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**ORIGINAL ARTICLE**

# To Determine the Frequency of Mortality in Neonates with Sepsis Having High MPV

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## ABSTRACT

**Introduction:** A high MPV on admission in septic patients may be a useful indicator associated with poor outcome especially when it is associated with decreasing platelet numbers.
**Objective:** To determine the frequency of mortality in neonates with sepsis having high MPV.
**Material & Method:**
**Study design:** Descriptive case series study
**Settings:** NICU, Shifa International Hospital, Islamabad
**Methodology:** All newborns of both genders up to 28th day of life who have culturally proven sepsis or probable sepsis with gestational age of ≥28 weeks, birth weight > 700gms were enrolled. The initial investigations on admission was carried out as per NICU septic screening protocol includes complete blood count CBC, C-Reactive Protein (CRP), electrolytes, renal function tests, blood C/S, urine R/E urine C/S, x-ray chest while the other investigations including CSF analysis, gram staining and culture, tracheal secretions and catheter tips for culture and sensitivity are performed when indicated clinically. Outcome was measured till discharge or death.
**Results:** Mean age of the patients was mean ±SD 6.58 ±5.72 days. Most of the neonates 59 (62.1%) were males whereas 36 (37.9%) were females. Mean CRP, TLC count, platelet count, TLC count at baseline were 21.23 ±42.34, 15190.5 ±4619.32, 254348.42 ±101479.87 respectively. MPV at baseline 10.56 ±0.85 and at 48 hours was 9.96 ±0.81 respectively. Mortality was observed in 22 (23.2%) neonates.
**Conclusion:** The frequency of mortality was found to be 23.2% in neonates with sepsis having high MPV.
**Keywords:** Mortality, Neonates, Sepsis, Mean Platelet Volume

## INTRODUCTION

Neonatal Sepsis is one of the leading cause of neonatal mortality and morbidity in developing countries. The proportion of neonatal mortality among children under the age of five has grown during the last 2 decades[1]. Pakistan has still high neonatal mortality rate of 55 per 1,000 live births[1]. Infection accounts for 36% and remains the most common cause of neonatal mortality. The incidence of neonatal sepsis in Pakistan is reported in the range of 1.13-3.8/1000 live births[2]. The disease is rapidly progressive and associated with 1.6 million deaths annually in developing countries.

The early signs and symptoms of sepsis in neonates are usually subtle and non-specific that can lead to critical delay in diagnosis and initiation of appropriate and aggressive management.

Many of the laboratory markers are used as early prognostic indicators in sepsis like high CRP, leucocytosis or leucopenia and thrombocytopenia. As CRP carries the positive predictive value up to 91 % and negative predictive value 83% for sepsis[3] and these indicators are considered very significant however the platelet indices including Mean platelet volume (MPV) have been reported to be reliable prognostic indicator in neonatal sepsis, the advantage of MPV remains that it's a part of complete blood count (CBC) requiring no extra cost or a separate blood specimen and it is performed by automated hematology analyzer by either optical or electrical impedence method that is available at most district level hospitals in Pakistan[4,5].

MPV is defined as the mean size of platelets in blood volume and it is most significant among all platelet indices having the positive predictive value (PPV) 76 % and negative predictive value 63% for sepsis. MPV is directly related to the rate of platelet production in bone marrow and is inversely related to the degree of platelet maturation[6,7]. The severity and invasiveness of systemic infection is directly related to increase in MPV. MPV tends to rise whenever there is platelet destruction as observed in sepsis due to inflammatory cytokinese[8].

A high MPV on admission in septic patients may be a useful indicator associated with poor outcome especially when it is associated with decreasing platelet numbers[9]. In a recent prospective study Oncel et al reported high MPVs in septic newborns. Catal F et al concluded that high MPV may simply predict the severity of sepsis in preterm infants and its serial monitoring can predict the progression of sepsis or response to therapy. He reported a cut-off value of 10.35 fl of MPV associated with sepsis and the value of 10.75 as a cut-off associated with high mortality with the sensitivity of 95.2% & specificity of 84.9% [10]. Fernando et al recorded mortality of 46% in his adult patients who had high MPVs on admission in a critical care unit[11].

