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# Evaluation of Various Risk Factors in Neonatal Sepsis

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## ABSTRACT

**Background:** Neonatal sepsis (NS) is a clinical syndrome characterized by signs and symptoms of infection in neonatal period of life. It covers various systemic infections of newborn such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections (UTIs).

**Objective:** This study aims to evaluate the risk factors of neonatal sepsis and early detection of neonatal sepsis with easily accessible, inexpensive, and widely used laboratory tests.

**Patients and methods:** This cross section study was conducted during a period of 6 months, on cases admitted to Atfal Misr Neonatal Intensive Care Unit (NICU) on 80 newborns who were divided into 3 groups: group A (n = 22): proven NS, group B (n = 18): clinical NS and Group C (n = 40): apparently healthy control.

**Results:** In current study, there was significant positive correlation between MPV with age (r= 0.22 and p= 0.04), WBC (r= 0.66 and p= 0.0001) and CRP (r= 0.77 and p= 0.0001). On the other hand, there was significant negative correlation between MPV with HB (r= -0.74 and p=0.0001), platelet (r= -0.62 and p=0.0001) and uric acid (r= -0.37 and p= 0.001). In current study, there was significant positive correlation between uric acid with HB (r= 0.31 and p= 0.005), and platelet (r= 0.46 and p= 0.0001). On the other hand, there was significant negative correlation between uric acid with age (r=-0.11 and p=0.3), WBC (r= -0.42 and p=0.0001) and CRP (r= -0.42 and p= 0.0001).

**Conclusion:** The presence of the particular set of risk factors can help in deciding the empirical antibiotic and thereby prevent delay in starting appropriate treatment. The combined use of CRP and MPV should be considered in the early diagnosis of NS; however uric acid levels may only be utilized as an additional tool to support diagnosis.

**Keywords:** Sepsis, Neonatal, Risk Factors, CRP, MPV.

## INTRODUCTION

Sepsis is a life-threatening condition that occurs when the body's response to an infection injures its own tissues and organs. The pathogenesis of sepsis involves a series of complex regulatory interactions, with concomitant and often antagonistic processes, resulting in a dysregulated host response with both exaggerated inflammation and immune suppression. The pro-inflammatory response to sepsis leads to activation of the coagulation system with concurrent inhibition of anticoagulant mechanisms and fibrinolysis. Consequently, fibrinolytic and fibrinogen products are consumed, clot forms, and bleeding shows itself in the form of disseminated intravascular coagulation (DIC) [(1)].

Neonatal sepsis represents an important cause of morbidity and mortality especially in low-resource settings. Early diagnosis and prompt treatment of neonatal sepsis improves outcome [(2)]. It is estimated that 20% of neonates develop sepsis and approximately 1% deaths are related to sepsis [(3)].

Though blood culture is gold standard for diagnosis but it is not always positive even in presence of clinical features of sepsis in a neonate. A high index of suspicion and its confirmation are necessary for early diagnosis of sepsis. Various tests are traditionally applied [(4)].

Neonatal sepsis is usually accompanied by thrombocytopenia, so platelet indices have gained more importance in the recent studies; amongst, the indices related to morphology and platelet kinetics such as mean platelet volume (MPV), platelet volume distribution width (PDW) and plateletcrit (PCT) [(5)].

MPV is an important predictor for many diseases, high MPV in the first hours of life may reflect the presence of a risk factor for the development of necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH) and neonatal sepsis [(6)].

The negative predictive value of various sepsis screen parameters is too low to confidently rule out sepsis. There is no ideal test or combination of tests which are bench markers of an excellent test [(7)].

This study aims to evaluate the risk factors of neonatal sepsis and early detection of neonatal sepsis with easily accessible, inexpensive, and widely used laboratory tests.

## PATIENTS AND METHODS

This cross section study was conducted during a period of 6 months, on cases admitted to Atfal Misr NICU.

**Study populations were divided into three groups:**

- **Group A: Cases with ( proven sepsis):** 22 full-terms neonates who had clinical picture of sepsis (lethargy, body temperature changes, poor neonatal reflexes, poor feeding, vasomotor instability, low/high blood sugar, seizures, signs of CNS infections, jaundice, etc.) and laboratory signs of sepsis (positive blood culture high titre of CRP, increase MPV, thrombocytopenia, etc.) .
- **Group B: Cases with (Clinical sepsis):** 18 full term neonates who had clinical picture of sepsis or





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laboratory signs of sepsis (with negative blood culture).

