient group | early onset (0-7) days | | Late onset(8-28)days | |
|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** |
| Culture +ve | 63 | 36% | 112 | 64% |
| Culture –ve | 6 | 24% | 19 | 76% |
| **Total** | **69** | **34.5%** | **131** | **65.5%** |

**P value > 0.07 ( not significant )**

As shown in table (6) gram negative bacteria accounted for 138/175 (78.8%) while Gram positive bacteria were isolated from 34/175 (19.42%) and Candida albicans from 3/175 (1.71%) .

**Table 6:** distribution of pathogenic agents of 175 culture +ve neonatal sepsis .

| Pathogenic agent | No. | Percentage |
|---|---|---|
| **Gram –ve** | 138 | 78.85 |
| ❖ Klebsiella | 58 | 33.14 |

| | | |
|---|---|---|
| ❖ E.coli | 47 | 26.8 |
| ❖ E.aerogenes | 24 | 13.7 |
| ❖ Pseudomonas | 3 | 1.7 |
| ❖ Proteus | 6 | 3.42 |
| **Gram +ve** | 34 | 19.42 |
| ❖ Strept.fecalis | 13 | 7.42 |
| ❖ GBS | 7 | 4 |
| ❖ Listeria | 1 | 0.57 |
| ❖ Pneumococcs | 5 | 2.85 |
| ❖ Staph. | 8 | 4.57 |
| **Candida albicans** | 3 | 1.73 |
| **Total** | **175** | |

**p value < 0.05 ( significant )**

Table (7)showed , In early onset disease Klebsiella and E.coli were the causes of 8 (12.69%) and 31 (49.20%) of cases respectively , compared to 50 (44.64%) and 16 (14.28%) in late onset disease. Other individual organisms did not show statistically significant differences in proportion of culture positive cases between early and late onset .

**Table 7**: classification of (175) cases of culture +ve sepsis according to age onset of disease .

| Patient group | early onset | late onset |
|---|---|---|

| | No. | % | No. | % |
|---|---|---|---|---|
| ❖ Klebsiella | 8 | 12.69 | 50 | 44.64 |
| ❖ Escherichia .coli | 31 | 49.20 | 16 | 14.28 |
| ❖ E.aerogenes | 6 | 9.52 | 18 | 16.07 |
| ❖ Proteus | 2 | 3.17 | 4 | 3.57 |
| ❖ Pseudomonas | 1 | 1.58 | 2 | 1.78 |
| ❖ GBS | 5 | 7.93 | 2 | 1.78 |
| ❖ Listeria | 1 | 1.58 | 0 | 0 |
| ❖ Strep.fecalis | 8 | 12.69 | 5 | 4.46 |
| ❖ Staph. | 1 | 1.58 | 7 | 6.25 |
| ❖ Pneumococci | 0 | 0 | 5 | 4.46 |
| ❖ Candida | 0 | 0 | 3 | 2.67 |
| **Total** | 63 | 36% | 112 | 64% |

**P value < 0.001 ( highly significant )**

As shown in table(8),32 (53.3%) of late onset Klebsiela sepsis , 12 (20%) of E.aerogenes sepsis and 6 (10%) of E.coli sepsis have prior hospitalization .

**Table 8:** History of prior hospitalization among different bacterial isolates in late onset disease.

| Patient group | Late onset disease | History of hospitalization | |
|---|---|---|---|
| | | No. | % |

| | | | |
|---|---|---|---|
| ❖ Klebsiella | 50 | 32 | 53.3 |
| ❖ E.aerogenes | 18 | 12 | 20 |
| ❖ E.coli | 16 | 6 | 10 |
| ❖ Proteus bacteria | 4 | 2 | 3.33 |
| ❖ Strep.fecalis | 5 | 1 | 1.66 |
| ❖ Staph. | 7 | 3 | 5 |
| ❖ Pseudomonas | 2 | 2 | 3.33 |
| ❖ GBS | 2 | 0 | 0 |
| ❖ Pneumococci | 5 | 1 | 1.66 |
| ❖ Candida | 3 | 1 | 1.66 |
| **Total** | 112 | 60 | 53.57% |

**P value >0.08 (not significant)**

As shown in table(9) overall death among the studied patients was 82/200 (41%) . in culture positive group , it was 24/63 (42.8%) in early onset and 52/112 (46.42%) in late onset sepsis , while among culture negative group 2/6 (33.33%) of early onset and 4/19 (21.05%) of late onset sepsis .

