

## Incidence of Neonatal Sepsis and the Causative Organisms in Neonatal Intensive Care Unit of Tanta University Hospital

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### Abstract

**Background:** Neonatal sepsis is considered a major cause of morbidity and mortality among neonates worldwide. Premature infants are more susceptible to sepsis. Diagnosis and management of sepsis are great challenges facing neonatologists in NICUs.

**Aim of Study:** The aim of this study was to evaluate the incidence of neonatal sepsis at neonatal Intensive Care Unit in Tanta University Hospital. The study was carried out on all admitted neonates with clinical signs and symptoms of sepsis at the time of admission or who developed sepsis during their hospital stay.

**Patients and Methods:** This study was prospectively conducted over a period of 12 months from August 2017 to August 2018, at NICU in Tanta University Hospital.

**Results:** A total of 330 neonates admitted to our TUH NICU along one year from August 2017 to August 2018 were divided into 2 groups as regard clinical and laboratory findings of sepsis. The 2 groups were: Group 1 (case): Sepsis group included (145) neonates who showed clinical presentation and laboratory findings of sepsis and Group 2 (control): Non sepsis group included (185) neonates who were free and not showing any manifestations of sepsis or any laboratory findings of sepsis.

**Conclusions:** The incidence of neonatal sepsis in our TUH NICU was about 43.94% along one year and the most common organisms was klebsiella (31.03%) followed by staph aureus (20%).

**Key Words:** Neonatal sepsis – Incidence – Klebsiella – Staph aureus.

### Introduction

NEONATAL sepsis is defined as a clinical syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of a bacterial pathogen from the blood stream [1].

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Neonatal sepsis is considered a major cause of morbidity and mortality among neonates worldwide [2].

Neonatal sepsis is broadly categorized into two categories: Early-Onset Sepsis (EOS) and late-onset sepsis according to the postnatal day of presentation [3].

Early-Onset Neonatal Sepsis (EOS) occurs within the first 72 hours of life, while late-onset sepsis occurs after 72h of life [4,5].

The microorganisms most commonly implicated in early-onset infection include the following: (Group B Streptococcus (GBS), Escherichia coli, Coagulase-negative Staphylococcus, Haemophilus influenza, Listeria monocytogenes) [6].

Early-onset sepsis is associated with acquisition of microorganisms from the mother. Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize the mother's Genitourinary (GU) tract; the neonate acquires the microorganisms as it passes through the colonized birth canal at delivery [7].

Organisms that have been implicated in causing late-onset sepsis include the following: (Coagulase-negative Staphylococcus, Staphylococcus aureus, E coli, Klebsiella, Pseudomonas, Enterobacter, Candida, GBS, Serratia, Acinetobacter, Anaerobes) [8].

Late-onset sepsis occurs after the third day of life and is acquired from the caregiving environment [9,10]. The signs and symptoms of neonatal sepsis are nonspecific. These include fever or hypothermia, respiratory distress including cyanosis and apnea, feeding difficulties, lethargy or irritability, hypotonia, seizures, bulging fontanel, poor

perfusion, bleeding problems, abdominal distention, hepatomegaly, guaiac-positive stools, unexplained jaundice, or more importantly, “just not looking right” [11].

Severe sepsis manifestations include cardiovascular organ dysfunction or acute respiratory distress syndrome or two or more other organ dysfunctions (respiratory, renal, neurologic, hematologic, or hepatic) [12].

Premature and ill infants are more susceptible to sepsis and subtle nonspecific initial presentations; considerable vigilance is therefore required in these patients so that sepsis can be effectively identified and treated [8].

Diagnosis and management of sepsis are great challenges facing neonatologists in NICUs. Clinical diagnosis of presentation is difficult due to non-specific signs and symptoms. In addition, laboratory diagnosis is time consuming. This matter necessitates the initiation of empirical antibiotic therapy till the suspected sepsis is ruled out [13].

Table (1): Major risk factors for neonatal sepsis [14].

Early-onset infection	Late onset infection
<ul style="list-style-type: none"> <li>• Maternal infection, usually primary infection</li> <li>• Prolonged premature rupture of membranes &gt;18 hours</li> <li>• Chorioamnionitis</li> <li>• Intrapartum fever &gt;37.5C</li> <li>• Pregnancy on intrauterine device or with cervical cerclage</li> <li>• Maternal colonization with GBS</li> <li>• Preterm labor</li> <li>• Prematurity</li> <li>• Septic or traumatic delivery</li> <li>• Perinatal asphyxia</li> <li>• Male sex</li> <li>• LBW (&lt;2,500gm.)</li> <li>• Maternal infection (usually urogenital)</li> <li>• Maternal poverty, poor/no prenatal care, preeclampsia, maternal cardiac disease</li> <li>• Congenital immune defects or asplenia</li> <li>• Multiple pregnancy</li> <li>• Neonatal obstructive uropathy</li> <li>• Galactosemia in neonates</li> </ul>	<ul style="list-style-type: none"> <li>• Extreme prematurity</li> <li>• VLBW (&lt;750gm)</li> <li>• Bronchopulmonary dysplasia</li> <li>• Complex congenital malformations</li> <li>• Short bowel syndrome</li> <li>• Delayed enteral feeding</li> <li>• Prolonged TPN</li> <li>• Previous broad spectrum antibiotic therapy.</li> <li>• Intravascular catheters</li> <li>• Endotracheal intubation</li> <li>• Assisted ventilation</li> <li>• Surgery including Necrotizing Enterocolitis (NEC)</li> <li>• Contact with hands of personnel colonized with pathogens</li> <li>• Contact with contaminated equipment</li> </ul>

LBW : Low Birth Weight.

TPN: Total Parenteral Nutrition.

VLBW : Very Low Birth Weight.

NEC: Total Parenteral Nutrition.

