ASSOCIATION BETWEEN MEAN PLATELET VOLUME AND CLINICALLY SUSPECTED NEONATAL SEPSIS

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ABSTRACT

Background: Neonatal sepsis is the major cause of mortality and morbidity in newborn both in developed and developing countries. Diagnosis is mainly done by clinical signs and symptoms and none of the investigations has been proven accurate for diagnosis of neonatal sepsis. This study demonstrated the association between mean platelet volume (MPV) and clinically suspected neonatal sepsis.

Method: Total 92 newborns with neonatal sepsis were included and Complete blood count [including MPV], C-reactive protein and blood C&S were done on Day 1 of sepsis period before commencing antibiotics and serial measurement were done on Day 3 and Day 7.

Results: MPV started to increase on Day 1(mean MPV=10.57 ± 0.87). Various clinical and laboratory findings may help in making diagnosis of neonatal sepsis. Blood culture remains as the gold standard diagnostic tool for neonatal sepsis but is time consuming and may produce false negative results, which can be attributed to the difficulties in discriminating a true infection from sample contamination[2].

The measurement of MPV has become available since 1970. MPV value increases as a result of raised platelet highest on Day 3 and decreased after appropriate antibiotics, and significant difference was observed between Day 3 and Day 7 (mean MPV; Day 3 =10.61 ± 0.98, Day 7 =10.39 ± 0.82, *p*=0.036).

Conclusion: MPV can be used to predict the diagnosis of neonatal sepsis and the response of antimicrobial treatment and is more useful in late onset sepsis, preterm and low birth weight infants.

INTRODUCTION

Neonatal sepsis is defined as a clinical syndrome of bacteremia with systemic signs and symptoms of infection in the first four weeks of life. Early onset neonatal sepsis is defined as infection occurring within 72 hours of birth.

MPV has high sensitivity and specificity for diagnosis of sepsis especially when combined with CRP [4]. A MPV value of 10.35fL was identified as the cut off value in patients probably resulting in sepsis with a sensitivity of 97.8% and specificity 78.7% (AUC = 0.949; $p < 0.001$) [5].

Although there are some studies of neonatal sepsis in Myanmar, none of these included measuring mean platelet volume as a predictive marker for neonatal sepsis. This study demonstrated the early rise of mean platelet volume in both clinical and proven sepsis and also detected the changes of it in response to disease activity.

MATERIALS AND METHODS

This was a hospital-based prospective study done in Neonatal intensive care unit of Central Women Hospital (Yangon) and the study period is from 1st January 2016 to 31st December 2016. A total of

92 neonates who met the inclusion criteria of clinical and proven sepsis were included in the study. These newborns were diagnosed as neonatal sepsis if they had one of the signs and symptoms of sepsis according to WHO criteria with raised CRP. History including maternal risk factors and clinical presentations were recorded and physical examinations were done. The day on which signs and symptoms of neonatal sepsis started was assumed as Day 1. Laboratory investigation such as CBC, CRP, blood culture & sensitivity on Day 1 was performed before commencing antibiotics. Serial measurements (CBC including MPV and CRP) were done on Day 3 and Day 7. The collected data were analyzed by using SPSS software version 16.

RESULTS

Among the study population, 40.2% were term infants, 28.3% late prem and 31.5% preterm infants. Regarding the sex distribution, 63% were males and 37 % were females. 33.7 % of the study infants had normal birth weight, 37% had low birth weight, 29.3% had very low birth weight. In the present study, 51 infants had early onset sepsis and 41 infants had late onset sepsis. Only 17.4 % had positive blood culture. The mean MPV was highest on Day 3 (10.61±0.98) and the difference between mean MPV of Day 3 and Day 7 were statistically significant (p=0.03). On Day 1 and 3, mean MPV of late onset sepsis is significantly higher than early onset. The more preterm the infant, the higher MPV value on Day 1,3,7. The mean MPV was highest in very low birth weight group in Day 3 and 7 of the sepsis period and these were statistically significant.