Our study is planned to determine the outcome for high MPV in neonates admitted with probable or culture proven sepsis as there is limited data available in this population. More so, we are in desperate need to limit our neonatal mortality and associated morbidity with limited available resources.

## MATERIAL AND METHODS

This descriptive case series was conducted 1st December to 30th May from Neonatology Department, NICU Shifa International Hospital, Islamabad. Sample size of 95 cases

is estimated using 95% confidence level, anticipated population proportion=46% 11 and absolute precision=10%

All newborns of both genders up to 28th day of life who have culturally proven sepsis or probable sepsis with gestational age of ≥28 weeks, Birth weight > 700 gms were included. All neonates with Congenital Anomalies, Congenital heart defects, Hypoxic Ischemic Encephalopathy, RDS and those who have received red blood cell and platelet transfusion in last 7days were excluded.

Informed consent was obtained from the parents. Demographic data (name, age, parity, gestational age, BMI) will be recorded. The initial investigations on admission was carried out as per NICU septic screening protocol includes complete blood count CBC, C-Reactive Protein (CRP), electrolytes, renal function tests, blood C/S, urine R/E urine C/S, x-ray chest while the other investigations including CSF analysis, gram staining and culture, tracheal secretions and catheter tips for culture and sensitivity are performed when indicated clinically.

Blood was drawn by nursing staff with proper aseptic measures, samples was taken to the lab by lab transporter and it takes maximum of 1 hour between drawing of blood and sample processing. CBC is performed using Exe5000 (Sysmax, Japan). Date was collected by using designed proforma. Outcome was measured till discharge or death.

The data was analyzed through SPSS V20. age, gestational age, weight, mean platelets volume, CRP, Total leucocyte count and platelet count was presented by mean ±SD. Gender, mortality was presented as percentage & frequency. Data was stratified for age, gender, gestational age, baseline MPV, probable or proven sepsis. Post stratification chi-square was applied keeping a p-value <0.05 as significant.

## RESULTS

Total 95 neonates, the mean age was 6.58 ±5.72. Majority of the neonates 65 (68.4%) were presented with ≤7 days of age whereas 30 (31.6%) neonates were presented with >7 days of age. There were 59 (62.1%) were males whereas 36 (37.9%) were females. Table: 1

The mean gestational age was 36.85 ±2.70. 50 (52.6%) had ≤37 weeks of gestational age whereas 45 (47.4%) had>37 weeks of gestation. Table: 2

The mean weight was 2.8 ±0.7 Kg whereas mean CRP, TLC count, platelet count, MPV count at baseline and MPV count at 48 hours were 21.23 ±42.34, 15190.5 ±4619.32, 254348.42 ±101479.87, 10.56 ±0.85 and 9.96 ±0.81 respectively. Significant difference was observed among mean MPV count at baseline and at 48 hours (p-value <0.001) Table: 3

Table 1: Distribution of Age & Gender

| | | Frequency(%) |
|---|---|---|
| Age | Mean ±SD | 6.58 ±5.72 |
| | <7 days | 65(68.40%) |
| | >7days | 30(31.60%) |
| Gender | Male | 59(62.10%) |
| | Female | 36(37.90%) |

Probable sepsis was observed in 93 (97.9%) neonates while proven sepsis was observed in 16 (16.8%) neonates. Mortality was observed in 22 (23.2%) neonates. Table: 4

Significant association of mortality was observed with proven sepsis and mortality (p-value <0.001) whereas age, gender, gestational age and probable sepsis showed insignificant association (p-value >0.05). Table: 5.