2- Any neonate with clinical symptoms and signs or laboratory data of neonatal sepsis as demonstrated in Griffin Score, Tollner Score and Hematological sepsis score.

*The following was done to all selected cases:*

#### History:

Full history was taken including (antenatal, natal, postnatal history) by collection of these data:

#### Aim and objectives:

The aim of this study is to evaluate the incidence of neonatal sepsis and the causative organisms in neonatal Intensive Care Unit in Tanta University Hospital.

#### Patients and Methods

This study was prospectively conducted over a period of 12 months from August 2017 to August 2018, at NICU in Tanta University Hospital. The study was carried out on all admitted neonates with clinical signs and symptoms of sepsis at the time of admission or who developed sepsis during their hospital stay were assessed.

#### Inclusion criteria:

All neonates (both preterm and full-term) admitted to our NICU all over one year but blood culture is recommended to:

1- Any neonate having risk factor for neonatal sepsis as in (Table 1), [14].

- *Maternal data was obtained including:* Gestational age, mode of delivery, and risk factors of sepsis such as Prolonged Rupture of Membrane (PROM), maternal fever.

- *Neonatal data was obtained including:* Sex, birth weight, and risk factors for sepsis such as (prematurity, chorioamnionitis, or insertion of umbilical catheter).

- Other data such as social, demographic data was recorded by qualified medical staff.

All these data was listed on a standardized data collection sheet.

#### *Clinical examination:*

Full clinical examination was done.

#### *Laboratory investigations and methods:*

##### *1- Laboratory investigations included:*

- CBC
- CRP.

• Blood Culture is recommended to those with risk factors of sepsis or those who were suspected having sepsis according to Griffin Score, Tollner Score and hematological score of sepsis.

##### *2- Laboratory methods included:*

###### *A- Collection of specimens:*

Blood samples were collected under complete aseptic conditions for CRP, CBC, and blood cultures. About (3.5-4ml) of blood was taken. 1ml for CBC, 1ml for CRP, (1.5-2ml) for blood culture.

Blood was collected from a peripheral vein. Approximately (1.5-2ml) of blood was inoculated directly into blood culture medium vials and was sent to our clinical microbiology laboratory for cultivation and subsequent processing.

###### *B- Processing of specimens:*

The blood cultures were incubated aerobically and anaerobically at 37°C in blood culture bottle. And subcultures were made every 3 days on enriched and selective media including blood, chocolate, MacConkey Agar plates and examined for growth after 24-48 hours. The same protocol was repeated until the 9<sup>th</sup> day before blood culture was considered to be free of microorganisms (to be negative blood culture). Isolates obtained were identified by standard microbiological techniques, namely, Gram staining, colony characteristics, and biochemical properties including catalase, coagulase, growth on mannitol salt agar, and hemolytic activity on blood agar plates for Gram-positive isolates, and Triple Sugar Iron (TSI), motility, indole, citrate utilization, urease, oxidase for Gram-negative bacilli. Candida isolates were confirmed by growth on Sabouraud media.

###### *C- Antimicrobial susceptibility testing:*

Antimicrobial susceptibility testing was done on Mueller-Hinton agar according to the isolated organisms.

#### *Consent:*

Written informed consent was obtained from the parents of all subjects of the study. The study was approved by Ethics Committee of Faculty of Medicine, Tanta University.

#### *The risk to the participants and measures used to minimize this risk:*

When we take any sample we can introduce infection to the patient, so to minimize this risk, samples were taken under complete aseptic conditions.

#### *Privacy:*

To maintain privacy of participants and confidentiality of the data we did the following:

- Code number was given to every patient symbol to the name and address that was kept in a special file.
- The name of the patient in the research was hidden.
- The results of the research were used only in scientific aim and not used in any other aims.

## **Results**

A total of 330 neonates admitted to our TUH NICU along one year from August 2017 to August 2018 were studied and were divided into 2 groups as regard clinical and laboratory findings of sepsis. The 2 groups were: Group 1 (case): Sepsis group included (neonates who showed clinical presentation and laboratory findings of sepsis, group 2 (control): Non sepsis group included neonates who were free and not showing any manifestation of sepsis or any laboratory findings of sepsis.

The incidence of neonatal sepsis in our TUH NICU was about 43.94% (number of sepsis cases =145) and the non sepsis cases 56.06% (number of non sepsis cases=185) of the total number of cases admitted to our TUH NICU along one year which was about 330 neonates (100%).

There was no significant difference between sepsis and non sepsis group as regard gestational age, sex and mode of delivery (*p*-value 0.288, 0.692, 0.167 respectively), but as regard mean body weight, it was significantly lower in the neonates with sepsis compared to nonsepsis group (*p*-value <0.001 \*).

Most of cases with sepsis showed manifestations of sepsis after admission to our NICU. The number of cases who showed sepsis manifestations before admission=61 cases of the total number of sepsis group (145 neonates) by percentage of (42.07%)

which was lower than the number of cases who showed sepsis after admission whose number=84 neonates by percentage of (57.93%).

Sepsis group was classified into 2 groups as regard to operated or not operated cases because the operated group may catch the organism of sepsis from the operating theater. We correlated the causative organisms of the cases undergoing operation and others who were not operated. The number of the operated cases=43 cases of the total number of sepsis group (145) neonates, by percentage of (29.66%) and the number of non operated cases who showed sepsis manifestations= 102 neonates by percentage of (70.34%).

Of the total number of neonates under study (330), 42 neonates had history of PROM. From which 32 neonates showed manifestations of sepsis who represented about (22.07%) of sepsis group. Thus PROM was considered an important risk factor for sepsis.

Of the total number of neonates under study (330), 15 neonates had history of chorioamnionitis which was considered an important risk factor to sepsis and all of them (15 neonates) showed manifestations of sepsis who represented about (10.34%) of sepsis group.