**Table 9:** Case fatality rate in early and late neonatal sepsis among 200 patients.

| Patient group | Early | Late | Total death |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Culture +ve | 24/63 (42.8%) | 52/112 (46.42%) | 76/175 (43.42%) |
| Culture -ve | 2/6 (33.33%) | 4/19 (21.05%) | 6/25 (24%) |
| **Total** | 26/69 (42.02%) | 56/131 (42.7 %) | 82/200 (41%) |

**P value >0.06 ( not significant )**

Individual case fatality rate for different pathogenic agents was varied greatly ranging from 100% in case of Pseudomonas and Candida albicans, to zero in case of Pneumococcal sepsis. Staph, GBS, and Klebsiella were the leading fatal pathogens in early onset sepsis, with mortality of 1/1 (100%), 3/5 (60%) and 4/8 (50%) respectively compared to Staph., Klebsiella, and Proteus in late onset sepsis, 4/7 (57.14%), 28/50 (56%) and 3/6 (50%) respectively as shown in table(10).

| **Pathogenic agent** | **No.** | **Death** | |
|---|---|---|---|
| | | **Early(%)** | **Late(%)** |
| ❖ Klebsiella | 58 | 4/8(50) | 28/50(56) |
| ❖ E.coli | 47 | 9/31(29.03) | 4/16(25) |
| ❖ E.aerogenes | 24 | 1/6(16.66) | 8/18(44.4) |
| ❖ Strp.fecalis | 13 | 3/8(37.5) | 1/5(20) |
| ❖ Staph. | 8 | 1/1(100) | 4/7(57.14) |

| | | | |
|---|---|---|---|
| ❖ Proteus | 6 | 0 | 3/6(50) |
| ❖ GBS | 7 | 3/5(60) | 0 |
| ❖ Pseudomonas | 3 | 1/1(100) | 2/2(100) |
| ❖ Listeria | 1 | 1/1(100) | 0 |
| ❖ Pneumococci | 5 | 0 | 0 |
| ❖ Candida | 3 | 1/1(100) | 2/2(100) |
| **Total** | 175 | 24 | 52 |

**Table 10:** Comparison of pathogenic isolates and case fatality in early and late onset sepsis among 175 culture +ve patients.

**P value < 0.05(significant).**

## Discussion

Neonatal sepsis, inspite of considerable progress in hygiene, introduction of newer effective antimicrobial agents and advanced technique in early diagnosis and treatment, remain one of the most important causes of mortality in this age group .

This study showed that sepsis occurred more frequently among preterm neonates (59%),such finding seems compatible with data reported by Asindi A.[13].

The study also showed that male babies are affected more frequently (60%) than female (male :female is 3:2), this result is similar to the studies done by Bennet R.(61%) & Samanci (58%) [14,15]. Premature rupture of amniotic membranes and maternal fever have been reported frequently in the neonates

with early onset , late onset septicemia 123 (61.5 %) and 130 (65%) respectively, such finding seems compatible data reported by Gladstone I.M. [16].

Early onset sepsis have occurred in 69 (34.5%) of cases, a figure is compatible with that reported by Al-Harthi A. , in Saudi Arabia (36%) [17], however it is lower than data reported by Sanghavi in USA (49%) and higher than that reported by David J. in London (29.25%) [18], such variation may be related to the character of our patients, since most cases are either referred from district hospital or presented after a period of hospitalization as nosocomial infection which is mostly manifested after( $8^{th}$) day of life (late onset disease) .

Gram –ve bacteria were the predominant isolate, both in early and late onset sepsis 138 (78.8%) as that reported by Koutouby A. in Saudi Arabia (80%), Stockholm (77%), and Emirates (77.8%), as Gram –ve bacteria are common in the neonatal care unit or even in the nurseries for well babies [19].

Other Gram –ve bacteria, like Pseudomonas aeroginosa appears as uncommon cause of sepsis, with 3 cases (1.78%), as a late onset disease in 2 cases, both of them were low birth weight and having a history of previous hospitalization for more than 6 days, such incidence is lower than that reported by Al-Harthi A. at Saudi Arabia (11.47%), and lower than data reported by Gladstone in London (7.0%) such variation in Pseudomonas sepsis incidence reflect the differences in the causative agents of nosocomial infection at different ICU, at our SCBU although Pseudomonas appears as uncommon cause of neonatal sepsis, it may need adequate further evaluation and follow up to control its spread , specially in view of its high mortality[19].

In this study, staphylococcal infection was reported in 8 (4.57%), 2 cases as S.aureus and the other 6 cases as S.epidermidis. The main factor associated with staph. Infection was prolonged hospitalization. This incidence was nearly

compatible with that reported by Mohammed S. in Kuwait (4.02%) [20] , while it is very low in comparison to that reported by Mitchison R. in Stockholm (25%) [20]. such low incidence, mostly due to exclusion of all babies who were received prior antibiotics, or due to lack of use of central vascular line for total parentral nutrition in our unit .