- **Group C: Controls group:** 40 healthy non-septic (no clinical picture of sepsis and negative blood culture) neonates of the same age and sex.
- **Inclusion criteria:** All neonates who were admitted to NICU with clinical picture of sepsis with or without positive blood culture. And age and sex matched apparently healthy non septic (no clinical picture of sepsis and negative blood culture) neonates.

  **Exclusion criteria:** Inborn errors of metabolism. Major congenital anomalies. Cases of hypoxic ischemic encephalopathy. And chromosomal abnormalities.

**All patients were subjected to:**

*1- History Taking:*

- **Prenatal history:** history of prenatal care, urinary tract infection, chronic diseases, laboratory investigations (especially CRP and or blood culture) and history of pervious pregnancies.
- **Antenatal history**: preterm or full-term baby, mode of delivery, history of rupture of membranes, vaginal bleeding and temperature of mother.
- **Postnatal history**: history of baby at resuscitation room (APGAR score …etc.), cause of admission at neonatal intensive care unit (NICU), fever, feeding history (breast/ artificial feeding, total parentally nutrition (TPN)), invasive procedures (including intravenous cannulas, peripherally inserted central catheters, endotracheal tubes).

*2- Clinical Examination:*

- Apgar score at 1 and 5 minutes.
- Gestational age using Ballard scores [8].
- Systemic examination of the baby.
- Anthrometric measurements (body weight, length, body mass index (BMI), occipitofrontal circumference (OFC).

***3-Laboratory Investigations:***

**A. Complete Blood Count (CBC):** (by using Cell – dyn Ruby automatic machine " Abbott company - Germany").

**Samples were collected to see:**

- White blood count (leukocytosis/leukopenia).
- Hemoglobin level (anemia).
- Platelet count (thrombocytopenia/thrombocytosis).
- MPV.

**B. Blood culture:** (by using Bectec media) whenever possible.

**C. CRP with titre.**

**D. Serum Uric Acid**.

**Ethical approval:**

**The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study.**

***Statistical analysis***

Data were entered in excel sheet, and then transferred to SPSS version 15 for data analysis. The description of the data done in form of Mean±SD and range for quantitative data and frequency and proportion for qualitative data. Chi-square ($X^2$) test and Fisher's exact test of significance was used in order to compare proportions between two qualitative parameters and to compare between 3 groups; one way ANOVA with Tukey post-hook test. Pearson's correlation coefficient (r) test was used for correlating data. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant if $P < 0.05$.

**Results**

**Table (1): Demographic data of the studied groups (n=80)**

| | Group A (N=22) Mean±SD or N (%) | Group B (N=18) Mean±SD or N (%) | Group C (N=40) Mean±SD or N (%) | P value |
|---|---|---|---|---|
| **Age** | | | | |
| **Mean±SD** | 4.1±1.3 | 4.5±1.6 | 3.7±1.4 | 0.1 |
| **Birth weight** | | | | |
| **Mean±SD** | 3±0.4 | 2.9±0.3 | 3±0.1 | 0.4 |
| **Sex** | | | | |
| **Male** | 15 (68.2%) | 10 (55.6%) | 19 (47.5%) | 0.3 |
| **Female** | 7 (31.8%) | 8 (44.4%) | 21 (52.5%) | |
| **Mode of delivery** | | | | |
| **Normal** | 10 (45.5%) | 8 (44.4%) | 22 (55%) | 0.7 |
| **CS** | 12 (54.5%) | 10 (55.6%) | 18 (45%) | |
| **Birth trauma** | | | | |
| **-ve** | 22 (100%) | 17 (94.4%) | 40 (100%) | 0.1 |
| **+ve** | 0 (0%) | 1 (5.6%) | 0 (0%) | |
| **Feeding** | | | | |
| **No feeding** | 3 (13.6%) | 0 (0%) | 0 (0%) | 0.002* |
| **Breast feeding** | 6 (27.3%) | 4 (22.2%) | 24 (60%) | |
| **Artificial feeding** | 13 (59.1%) | 14 (77.8%) | 16 (40%) | |