Loss of interest for feeding and poor suckling was the most frequent clinical finding of sepsis (27.59%) followed by hypothermia (20.69%), NEC (15.86%), cyanosis, grunting, persistent vomiting, fever (13.79%), mottling (13.10%) and not doing well and lethargy (12.41 %).

The percentage of blood culture negative patients showing manifestations of sepsis was (27.59%), but blood culture positive cases were about (72.41%). Among positive cultures, Klebsiella was the most prevalent organism (31.03%) followed by Staphylococcus aureus (20%).

Among positive culture cases of operated group, the most prevalent organism was staph.aureus (25.58%) followed by Klebsiella (16.28%). On the contrary, non operated group showed that the most prevalent organism was Klebsiella (37.25%) followed by staphylococcus aureus (17.65%).

As regard CRP which was considered acute phase reactant non specific to sepsis. Among sepsis group, CRP was positive in about (78.62%) only and among non sepsis group, CRP was positive in about (11.89%) with sensitivity, specificity, PPV, NPV of (79%, 25%, 79%, 24% respectively).

As regards blood culture positive cases of sepsis group, only 80% had CRP positive (>6mg/dl) and about 20% had negative CRP inspite showing manifestation of sepsis and positive blood culture for organism and this means that CRP is acute phase reactant highly sensitive, non specific to sepsis. The sensitivity, specificity, PPV, NPV of CRP were (79%, 25%, 79%, 24% respectively).

Sepsis group had high incidence of mortality (57.42%). On the contrary to non sepsis group which showed low mortality rate (13.51%).

Among died cases of sepsis group, the most common organism causing sepsis was Klebsiella (22.89%) followed by Staph. aureus (19.28%) then E. Coli then Proteus, Pseudomonas, Candida and Yeast.

HB level and platelet count were significantly lower in sepsis group than non sepsis group ( $p$ -value <0.001 \*, <0.001 \* respectively). While WBCS count was significantly higher in sepsis group than non sepsis group ( $p$ -value=<0.001 \*).

Some cases of sepsis group responded to sepsis by leukopenia (WBCS <5000) who represented about (10.3%) of cases and others responded by leukocytosis (WBCS >20000) who represented about (24.1%). This classification was according to hematological score of sepsis which was done by (Pinky P., Laishram R.S. & Devi K.A., 2018), [15].

## Discussion

Neonatal sepsis is the third leading cause of neonatal mortality, only behind prematurity and intrapartum-related complications (or birth asphyxia) [16].

The aim of this study was to evaluate the incidence of neonatal sepsis in the NICU of TUH and the causative organisms causing sepsis.

In the present study, the incidence neonatal sepsis was (43, 94%), this agreed with other studies [17-19] who showed that the incidence of sepsis was (45.9%, 62%, 41, 7% respectively) and this disagreed with other studies [20,21] which showed low incidence of sepsis (7.6%, 7.8%) respectively.

The mean gestational age of sepsis group was  $35.710 \pm 2.970$  weeks, this agreed with another study [22] in which the mean gestational age for sepsis cases was  $34.4 \pm 3, 8$  weeks.

This study showed that there were no significant differences between the 2 groups as regard to

gestational age, sex and mode of delivery ( $p$ -value = 0.288, 0.692, 0.167 respectively) and this agreed with other studies [23-26] who found that there was no significant difference between sepsis group and non sepsis group with respect to their gestational age, sex and mode of delivery.

As regard gestational age, the present study disagreed with other studies [20,27] who found that sepsis was common in LBW infants (both preterm and term babies small for gestational age). This may be due to:

- a- Innate immunity is affected by impaired cytokine production, decreased expression of adhesion molecules in neutrophils and a reduced response to chemotactic factors [27].
- b- Also, transplacental passage of antibodies starts during the second trimester and achieves its maximal speed during the third trimester. As a result, most preterm newborns have significantly reduced humoral responses [20,27].

Our present study also disagreed with other studies [17,28] who found term babies' incidence to sepsis more than preterm babies.

As regard sex, neonatal septicemia was found to be more common in males. The factors regulating the synthesis of gammaglobulin are probably situated on X chromosomes in the male infants thus confers less immunological protection compared to female counterpart [34].

Our present study disagreed with other studies [17,20,29-33] that showed that males were more affected by neonatal sepsis than females.

Also the present study disagreed with another study [35] who stated that females accounted for 53.6% of the studied septic cases and males accounted for 46.4%.

This disagreed with Kardana 2011 study [36] who observed that babies born by vaginal delivery were more likely to have sepsis than those delivered by caesarean section. This may be related to good sterilization and intrapartum chemoprophylaxis which dramatically decreased the risk of sepsis in neonates delivered by caesarian section.

On the contrary, our present study disagreed with another studies [17,33,37-39] who found the incidence of sepsis was higher in neonates born via CS than in those born via VD.

The present study showed that the mean body weight was significantly lower in the neonates with neonatal sepsis compared to the control group

(mean  $\pm$  SD = 2.309  $\pm$  0.770, 2.948  $\pm$  0.939 respectively) ( $p < 0.001$  \*), this agreed with the study of Schrag 2011 study [40] who found that low birth weight was associated with higher risk for sepsis, and disagreed with Mike 2011 study [23].

This agreed with studies which said that low birth weight LBW (IUGR & prematurity) were risk factors for neonatal sepsis, a result similar to many previous studies carried in different countries whether developing and developed world [17,18,20, 42-46]. This is caused by an immature inexperienced immune system; a fragile cutaneous barrier; and a prolonged hospital stay with increased exposure to the Neonatal Intensive Care Unit (NICU) environment, including various invasive devices and procedures [18,41].

In the current study among the septic group patients, the number of cases showing sepsis before admission was 61 representing (42,07%), and the number of cases showing sepsis after admission was 84 representing (57,93%), similar finding was reported by seliem 2018, [17] who found that the percentage of sepsis cases before admission was 44,2% and after was 55,8%.