Over all mortality rate of 82 (41%) in this study is unacceptably high in comparison to that reported by Battistio O. in USA (18.8%) and Schat A. in Stockholm (22%) [20,21], such high mortality in our unit may be related to the infectious process and other factors, because most of infected neonates in our unit were preterm. Also most our patients were transferred from district hospital, so their diagnosis will be late. Other important factor is most of patients were presented with serious complications ( apnea, DIC, intra ventricular hemorrhage, ……etc.), such neonates died shortly after their admission inspite of usage of the available treatment and supportive measures .

**Conclusion** Neonatal septicemia generally is present in developing countries more common than developed countries, the pathogen allocation is different with a prevalence of Gram -ve bacteria and mortality rate is very high.

Prematurity , prolonged rupture of membranes and maternal fever during pregnancy are an important risk factors of neonatal sepsis

**Recommendations**

Good antenatal care and good obstetric treatment in early detecting and treating of the mothers at risk .

Prevention of prematurity and LBW in an attempt to reduce the incidence of neonatal sepsis.

Effective control measures to eradicate and limit the spread of nosocomial infection in our units is mandatory , because of its relative high frequency and poor outcome,provision of antibiotics and good intensive care unit .

**References**


1.Reinhart, K. Recognizing sepsis as a global health priority—a WHO resolution. *N. Engl. J. Med.* **377**, 414–417 (2017).

2.Fleischmann-Struzek, C. et al. The global burden of paediatric and neonatal sepsis: a systematic review. *Lancet Respir. Med.* **6**, 223–230 (2018).

3.Singer, M. et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA* **315**, 801–810 (2016).

4. Matics, T. J. & Sanchez-Pinto, L. N. Adaptation and validation of a pediatric sequential organ failure assessment score and evaluation of the sepsis-3 definitions in critically ill children. *JAMA Pediatr.* **171**, e172352 (2017).

5. Wynn, J. L. & Polin, R. A. A neonatal sequential organ failure assessment score predicts mortality to late-onset sepsis in preterm very low birth weight infants. *Pediatr Res*. https://doi.org/10.1038/s41390-019-0517-2 (2019).

6. Zhang, X., Zhivaki, D. & Lo-Man, R. Unique aspects of the perinatal immune system. *Nat. Rev. Immunol.* **17**, 495–507 (2017).

7. Olin, A. et al. Stereotypic immune system development in newborn children. *Cell* **174**, 1277–1292 (2018).

8. Achten, N. B. et al. Association of use of the neonatal early-onset sepsis calculator with reduction in antibiotic therapy and safety: a systematic review and meta-analysis. *JAMA Pediatr*. https://doi.org/10.1001/jamapediatrics.2019.2825 (2019).

9. Agyeman, P. K. A. et al. Epidemiology of blood culture-proven bacterial sepsis in children in Switzerland: a population-based cohort study. *Lancet Child Adolesc. Health* **1**, 124–133 (2017).

10. Higgins, R. D. et al. Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis: summary of a workshop. *Obstet. Gynecol.* **127**, 426–436 (2016).
11. Molloy, E. J. et al. Developing core outcome set for women's, newborn, and child health: the CROWN Initiative. *Pediatr. Res.* **84**, 316–317 (2018).
12. Molloy, E. J., Mader, S., Modi, N. & Gale, C. Parent, child and public involvement in child health research: core value not just an optional extra. *Pediatr. Res.* **85**, 2–3 (2019).
13.Asindi A.A.,Bilal N. E.,et al."Neonatal septicemia".Saudi medical Journal.2004;25(14):822-25.
14.Bennet R., Eriksson M."Increasing incidence of neonatal sepsis". Chin J. and Charles M.D, Rudolf Text book of pediatrics 18th ed. Churchill living stone . 2003 ;34(8):128-32
15.Samanci N., Ovali F. Akdogan Z." Neonatal septicemia in a neonatal ICU, Result of four years " .American public Health Association 2005.(WWW.emedicine . com) .
16.Gladstone I.M., Ehreenkranz R.A., Edberg S. "A ten years review of neonatal sepsis and comparison with the previous fifty years experience". Journal of child health. 2000:91-94.
17.Al-Harthi A., Dagriri K.A."Neonatal sepsis". Saudi Medical Journal 2000 ; 30(4) : 331-35 .
18.Sanghavi K.P., Tudehope D. "Neonatal bacterial sepsis in intensive care unit". Pediatrics Child health . 2004;58 :93-96 .
19.Koutouby A., Habibulla J." Neonatal sepsis in Dubai, United Arab Emirates". Journal of tropical pediatrics 2007 ; 21(28) : 251-53 .
20.Battisti O., Mitchison R. Davies P."Changing blood culture isolate in referral neonatal ICU". Archives of diseases in childhood . 2000; 42:610-13.
21.Schat A., Zywicki S., Smoor M. "Risk factors and prevention of early neonatal sepsis ". Journal of tropical pediatrics. 2005; 26(12):27-31 .