**Table (2): Clinical criteria indicating sepsis in the studied groups (n=40)**

| | | Group A (N=22) N (%) | Group B (N=18) N (%) | P value |
|---|---|---|---|---|
| **Poor suckling** | **-ve** | 3 (13.6%) | 2 (11.1%) | 0.8 |
| | **+ve** | 19 (86.4%) | 16 (88.9%) | |
| **Lethargy** | **-ve** | 4 (18.2%) | 8 (44.4%) | 0.07 |
| | **+ve** | 18 (81.8%) | 10 (55.6%) | |
| **Poor Moro reflex** | **-ve** | 3 (13.6%) | 4 (22.2%) | 0.5 |
| | **+ve** | 19 (86.4%) | 14 (77.8%) | |
| **Respiratory distress** | **No** | 3 (13.6%) | 2 (11.1%) | |
| | **Grade 1** | 8 (36.4%) | 4 (22.2%) | |
| | **Grade 2** | 0 (0%) | 1 (5.6%) | 0.5 |
| | **Grade 3** | 2 (9.1%) | 4 (22.2%) | |
| | **Grade 4** | 9 (40.9%) | 7 (38.9%) | |
| **Pallor** | **-ve** | 3 (13.6%) | 4 (22.2%) | 0.5 |
| | **+ve** | 19 (86.4%) | 14 (77.8%) | |
| **Cyanosis** | **-ve** | 12 (54.5%) | 11 (61.1%) | 0.7 |
| | **+ve** | 10 (45.5%) | 7 (38.9%) | |
| **Jaundice** | **-ve** | 13 (59.1%) | 14 (77.8%) | 0.2 |
| | **+ve** | 9 (40.9%) | 4 (22.2%0 | |
| **Abdominal distension** | **-ve** | 2 (9.1%) | 14 (77.8%) | 0.0001* |
| | **+ve** | 20 (90.9%) | 4 (22.2%) | |
| **Intestinal sound** | **Sluggish or absent** | 6 (27.3%) | 3 (16.7%) | 0.4 |
| | **Audible** | 16 (72.7%) | 15 (83.3%) | |
| **Seizures** | **-ve** | 2 (9.1%) | 14 (77.8%) | 0.0001* |
| | **+ve** | 20 (90.9%) | 4 (22.2%) | |
| **Vomiting** | **-ve** | 14 (63.6%) | 13 (72.2%) | 0.6 |
| | **+ve** | 8 (36.4%) | 5 (27.8%) | |
| **Bleeding** | **-ve** | 9 (40.9%) | 12 (66.7%) | 0.1 |
| | **+ve** | 13 (59.1%) | 6 (33.3%) | |
| **HSM** | **-ve** | 13 (59.1%) | 13 (72.2%) | 0.3 |
| | **+ve** | 9 (40.9%) | 5 (27.8%) | |
| **Hyperthermia** | **-ve** | 12 (54.5%) | 14 (77.8%) | 0.1 |
| | **+ve** | 10 (45.5%) | 4 (22.2%) | |
| **Diarrhea** | **-ve** | 20 (90.9%) | 16 (88.9%) | 0.8 |
| | **+ve** | 2 (9.1%) | 2 (11.1%) | |
| **Sclerema** | **-ve** | 9 (40.9%) | 11 (61.1%) | 0.2 |
| | **+ve** | 13 (59.1%) | 7 (38.9%) | |
| **Umbilical sepsis** | **-ve** | 16 (72.7%) | 15 (83.3%) | 0.4 |
| | **+ve** | 6 (27.3%) | 3 (16.7%) | |
| **Skin infection** | **-ve** | 19 (86.4%) | 15 (83.3%) | 0.7 |
| | **+ve** | 3 (13.6%) | 3 (16.7%) | |
| **Hypoactive** | **-ve** | 6 (27.3%) | 3 (16.7%) | 0.4 |
| | **+ve** | 16 (72.7%) | 15 (83.3%) | |

***HSM: Hepatosplenomegally**

**Table (3): Comparison between studied groups regarding laboratory investigations (n=80)**

| | Group A (N=22) | Group B (N=18) | Group C (N=40) | P values |
|---|---|---|---|---|
| **WBCs (mcL) Mean±SD** | 21041±602 | 18250±788 | 6490±477 | P1 0.3<br>P2 0.0001*<br>P3 0.0001* |
| **HB (gm/dl) Mean±SD** | 9.6±1.8 | 11.2±3.06 | 15.2±1.3 | P1 0.04*<br>P2 0.0001*<br>P3 0.0001* |
| **Platelets (mcL) Mean±SD** | 120273±12304 | 141278±15681 | 264375±3476 | P1 0.7<br>P2 0.0001*<br>P3 0.0001* |
| **MPV (mcL) Mean±SD** | 15.7±3.3 | 14.9±3.5 | 6.2±0.4 | P1 0.5<br>P2 0.0001*<br>P3 0.0001* |
| **Serum uric acid (mg/dl) Mean±SD** | 2.41±0.44 | 2.47±0.49 | 2.8±0.4 | P1 0.8<br>P2 0.001*<br>P3 0.01* |
| **CRP (mg/L) Mean±SD** | 70.3±7.7 | 56.1±3.8 | 0 | P1 0.09<br>P2 0.0001*<br>P3 0.0001* |