In the current study it was found that the septic group had highly significant increase in occurrence of PROM when compared to non sepsis group ( $p < 0.001$  \*). And this agreed with Selimovic 2010 study [47] who reported the same results.

In the present study, 12.72% (42 cases) of all cases under the study (330) had PROM, but only 32 cases of PROM were proved as sepsis which represented about 22.07% of sepsis group. This agreed with other studies [20,28,48,49] who found that PROM represent about (12, 9%, 61%, 45%, 75% of sepsis cases respectively).

This higher incidence of prolonged PROM in some of the previous studies might be due to low socioeconomic state and lack of antenatal care of the mothers as mentioned by Sakr 2016 [50].

In the current study it was found that the septic group has highly significant increase in occurrence of chorioamnionitis when compared to non sepsis group ( $p < 0.001$  \*). And this agreed with other studies [51,52].

But as regard chorioaminionitis as an important risk factor to sepsis, 15 neonates of the total number of neonates under study (330) had history of chorioaminionitis and showed manifestations of sepsis who represented about 10.34% of sepsis group. This agreed with other studies [20,28] who found

that chorioamionitis represented about (15, 1%, 33, 33%) of sepsis group respectively.

In the current study, clinical evaluation of neonates with sepsis revealed that that loss of interest for feeding and poor suckling were the most frequent clinical findings of sepsis (27,59%) followed by hypothermia (20,69%) and this agreed with other studies [18,20,27,53] who found that loss of interest for feeding and poor suckling was the most common presentation of neonatal sepsis.

This finding disagreed with a study [17] at Mansoura hospital in Egypt and also disagreed with other studies [25,54-56] who found that respiratory distress was the most prevalent presentation of sepsis. It also disagreed with Tewabe 2017 [28] who found that fever was the most common presentation of sepsis and also disagreed with Shitaye 2008 [35] who found that hypothermia (84.8%) was the most common presentation.

In the current study, among sepsis group who showed clinical presentation of sepsis (145 neonates), there were neonates negative for blood culture without growth although they showed high CRP and the CBC was showing sepsis (low HB, low Platelets, leukopenia or leukocytosis), there number was 40 neonates with percentage of (27, 59%) of sepsis group, but positive culture cases were 105 neonates with percentage of (72, 41%) of sepsis group.

This agreed with another studies [17,20,25,29, 53,57] who found that the incidence of bacteriologically positive cases was (40.7%, 48%, 45,2%, 34.78%, 45%, 30%) respectively.

Among the positive group 31,03% were caused by Klebsiella, 20% were caused by Staphylococcus aureus, 10,34% were caused by Escherichia coli organism, 5,52% were caused by proteus, 2,76% were caused by Candida, 1,38% were caused by Pseudomonas and 1,38% were caused by yeast.

Also this agreed with other studies [18,20,41, 53,58,59] who found that the most common microorganisms isolated from blood culture positive cases was Klebsiella.

Our present study disagreed with other studies [25,46,60,61] who found that staph.aureus was the predominant isolate. It also disagreed with another study [22] who found that the commonest organism isolated was S. epidermidis followed by S. haemolyticus.

The causative organisms in neonatal sepsis vary from place to place and the frequency of the caus-

ative organisms is different in different hospitals and even in the same hospital at different time. Also there is increasing trend of antibiotic resistance to the commonly used and available drugs. Continuous surveillance is needed to monitor changing epidemiology of pathogens and antibiotic susceptibility pattern) [25,62].

Our present study disagreed with Bhatt 2015 study [59] which showed higher incidence of post-operative sepsis in neonates which was found to be 73.75%.

Also our study disagreed with another study [63] who reported low incidence of post-operative sepsis (6.9%) which was much lower than our incidence. This was done in well-developed setups; so, their sepsis rate was much low. Hence, precise and well-organized strategies are required in developing countries such as India for the prevention of post-operative sepsis rates.

In our current study, the percentage of the negative blood cultures among operated sepsis group was 23,26% which is lower than that of the non operated sepsis group (29,41%) and among positive cultures, it showed that the most prevalent organism was staph.aureus (25,58%) on the contrary to non operated group was Klebsiella (37, 25%) followed by Staphylococcus aureus (16,28%) then Escherichia coli (18,60%), Proteus (11,63%), Candida (2,33%), Yeasts (2,33%), Pseudomonas (0%).

Our present study agreed with Bhatt 2015 study [59], but disagreed with others [63,64] who found that coagulase-negative staphylococcal sepsis (E. coli and K. pneumonia respectively) were the most common organisms in post operative sepsis.

In the current study, the mean Hb of sepsis group was (10.561 ± 2.975 gm/dl) and was significantly lower than that of non sepsis group (14.132 ± 1.587 gm/dl) ( $p < 0.001$  \*) and this agreed with other studies [53,65,66] who found mean Hb of the patients was significantly lower than that of the control group.

In the current study the mean platelets count of the septic group (172.322 ± 145.020 X 10<sup>3</sup>/cmm) was significantly lower than that of the controls (322.286 ± 91.290 X 10<sup>3</sup>/cmm) ( $p < 0.001$  \*), this was in agreement with others [53,65-67] who found that platelets count of the septic group was significantly lower than that of the control group.

Also, this agreed with similar studies [23,48] who stated that low platelet count is associated

with sepsis. This could be due to direct toxic injury of platelets, megakaryocytic suppression, increased peripheral consumption as in DIC or presence of immune component due to increased level of platelet associated immunoglobulins. Abdel-Hakim (2019) study [67] found that thrombocytopenia was consistently associated with poor prognosis in infant with sepsis.

The present study disagreed with Gonzalez 2003 [68] who found that there is no statistical difference between patients and controls as regards to and platelet count.