DISCUSSION

Neonatal sepsis is the life threatening emergency and any delay in treatment may be fatal. If diagnosed early and treated aggressively with antibiotics and good supportive care, it can be possible to save most cases of neonatal sepsis. Despite many screening tests being employed in the early diagnosis of sepsis investigating the possibility of infection, none of these methods has been proven sufficiently accurate when used alone and the sensitivity of these tests varies between 30% and 90%[6].

In the present study, nearly two third of the infants were late preterm and preterm and almost two third of the infants were low birth weight. 58 infants (63%) of the study population were male whereas 34 infants (34%) were female. Out of the 92 infants, bacterial pathogens were isolated from 16 infants. The positivity rate was 17.4%. A total of 16 proven neonatal sepsis in the present study was small and may have in incorrect estimation. There may be a flaw in technique of blood culture collection, volume of blood, or prior antibiotics given to mother. Culture is the gold standard for detection of bacteremia. However, negative culture result occurs sometimes although they are presented with highly suggestive clinical signs and symptoms for infection.

In the present study, early onset sepsis (55.4%) was documented more as compared to late onset sepsis (44.6%). The study of Hnin-Thuzar-Aung (2005)[7] reported that late onset sepsis (27.6%) was more common than early onset sepsis (21.9%). Similar observation has been made by Hnin Yee Win (2004)[8]. Perhaps it was due to the fact that mortality in early-onset cases is relatively high and some

neonates might have died before being admitted to the hospital. In the present study, all of the study population was inborn patients and there was more opportunity to detect early onset sepsis.

MPV levels were significantly higher in newborns with sepsis compared to healthy group. Mean baseline levels of CRP and MPV were significantly higher in proven sepsis compared to clinical sepsis[9]. No significant changes were found in MPV of infants between those with early onset and late onset sepsis. Additionally, these levels were not different between culture proven and non-proven sepsis[5]. In contrast, the present study showed significantly higher MPV in infants with late onset sepsis than in those with early onset sepsis on Day 1 and Day 3 and there was a statistical significance in association of MPV and type of sepsis according to onset. This means that MPV is more useful in the diagnosis of late onset sepsis.

Regarding the gestational age, preterm infants had higher MPV (preterm; 10.1 ± 1.3, term; 9.7 ± 1.2, p=0.002)[4]. Similarly, in the present study, the more preterm the infant groups, the higher the MPV values on all consecutive days and it was statistically significant (Day 1; p=0.000, Day 3; p=0.001, Day 7; p=0.006) . This means that MPV changes are more pronounced in premature neonates and it may be useful as a predictor of sepsis in preterm infants. The present study documented that MPV changes were inversely related to birth weight especially on Day 3 and Day 7 which were statistically significant (Day 3; p=0.001, Day 7; p=0.007). Therefore, MPV may be useful in the diagnosis of sepsis in low birth weight infants.

Regarding the serial MPV changes in the present study, on the first day of the sepsis period, MPV started to increase (Day 1; mean MPV=10.57 ± 0.87). The value was highest on Day 3 and after appropriate antibiotics, MPV decreased and significant difference had been observed between Day 3 and Day 7 (Day 3; mean MPV=10.61 ± 0.98, Day 7; mean MPV=10.39 ± 0.82, p=0.036). It might be useful for both diagnosis, follow up and antimicrobial response in neonatal sepsis.

CONCLUSION

In the present study, it was found that early onset sepsis was more common than late onset sepsis. The blood culture positivity rate was 17.4% in the present study which was lower than some local and international studies. The results of the present study demonstrated that MPV levels were significantly increased during the sepsis period, reached the maximum level at the height of severity and then declined after treatment that was thought to be a response to the treatment. Additionally, MPV values were significantly higher in late onset sepsis than in early onset sepsis. It demonstrated that MPV is more useful in diagnosis of late onset sepsis. Moreover, MPV changes were more pronounced in preterm infants and low birth weight infants. This means that it may be useful as a predictor of sepsis in preterm infants and low birth weight infants.