*MPV: Mean Platelet Volume *CRP: C-reactive protein

P1 (p value between group A and B), P2 (p value between group A and C) and P3 (p value between group B and C).

**Table (4): Blood culture of studied groups (n=40)**

| | Group A (N=22) N (%) | Group B (N=18) N (%) | P value |
|---|---|---|---|
| **Blood culture** | | | |
| **Klebsiella** | 15 (68.2%) | 0 (0%) | |
| **CONS** | 5 (22.7%) | 0 (0%) | |
| **Pseudomonas** | 1 (4.5%) | 0 (0%) | 0.0001* |
| **E. Coli** | 1 (4.5%) | 0 (0%) | |
| **-ve blood culture** | 0 (0%) | 18 (100%) | |

***CONS: Coagulase Negative Staphylococci**

**Table (5): Correlation between MPV and uric acid with different variables.**

| Studied variables | MPV | | Uric acid | |
|---|---|---|---|---|
| | Pearson's r | P value | Pearson's r | P value |
| **Age (Years)** | 0.22 | 0.04* | -0.11 | 0.3 |
| **WBCs (mcL)** | 0.66 | 0.0001* | -0.42 | 0.0001* |
| **Hb (gm/dl)** | -0.74 | 0.0001* | 0.31 | 0.005* |
| **Platelets (mcL)** | -0.62 | 0.0001* | 0.46 | 0.0001* |
| **CRP (mg/L)** | 0.77 | 0.0001* | -0.42 | 0.0001* |
| **Serum uric acid (mg/dL)** | -0.37 | 0.001* | | |

*CRP: C-reactive protein

**Table (6): Risk factors of neonatal sepsis.**

| | Group A(N=22) Mean±SD or N (%) | Group B(N=18) Mean±SD or N (%) | Group C(N=40) Mean±SD or N (%) | P value |
|---|---|---|---|---|
| **PROM** | | | | |
| **-ve** | 12 (54.5%) | 9 (50%) | 38 (95%) | 0.0001* |
| **+ve** | 10 (45.5%) | 9 (50%) | 2 (5%) | |
| **UTI** | | | | |
| **-ve** | 16 (72.7%) | 12 (66.7%) | 37 (92.5%) | 0.03* |
| **+ve** | 6 (27.3%) | 6 (33.3%) | 3 (7.5%) | |
| **Intrapartum fever** | | | | |
| **-ve** | 12 (54.5%) | 14 (77.8%) | 38 (95%) | 0.001* |
| **+ve** | 10 (45.5%) | 4 (22.2%) | 2 (5%) | |
| **Feeding** | | | | |
| **-ve** | 3 (13.6%) | 0 (0%) | 0 (0%) | 0.002* |
| **Breast** | 6 (27.3%) | 4 (22.2%) | 24 (60%) | |
| **Artificial** | 13 (59.1%) | 14 (77.8%) | 16 (40%) | |
| **Mode of delivery** | | | | |
| **Normal** | 10 (45.5%) | 8 (44.4%) | 22 (55%) | 0.6 |
| **CS** | 12 (54.5%) | 10 (55.6%) | 18 (45%) | |
| **Mechanical ventilation** | | | | |
| **Yes** | 8 (36.4%) | 7 (38.9%) | ——— | 0.8 |
| **No** | 14 (63.6%) | 11 (61.1%) | | |
| **CVL** | | | | |
| **Yes** | 6 (27.3%) | 5 (27.8%) | ——— | 0.8 |
| **No** | 16 (72.7%) | 13 (72.2%) | | |

*PROM: Premature rupture of membranes
*CVL: Central Venous Line

## DISCUSSION

In current study, there was non-significant difference between the three groups in age, birth weight, and sex.