In the current study the total leucocytic count of patients ( $17.969 \pm 6.776 \times 10^3/\text{cmm}$ ) was significantly higher than controls ( $6.344 \pm 3.670 \times 10^3/\text{cmm}$ ) ( $p < 0.001$  \*), this agreed with other studies [23,53,65,66]. However our present study disagreed with [67,68] who found that there was no significant difference between sepsis and control group ( $p$ -value  $> 0.05$ ).

Sometimes neonates respond to infection by decreasing WBCS count  $< 5000$  (leukopenia), others respond by increasing WBCS  $> 20000$  (leukocytosis) [48].

Boseila 2011 [48] found that Total Leucocytic Count (TLC) was not much informative for the diagnosis of neonatal sepsis. This may be because septic infants, in contrast to adults in whom hematopoiesis is developmentally mature, may deplete their neutrophil reserve and develop neutropenia during overwhelming infection.

In our study, some cases of sepsis group responded to sepsis by leukopenia (WBCS  $< 5000$ ) who represented about (10.3%) and others responded by leukocytosis (WBCS  $> 20000$ ) who represented about (24.1%). This agreed with [22] who reported that (6.9%) of sepsis cases had leukopenia (WBC  $< 5,000/\text{mm}^3$ ) and (22.3%) was showing leukocytosis (WBC  $> 20,000/\text{mm}^3$ ). This classification was according to hematological score of sepsis which was done by (Pinky P., Laishram R. S. & Devi K.A., 2018), [15].

Our present study showed that among sepsis group (145 cases), only 78.62% (114 cases) were CRP positive. Then we classified the sepsis group into 2 subgroups, blood culture negative cases (out of which 20% were CRP positive), blood culture positive cases (out of which only 80% were CRP positive). Also we found that CRP was positive in about (11.89%) of the control group due to non sepsis causes. Thus CRP is highly sensitive to sepsis but not specific. This agreed with another

studies [17,20] in which CRP was positive ( $> 6\text{mg/dl}$ ) in (85, 3%), (56.9%) of suspected sepsis cases respectively.

Predictive accuracy of CRP of this study was compared with other studies. In the present study, CRP had high sensitivity (79%) specificity (25%), PPV (79%) NPV (24%). This agreed with a study [25] in which CRP had a high sensitivity (77.8%), specificity (66.7%), positive predictive value (68.2%) and negative predictive value (76.5%). Our study also agreed with another study [18] who found that CRP had high sensitivity of (90.32%), specificity (42.10%), positive predictive value (71.79%) and negative predictive value (72.72%).

Since our neonatal unit is a referral unit, it attracts mainly the high risk patients and so in this study high mortality rate was reported to be about (57, 24%), and this agreed with another study [41] who also showed high incidence of mortality (44.2%).

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, incubators, different microorganisms and use of different antibiotics [41].

In our study, it was found that among died cases of sepsis group, the most common organism causing sepsis was Klebsiella followed by Staph then E. Coli then Proteus, Pseudomonas, Candida and Yeast. This agreed with another study [20] where the mortality rate due to Klebsiella was 33.33% which was the commonest organism among died cases as our present study.

Our study observed that higher mortality rate was reported with culture positive cases (66, 27%) than culture negative cases (33.73%). This agreed with a study [20] who observed higher mortality rates with culture positive cases (35.71%) than culture negative cases (19.67%). Higher mortality in culture positive group was due to invasion of blood stream by larger number of bacteria.

Blood culture positive cases showed the causative organisms causing sepsis, and also showed their sensitivity and resistance to antibiotics which agree with other studies [17,20,46,58].

#### Conclusions:

The incidence of neonatal sepsis in our TUH NICU was about 43, 94% along one year. The most common causative organism was Klebsiella (31.03%) followed by Staphylococcus aureus (20%).

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**Conflicts of interest:**

No conflicts of interest declared.

**Authors' contributions:**

All authors had equal role in design, work, statistical analysis and manuscript writing.