Table 2: Distribution of Gestational Age in weeks

| | | Frequency (%) |
|---|---|---|
| Gestational Age | Mean ±SD | 36.85 ±2.70 |
| | <37 | 50(52.60%) |
| | >37 | 45(47.40%) |

Table 3: Statistics of Weight, CRP, TLC, Platelets, MPV level at baseline and 48 hours

| | Mean + SD |
|---|---|
| Weight(Kg) | 2.8 ±0.71 |
| CRP level | 21.23 ±42.34 |
| TLC | 15190 ±4619.32 |
| Platelets | 245648.42 ±101479.87 |
| MPV level at baseline | 10.56 ±0.85 |
| MPV level at 48 hours | 9.96 ±0.81 |

Table 4: Frequency Distribution of Probable & Proven Sepsis & Mortality

| | Yes | No |
|---|---|---|
| Probable Sepsis | 93(97.90%) | 2(2.10%) |
| Proven Sepsis | 16(16.80%) | 79(83.20%) |
| Mortality | 22(23.20%) | 73(76.80%) |

Table 5: Comparison of mortality with respect to age of the neonates

| | | Mortality | | P value |
|---|---|---|---|---|
| | | Yes | No | |
| Age | <7 days | 47(64.4%) | 18(81.8%) | 0.12 |
| | >7 days | 26(35.6%) | 4(18.2%) | |
| Gender | Males | 1(1.4%) | 0 | 0.37 |
| | Females | 25(34.2%) | 11(50%) | |
| Gestational Week | <37 weeks | 41(56.2%) | 9(40.9%) | 0.232 |
| | >37 weeks | 32(43.8%) | 13(59.1%) | |
| Probable Sepsis | Yes | 72(98.6%) | 21(95.5%) | 0.411 |
| | No | 1(1.4%) | 1(4.5%) | |
| Proven Sepsis | Yes | 2(2.7%) | 14(63.6%) | 0.001 |
| | No | 71(97.3%) | 8(36.4%) | |

## DISCUSSION

Sepsis is a complex syndrome with significant morbidity and mortality. Despite current advances in diagnosis, it may be challenging to establish precise diagnostic criteria. Developmental differences between adults % children lead to distinct changes in the pathophysiology, epidemiology diagnosis & management in children compared with adults[12]. The proportion of neonatal mortality among children under the age of five has increased during the last 20 years. Pakistan's neonatal death rate remains high, at 55 per 1,000 live births[1].

Platelet indices are a set of measurements that are used to determine platelet count & morphology. The platelets amount in blood can also be maintained in a balanced state through regeneration and removal under Physiological conditions. As a result, both the numbers of platelets & their morphology remain constant. Under pathophysiological1conditions, any factor that could inhibit

platelets from regenerating, Enhance their activation or accelerate their mortality once their capacity for self-regulation is overwhelmed, resulting the changes in platelet count & morphology, as well as a variation in platelet indices[13]. Platelet volume is measured by MPV, but when platelet consumption rises, the bone marrow generates extra immature platelets. As a result, the MPV value increases[13].

According to Catal et al. and other studies, Platelet indices could not differentiate between different bacteria or between culture confirmed & non-culture proven in preterm newborns with sepsis. He reported a cut-off value of 10.35 fl of MPV associated with sepsis and the value of 10.75 as a cut-off associated with high mortality with the sensitivity of 95.2% & specificity of 84.9% [9,10].

In this study, mortality was observed in 22 (23.2%) neonates. However, in Fernando et al recorded mortality of 46% in his adult patients who had high MPVs on admission in a critical care unit.(11) R İşgüder, et al said that 32(17.2%) mortality in neonates who had high MPV on admission[14].

Invasive infections are thought to be responsible for more than 1.4 million newborn deaths per year around the world. However, even in countries with good medical standards, newborn sepsis significantly increases morbidity & mortality[15].

Thrombocytopenia is commonly associated with gram-negative or fungal sepsis and is mostly caused by intravasal consumption, according to clinical experience in neonatal intensive care units, although increase thrombopoietin, during sepsis serum levels have been described[16].

## CONCLUSION

The frequency of mortality was found to be 23.2% in neonates with sepsis having high MPV.

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