This is in agreement with **Shalaby *et al.*** [9] case-control study, which was done on 80 newborns divided into 3 groups: group A: clinical NS, group B: Proven NS and Group C: apparently healthy control. Their study showed that, there was no statistically significant difference between patient groups (group A and group B) and control group (group C) as regard to sex, and age.

In current study, there was non-significant difference between the three groups in mode of delivery and birth trauma.

In contrast to us, a meta-analysis by **Murthy *et al.*** [10]**,** was performed for gestational age, which was associated with a significantly higher odds of neonatal sepsis.

Also, our finding was supported by **Oncel *et al.*** [11]**,** study included a total of 100 newborns, 35 had proven sepsis (Group 1a) and 65 had clinical sepsis (Group 1b). The control group (Group 2) consisted of 50 healthy controls. The difference between patients with sepsis (Group 1 either a or b) and healthy controls (Group 2) with regard to mode of delivery was statistically insignificant.

In current study, as regard the type of feeding, the majority of group A and B received artificial feeding, while the majority of group C received breast feeding with significant difference between the three groups. Our findings indicate, however, that early breast milk may have a direct anti-infective action and may stimulate neonatal immune function as well as decreasing the ingestion of infectious pathogens. Close contact between the infant-mother and stimulation of the entero-mammary mucosa-associated lymphoid tissue system may also contribute [12].

This results was supported by **Bhargava *et al.*** [13]**,** showed that, neonates on expressed and formula feed had more chances of acquiring sepsis and they had 14.48 times more common in neonates with delayed enteral feeding as seen in our study.

In current study, as regard to clinical presentation, the incidence of poor suckling, lethargy, poor Moro reflex, respiratory distress and its grades, pallor, cyanosis, jaundice, absent intestinal sound, vomiting, bleeding, HSM, hyperthermia, diarrhea, sclerema, umbilical sepsis, skin infection and hypoactive were comparable in group A and B.

This in agreement with **Shalaby *et al.*** [9] who observed that the most frequent symptoms in their cases were poor suckling (87.5%), respiratory distress

(RD) (82.5%), lethargy and poor Moro reflex (77.5%) without significant difference between cases groups.

Similarly, the common clinical presentation in the **Jajoo *et al.*** [14] study was lethargy/refusal to feed 63 (77%), respiratory distress 36 (44%), and hypothermia 39 (47.5%).

These differences in percentage and predominance of signs may be due to the difference in the causative organisms and the course of sepsis or owing to the nonspecific clinical symptoms and signs of neonatal sepsis. Also, the variance in clinical features of neonatal sepsis further gives credence to the nonspecific nature of its manifestations and the need for a high index of suspicion.

On the other hand in current study, the majority of group A had significantly higher incidence of either abdominal distension or seizures than in group B. Necrotizing enterocolitis (NEC) and associated abdominal distension is an acute inflammatory necrosis of the bowel and may be the underlying cause of neonatal sepsis [2].

According to blood culture results in current study,, the most common organism in group A was klebsiella (68.2%), followed by coagulase negative staphylococci (CONS) in (22.7%), pseudomonas and E. Coli in (4.5%) while in group B, all had -ve blood culture with significant difference between both groups.

This comes in agreement with study by **El Nemer *et al.*** [15]**.** The study found that positive blood cultures were (100%) in the confirmed sepsis group and was (58.8%) in the suspected sepsis group. They found that klebsiella showed the highest incidence being (36.8%) followed by staph aureus (28.3%) followed by E. coli (18.4%) followed by pseudomonas (15.8%), and lastly staph. epidermidis (2.6%).

In current study, there was significant decrease in HB in group A than group B.

Also, there was significant increase in WBCs, MPV and CRP and significant decrease in HB, platelets and serum uric acid in group A than group C and in group B than group C. Most of our studied patients in the infected group were thrombocytopenic, which is similar to previous studies. 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 [16].

The evaluation of immune response during sepsis newborn showed that mediators of innate immune response, as C-reactive protein (CRP) was increased [17].

This was in agreement with **Abdel Fadil *et al.*** [18]**,** case-control study, which had been carried out in NICU of El-Minia University Hospital. The subjects were classified into one of the following three groups: Group I: clinical NS; Group II: culture proven NS; Group III: healthy control. The patients in Group II had the highest CRP levels, lowest platelet counts and lowest uric acid levels when compared to Group I and Group III ($p<0.05$ for all comparisons). Leukocyte, and MPV values were higher in Group I and Group II in comparison with Group III ($p<0.05$), although there was no difference between Group I and Group II for these parameters ($p>0.05$).