**References**

- 1- DELANGHE J.R. and SPEECKAERT M.M.: Translational research and biomarkers in neonatal sepsis. *Clinicachimica acta*, 451 (39): 46-64, 2015.
- 2- TZIALLA C., MANZONI P., ACHILLE C., et al.: New diagnostic possibilities for neonatal sepsis. *American Journal of Perinatology*, 35 (06): 575-7, 2018.
- 3- CARR R., BROCKLEHURST P., DORÉ C.J., et al.: Granulocyte-macrophage colony stimulating factor administered as prophylaxis for reduction of sepsis in extremely preterm, small for gestational age neonates (the PROGRAMS trial): A single-blind, multicenter, randomized controlled trial. *The Lancet*, 373 (9659): 226-33, 2009.
- 4- HORNIK C.P., FORT P., CLARK R.H., et al.: Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early human development*, 88 (6): S69-S74, 2012.
- 5- EDWARDS M.S. and GONIK B.: Preventing the broad spectrum of perinatal morbidity and mortality through group B streptococcal vaccination. *Vaccine*, 31 (8): D66-D71, 2013.
- 6- ANDERSON-BERRY A.L., BELLIG L.L. and OHNING B.L.: Incidence and antibiotic profile of bacterial isolates from neonatal septicemia in national medical college and teaching hospital, Birgunj, Nepal. *Research Journal of Pharmacy and Technology*, 11 (6): 2238-42, 2018.
- 7- KLINGER G., LEVY I., SIROTA L., et al.: Epidemiology and risk factors for early onset sepsis among very-low-birth weight infants. *American Journal of Obstetrics and Gynecology*, 201 (1): 38-40, 2009.
- 8- DUNKEL B. and CORLEY K.T.T.: Pathophysiology, diagnosis and treatment of neonatal sepsis. *Equine Veterinary Education*, 27 (2): 92-8, 2015.
- 9- VAN DEN HOOGEN A., GERARDS L., VERBOON-MACIOLEK M.A., et al.: Long-term trends in the epidemiology of neonatal sepsis and antibiotic susceptibility of causative agents. *Neonatology*, 97 (1): 22-8, 2010.
- 10- LIN F.Y., WEISMAN L.E., AZIMI P., et al.: Assessment of intrapartum antibiotic prophylaxis for the prevention of early-onset group B Streptococcal disease. *The Pediatric Infectious Disease Journal*, 30 (9): 759, 2011.
- 11- GERDES J.S.: Diagnosis and management of bacterial infections in the neonate. *Pediatric Clinics of North America*, 51 (4): 939-59, 2004.
- 12- GOLDSTEIN B., GIROIR B. and RANDOLPH A.: International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. *Pediatric Critical Care Medicine*, 6 (1): 2-8, 2005.
- 13- PATEL S.J. and SAIMAN L.: Antibiotic resistance in neonatal intensive care unit pathogens: Mechanisms, clinical impact, and prevention including antibiotic stewardship. *Clinics in Perinatology*, 37 (3): 547-563, 2010.
- 14- MITRA D.K., MULLANY L.C., HARRISON M., et al.: Incidence and risk factors of neonatal infections in a rural Bangladeshi population: A community-based prospective study. *Journal of Health, Population and Nutrition*, 37 (1), 6, 2018.
- 15- PINKY P., LAISHRAM R.S., AMBALA DEVI K., et al.: Hematological changes in neonatal sepsis-a study in a tertiary care hospital. *J. Evid. Based Med. Healthc*, 5 (33): 2415-2418, 2018.
- 16- LIU L., JOHNSON H.L., COUSENS S., et al.: Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. *The Lancet*, 379 (9832): 2151-2161, 2012.
- 17- SELIEM W.A. and SULTAN A.M.: Etiology of early onset neonatal sepsis in neonatal intensive care unit-Mansoura, Egypt. *Journal of Neonatal-Perinatal Medicine*, 11 (3): 323-330, 2018.
- 18- HOFER N., ZACHARIAS E., MÜLLER W., et al.: An update on the use of C-reactive protein in early-onset neonatal sepsis: Current insights and new tasks. *Neonatology*, 102 (1): 25-36, 2012.
- 19- LAMICHHANE A. and MISHRA A.: Correlation between C-reactive protein and Blood Culture in Neonatal Sepsis at a Tertiary Care Centre in Western Nepal. *Journal of Lumbini Medical College*, 7 (2): 5, 2019.
- 20- VERMA P., BERWAL P.K., NAGARAJ N., et al.: Neonatal sepsis: Epidemiology, clinical spectrum, recent antimicrobial agents and their antibiotic susceptibility pattern. *International Journal of Contemporary Pediatrics*, 2 (3): 176-180, 2015.
- 21- JOSEPH C.J., LIAN W.B. and YEO C.L.: Nosocomial infections (late onset sepsis) in the Neonatal Intensive Care Unit (NICU). *Proceedings of Singapore Healthcare*, 21 (4): 238-244, 2012.
- 22- NABIH M., ELTAHLAWY E. and REDA N.M.: Pattern of bacterial profile and antibiotic susceptibility among neonatal sepsis cases at Cairo University Children Hospital". *Journal of Taibah University Medical Sciences*, Vol. 15 (1): 39-47, 2020.
- 23- MIKE S., JOLANTA W. and ANNA S.: Serum and Urinary NGAL in Septic Newborns, *Bio. Med. Research International*, (24): 1-8, 2014.
- 24- EL-SHIMI M.S., MOHAMED M.H., ABDEL AL AHMED, et al.: Human Neutrophil Lipocalin in Early Diagnosis of Neonatal Sepsis. *Egyptian Journal of Pediatrics*, 394 (3587): 1-15, 2014.
- 25- LAKHEY A. and SHAKYA H.: Role of Sepsis Screening in early diagnosis of Neonatal Sepsis. *Journal of Pathology of Nepal*, 7 (1): 1103-1110, 2017.
- 26- MONDAL S., BANDYOPADHYAY R., SINHA S., et al.: Neonatal sepsis: Role of a battery of immunohematological tests in early diagnosis. *International Journal of Applied and Basic Medical Research*, 2 (1): 43, 2012.
- 27- ZEA-VERA A. and OCHOA T.J.: Challenges in the diagnosis and management of neonatal sepsis. *Journal of Tropical Pediatrics*, 61 (1): 1-13, 2015.