As a result, it has suggested that MPV can be used in addition to other markers and clinical findings to predict the diagnosis of neonatal sepsis and the response to antimicrobial treatment. However this is the first study in Myanmar to demonstrate significant changes of MPV in neonate

with sepsis and possible limitations of this study may be relatively small study population compared to the international studies and the lack of control group. Therefore, to attain the more precise results, similar studies with larger study population should be done in Myanmar.

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TABLES

Table (1) Profile of neonates enrolled for study (n=92)

Characteristics		Number	%
Gestation	Term	37	40.2
	Late-prem	26	28.3
	Preterm	29	31.5
Sex	Male	58	63
	Female	34	37
Birth weight (kg)	≥2.5	31	33.7
	1.5 – 2.49	34	37.0
	1-1.49	27	29.3
Mode of delivery	NSVD	40	43.5
	Instrumental	4	4.3
	LSCS	48	52.2
Sepsis	Early onset	51	55.4
	Late onset	41	44.6
Blood culture	positive	16	17.4
	negative	76	82.6

Table (2) Comparison between mpv values of day 1, 3 and 7 of sepsis in study infants

	MPV	Frequency	Mean	Standard Deviation	Pair t test	P value
Pair 1	MPV1	92	10.57	0.87	-0.39	0.69
	MPV3	92	10.61	0.98		
Pair 2	MPV1	92	10.57	0.87	1.76	0.08
	MPV7	92	10.39	0.82		
Pair 3	MPV3	92	10.61	0.98	2.12	0.03
	MPV7	92	10.39	0.82		

Table (3) Onset of the sepsis of study infants and mean platelet volume

	Onset of sepsis	Frequency	Mean	Standard Deviation	t test	P value
MPV1	early onset (<72 hours)	51	10.32	0.75	-3.12	0.002
	late onset (>72 hours)	41	10.88	0.93		
MPV3	early onset (<72 hours)	51	10.30	0.86	-3.48	0.001
	late onset (>72 hours)	41	10.99	1.00		
MPV7	early onset (<72 hours)	51	10.33	0.78	-0.79	0.430
	late onset (>72 hours)	41	10.47	0.87		

Table (4) Gestational age of study infants and mean platelet volume

MPV	Gestational age	Frequency	Mean	Standard Deviation	F test	P value
MPV1	Term	37	10.21	0.68	8.42	0.000
	Late prem	26	11.07	0.94		
	Preterm	29	10.58	0.84		
MPV3	Term	37	10.17	0.92	7.01	0.001
	Late prem	26	10.83	0.99		
	Preterm	29	10.96	0.86		
MPV7	Term	37	10.06	0.63	5.36	0.006
	Late prem	26	10.58	0.77		
	Preterm	29	10.64	0.95		

Table (5) Birth weight of study infants and mean platelet volume

MPV	Birth Weight	Frequency	Mean	Standard Deviation	F test	P value
MPV1	Normal birth weight (≥2.5kg)	31	10.28	0.71	2.66	0.075
	Low birth weight (1.5 to 2.49 kg)	34	10.70	0.67		
	Very low birth weight (1 to 1.49 kg)	27	10.74	1.17		
MPV3	Normal birth weight (≥2.5kg)	31	10.15	0.98	8.07	0.001
	Low birth weight (1.5 to 2.49 kg)	34	10.62	0.86		
	Very low birth weight (1 to 1.49 kg)	27	11.12	0.91		
MPV7	Normal birth weight (≥2.5kg)	31	10.05	0.60	5.22	0.007
	Low birth weight (1.5 to 2.49 kg)	34	10.44	0.93		
	Very low birth weight (1 to 1.49 kg)	27	10.71	0.77		