In current study, there was significant positive correlation between MPV with age, WBC and CRP. On the other hand, there was significant negative correlation between MPV with HB, platelet and uric acid.

This in agreement with **Shalaby *et al.*** [9]. Their study revealed that MPV showed a statistically significant positive correlation with WBCs and CRP, and a statistically significant negative correlation with platelet count.

This comes in agreement with the work of **Aydin *et al.*** [19]**,** who found negative correlations between MPV and platelet count ($r = -0.18$, $p = 0.002$) and uric acid levels ($r = -0.20$, $p < 0.001$). Positive correlations were found between MPV and leukocyte count ($r = 0.11$, $p = 0.04$), and CRP values ($r = 0.32$, $p < 0.001$).

In current study, there was significant positive correlation between uric acid with HB, and platelet. On the other hand, there was significant negative correlation between uric acid with age, WBC and CRP.

Also, according to **El-Mashad *et al.*** [20]**,** uric acid showed a significant positive correlation with the platelet count and a significant negative correlation with the I/T neutrophil ratio, MPV, and CRP.

This in accordance with **Shalaby *et al.*** [9] who found that serum uric acid (SUA) showed a statistically negative correlation with CRP.

In current study, there was significant difference in the incidence of PROM, UTI, intrapartum fever, and type of feeding; the majority of group A and B received artificial feeding, while the majority of group C received breast feeding. On the other hand, the mode of delivery, mechanical ventilation and CVL was comparable between the three groups. Whilst infections can occur in utero, birth represents an abrupt transition from a highly protected environment to exposure to a vast array of new pathogens ex utero. Parturition also places the baby in direct contact with maternal blood or genital secretions and infections may result, especially if there was prolonged or early rupture of membranes.

Similar to our study, **Yismaw *et al.*** [21]**,** reported that health related risk factors among mothers were 40% UTI, 26% foul-smelling vaginal discharge, 16% febrile illness, and 15% chronic illness. Out of the 423

neonates 47(11.1%) with (95% CI 8.2, 14.4) had positive blood culture for sepsis.

In contrast, **Anggara *et al.* [22],** showed that neonatal sepsis was predisposed by several maternal risk factors, with premature rupture of membrane (PROM) occurring in eight neonates (34.8%), and maternal fever during delivery in two infants (8.7%); the two groups differed non significantly.

Furthermore, a caesarean section and the duration of stay on admission also had a significant association with neonatal sepsis ($p<0.001$ and $p<0.001$, respectively) according to **Adatara *et al.* [23].**

In current study, the majority of group A and group B was alive and only 36.4% in group A and 38.9% in group B died. There was no significant difference between group A and B in outcome.

In agreement with current study, **El-Lahony *et al.* [24],** found no statistically significant difference between them as regards neonatal mortality between diagnosis (sepsis, neonatal infection, or no infection).

In current study, the majority of group A, B and C had no maternal history of chronic disease as DM and HTN with no significant difference between the three groups regarding the incidence of chronic disease.

In agreement, the **Adatara *et al.* [25],** study, a total of 103 neonates who had sepsis (cases) with their index mothers and 797 neonates who had no sepsis (controls) with their index mothers were enrolled. They found that, no significant difference between groups in maternal history of hypertensive disease ($P= 0.875$).

In contrast, rates of neonatal sepsis were higher among infants born to mothers with diabetes mellitus and gestational diabetes than among infants born to mothers without diabetes. Rates of neonatal sepsis were higher among infants born to mothers with chronic hypertension than among those born to healthy mothers ($p<0.001$) according to **Birch *et al.* [26].**

## CONCLUSION

To define effective strategies to prevent neonatal sepsis, risk-factor analysis should be done and possible sources of infections should be defined. The most identified bacteria causing neonatal sepsis were gram negative bacteria. As regard to risk factors of neonatal sepsis, artificial feeding, PROM, intrapartum fever, UTI, CS, CVL and mechanical ventilation significantly increased the incidence of sepsis.

The presence of the particular set of risk factors can help in deciding the empirical antibiotic therapy and thereby prevent delay in starting appropriate treatment.

The combined use of CRP and MPV should be considered in the early diagnosis of NS; however uric acid levels may only be utilized as an additional tool to support diagnosis.

Present study concluded that MPV increases significantly in neonates with sepsis while SUA decreases significantly in neonates with sepsis. So, MPV and SUA could be a useful early diagnostic marker in neonatal sepsis.

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