- 28- TEWABE T., MOHAMMED S., TILAHUN Y., et al.: Clinical outcome and risk factors of neonatal sepsis among neonates in Felege Hiwot referral Hospital, Bahir Dar, Amhara Regional State, North West Ethiopia 2016: A retrospective chart review. *BMC Research Notes*, 10 (1): 265, 2017.
- 29- ZAKA-UR-RAB Z., KAR M., GUPTA V., et al.: Evaluation of laboratory markers of sepsis screen in the diagnosis of early onset neonatal septicemia. *International Journal of Contemporary Pediatrics*, 3 (4): 1144-9, 2016.
- 30- MASOOD M.K., BUTT N., SHARIF S., et al.: Clinical spectrum of early onset neonatal sepsis. *Annals of King Edward Medical University*, 17 (1): 27-9, 2011.
- 31- HAFSA A., FAKRUDDIN M., HAKIM M.A., et al.: Neonatal bacteremia in a neonatal intensive care unit: Analysis of causative organisms and antimicrobial susceptibility. *Bangladesh Journal of Medical Science*, 10 (3): 187-94, 2011.
- 32- HASAN M.S. and MAHMOOD C.B.: Predictive values of risk factors in neonatal sepsis. *Journal of Bangladesh College of Physicians and Surgeons*, 29 (4): 187-95, 2011.
- 33- BATES M., KABWE M. and ZUMLA A.: Neonatal sepsis and antibiotic resistance in developing countries. *The Pediatric Infectious Disease Journal*, 33 (10): 1097, 2014.
- 34- DESAI K.J. and MALEK S.S.: Neonatal septicemia: Bacterial isolates & their antibiotics susceptibility patterns. *NJIRM*, 1 (3): 12-5, 2010.
- 35- SHITAYE D.: Neonatal Sepsis: Bacterial Etiologic Agents and Their Antibiotic Susceptibility Pattern in Tikur Anbesa University Hospital, Addis Ababa, Ethiopia. Faculty of Medicine Ababa University (MSc Thesis), 1 (1): 12, 2008.
- 36- KARDANA I.M.: Incidence and factors associated with mortality of neonatal sepsis. *Paediatrica Indonesiana*, 51 (3): 144-8, 2011.
- 37- AFSHARPAIMAN S., TORKAMAN M., SABURI A., et al.: Trends in incidence of neonatal sepsis and antibiotic susceptibility of causative agents in two neonatal intensive care units in Tehran, IR Iran. *Journal of clinical neonatology*, 1 (3): 124, 2012.
- 38- GANDHI S., RANJAN K., RANJAN N., et al.: Incidence of neonatal sepsis in tertiary care hospital: An overview. *Int. J. Med. Sic. Public Health*, 2 (3): 548-52, 2013.
- 39- UTOMO M.T.: Risk factors of neonatal sepsis: A preliminary study in Dr. Soetomo hospital. *Indonesian Journal of Tropical and Infectious Disease*, 1 (1): 23-6, 2010.
- 40- SCHRAG S.J., CUTLAND C.L., ZELL E.R., et al.: Risk factors for neonatal sepsis and perinatal death among infants enrolled in the prevention of perinatal sepsis trial, Soweto, South Africa. *The Pediatric Infectious Disease Journal*, 31 (8): 821-6, 2012.
- 41- JUMAH D.S.: Predictors of mortality outcome in neonatal sepsis. *The Medical Journal of Basrah University*, 25 (1): 11-8, 2007.
- 42- RODRIGUEZ M., CANADIANI C., GARCIA J., et al.: Morbidity and Mortality from neonatal sepsis in a tertiary care level hospital. *Salud publica de Mexico*, 45 (2): 90-5, 2003.
- 43- HENGST J.M.: The role of C-reactive protein in the evaluation and management of infants with suspected sepsis. *Advances in neonatal care: Official journal of the National Association of Neonatal Nurses*, 3 (1): 3-13, 2003.
- 44- SHITAYE D., ASRAT D., WOLDEAMANUEL Y., et al.: Risk factors and etiology of neonatal sepsis in Tikur Anbesa University Hospital, Ethiopia. *Ethiopian Medical Journal*, 48 (1): 11-21, 2010.
- 45- STOLL B., HANSEN N., BELL E., et al.: Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. *Pediatrics*, 126 (3): 443-56, 2010.
- 46- MOHAMMADI P., KALANTAR E., BAHMANI N., et al.: Neonatal bacteremia isolates and their antibiotic resistance pattern in Neonatal Insensitive Care Unit (NICU) at Beasat Hospital, Sanandaj, Iran. *Acta. Medica Iranica*, 4 (1): 337-40, 2014.
- 47- SELIMOVIC A., SKOKIC F., BAZARDZANOVIC M., et al.: The predictive score for early-onset neonatal sepsis. *Turk J. Pediatr.*, 52 (2): 139-44, 2010.
- 48- BOSEILA S., SEOUD I., SAMY G., et al.: Serum neopterin level in early onset neonatal sepsis. *Journal of American Science*, 7 (7): 343-52, 2011.
- 49- KHAIR K.B., RAHMAN M.A., SULTANA T., et al.: Role of hematologic scoring system in early diagnosis of neonatal septicemia. *Bangabandhu Sheikh Mujib Medical University Journal*, 3 (2): 62-7, 2010.
- 50- SAKR M.A. and MAKSOUD H.M.A.: Evaluation of Serum Leptin Level as Early Marker in Early Onset Neonatal Sepsis. *Trends in Medical Research*, 11 (3): 113-7, 2016.
- 51- MADAVI D., AZIZ F. and AGRAWAL G.: Clinico-bacteriological profile and antibiotic sensitivity pattern of neonatal septicemia-a prospective observational study. *International Journal of Current Research and Review*, 7 (5): 13, 2015.
- 52- SHAH G.S., BUDHATHOKI S., DAS B.K., et al.: Risk factors in early neonatal sepsis. *Kathmandu University medical journal (KUMJ)*, 4 (2): 187-91, 2006.
- 53- SHALABY M.M., SOBEIH A.A., ABDULGHANY W.E., et al.: Mean platelet volume and serum uric acid in neonatal sepsis: A case-control study. *Annals of Medicine and Surgery*, 20 (2): 97-102, 2017.
- 54- BASU R. and BANDYOPADHYAY S.: Study on correlation between sepsis screening and blood culture in neonatal sepsis. *Morbidity and Mortality*, 6 (2): 7, 2014.
- 55- BEKHOF J., REITSMA J.B., KOK J.H., et al.: Clinical signs to identify late-onset sepsis in preterm infants. *European Journal of Pediatrics*, 172 (4): 501-8, 2013.
- 56- TAMAYO E., FERNÁNDEZ A., ALMANSA R., et al.: Pro-and anti-inflammatory responses are regulated simultaneously from the first moments of septic shock. *European Cytokine Network*, 22 (2): 82-7, 2011.
- 57- HISAMUDDIN E., HISAM A., WAHID S., et al.: Validity of C-Reactive Protein (CRP) for diagnosis of neonatal sepsis. *Pakistan Journal of Medical Sciences*, 31 (3): 527, 2015.

- 58- PANIGRAH P., CHANDEL D.S., HANSEN N.I., et al.: Neonatal sepsis in rural India: Timing, microbiology and antibiotic resistance in a population-based prospective study in the community setting. *Journal of Perinatology*, 37 (8): 911-21, 2017.
- 59- BHATT S., AGRAWAL P., PATEL A., et al.: Audit of sepsis in neonatal surgeries at tertiary-care level hospital in India. *Internasional Journal of Medical Sciences and Public Health*, 14 (12): 1715-9, 2015.
- 60- MATHAI E., CHRISTOPHER U., MATHAI M., et al.: Is C-reactive protein level useful in differentiating infected from uninfected neonates among those at risk of infection. *Indian Pediatr*, 41 (9): 895-900, 2004.
- 61- GARG D and AGRAWAL N.: Etiology and presentation of neonatal septicemia at tertiary care hospital of southern Rajasthan. *International journal of Medical Science and Education*, 11 (2): 12-20, 2014.
- 62- YADAV S.K. and GIRI A.: Bacteriological Profile of Neonatal Sepsis in a Neonatal Intensive Care Unit of a Tertiary Care Hospital of Eastern Nepal. *Journal of College of Medical Sciences-Nepal*, 15 (2): 93-7, 2019.
- 63- KESSLER U., EBNETER M., ZACHARIOU Z., et al.: Post-operative sepsis in infants below 6 months of age. *World Journal of Pediatrics*, 5 (2): 113-7, 2009.
- 64- OSIFO D.O. and ORIAIFO I.A.: Factors affecting the management and outcome of neonatal surgery in Benin City, Nigeria. *European Journal of Pediatric Surgery*, 18 (02): 107-10, 2008.
- 65- MAKKAR M., GUPTA C., PATHAK R., et al.: Performance evaluation of hematologic scoring system in early diagnosis of neonatal sepsis. *Journal of Clinical Neonatology*, 2 (1): 25, 2013.
- 66- NARASIMHA A. and KUMAR M.H.: Significance of hematological scoring system (HSS) in early diagnosis of neonatal sepsis. *Indian Journal of Hematology and Blood Transfusion*, 27 (1): 14-7, 2011.
- 67- ABDEL-HAKIM G., SHEHATA N., ABDEL-HAMEED W., et al.: Cord Blood Interleukin-6 as a Predictor of Early Onset Sepsis in High Risk Neonates. *Annals of Neonatology Journal*, 1 (2): 38-48, 2019.
- 68- GONZALEZ B.E., MERCADO C.K., JOHNSON L., et al.: Early markers of late-onset sepsis in premature neonates: Clinical, hematological and cytokine profile. *Journal of Perinatal Medicine*, 31 (1): 60-8, 2003.

## نسبة حدوث التسمم الوليدي والميكروبات المسببة له بوحدة العناية المركزة للأطفال حديثي الولادة بمستشفيات جامعة طنطا

يعد التسمم الدموي الوليدي أو ما يعرف بالانتان الوليدي من الأسباب الهامة والأساسية وراء ارتفاع معدلات المرض والوفيات في الأطفال حديثي الولادة وخصوصاً المبتسرين والرضع ذوي الوزن المنخفض عند الولادة.

وتعد مزرعة الدم هي حجر الأساس لتشخيص وإثبات التسمم الدموي الوليدي، ولكنها تتطلب على الأقل من ٤٨ ساعة حتى ٧٢ ساعة حتى تعطينا نتائج دقيقة وموثوقة، ومن عيوبها أيضاً أنها تعطي نتائج إيجابية فقط في نسبة من ٣٠ إلى ٧٠٪ من الأطفال المصابين بالتسمم الدموي الوليدي ورغم وجود أعراض وعلامات التسمم الدموي على المرضى الذين لديهم مزرعة الدم سالبة وأيضاً قد تكون غير متاحة في بعض المستشفيات وتتاثر في نتائجها بكمية الدم المستخدمة التي تم سحبها من الطفل المصاب والتي قد تكون قليلة، كما تتأثر بالمضادات الحيوية التي قد تكون تم إعطائها للأم ما قبل الولادة أو أثناء الولادة أو للجنين ما بعد الولادة كما تعتمد أيضاً على كمية الميكروب الموجودة بالدم وكفاءة المعمل.

الهدف من البحث: يتمثل الهدف من هذه الدراسة في تحديد نسبة حدوث التسمم الدموي الوليدي والميكروبات المسببة له بوحدة العناية المركزة للأطفال حديثي الولادة بمستشفيات جامعة طنطا على مدار عام.

مواد وأساليب البحث: أخذ التاريخ الطبي الكامل، إجراء فحص إكلينيكي كامل، عمل صورة دم كاملة وعمل مزرعة دم.

النتائج: لقد وجد أن هذه الدراسة قد شملت ٣٣٠ حالة لحديثي الولادة تم دخولهم لوحدة العناية المركزة للأطفال حديثي الولادة بجامعة طنطا وأسفرت النتائج عن:

– نسبة حدوث التسمم الدموي الوليدي بوحدة العناية المركزة للأطفال حديثي الولادة بجامعة طنطا لدينا حوالي (٤٣.٩٤٪) من إجمالي عدد الحالات التي تم دخولها لوحدة حديثي الولادة خلال سنة واحدة.

– كان الميكروب السائد المسبب للتسمم الدموي الوليدي بين الحالات الإيجابية لمزرعة الدم هو الكليسييلة بنسبة (٣١.٠٣٪)، يليه بكتريا المكورات العنقودية الذهبية بنسبة (٢٠٪).

– كانت الأعراض والعلامات المرضية الأكثر شيوعاً للإنتان فقدان القدرة على الرضاعة ورفضها بنسبة (٢٧.٥٩٪).

– يعتبر بروتين سي التفاعلي متفاعل طوري حاد غير محدد للإنتان ولكنه حساس للغاية في الدراسة الحالية.