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Association between Adiponectin Level and Mean Platelet Volume in Neonates with Respiratory Distress Syndrome: A Prospective Cohort Study

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ABSTRACT

Background: Respiratory distress is a serious condition affecting preterm neonates. The present study was designed to evaluate the association between mean platelet volume (MPV) and adiponectin (APN) levels and the development of respiratory distress syndrome (RDS) in preterm neonates.

Methods: This prospective cohort study was conducted at a tertiary hospital. The target population was preterm neonates (≤ 34 weeks) admitted to the incubator and diagnosed with RDS. A control group was recruited and composed of age-matched neonates seen at the delivery room and required no admission or ventilatory support. Blood samples were withdrawn on days 1 and 7 of life for a complete blood count and another one for APN level measurement .

Results: The study group showed a higher MPV at day 1 and day 7 than the control group (P<0.001) and lower mean APN at day 1 and day 7 than the control group (P<0.001). The MPV had cut-off levels of more than 7.7 (sensitivity of 86.96% and specificity of 100%) and 8.15 (sensitivity of 78.26% and specificity of 91.3%) on days 1 and 7, respectively, to predict RDS. The APN had cut-off levels ≤ 37 (sensitivity of 86.96% and specificity of 60.87%) and ≤ 22.4 (sensitivity of 82.61% and specificity of 69.57%) on days 1 and 7, respectively, to predict RDS.

Conclusion: Based on the findings of the present research, the MPV significantly increased while APN levels were lower in preterm neonates with RDS. Both markers predicted RDS development significantly.

Keywords: Adiponectin, Mean platelet volume, Neonates, Preterm, Respiratory distress syndrome

Introduction

Respiratory distress syndrome (RDS) is a fundamental cause of neonatal intensive care unit admission and causes significant morbidity and mortality in preterm infants. The RDS develops in the first 4–6 h of life and is manifested by increased respiratory rate, respiratory distress with retraction, grunting, and cyanosis (1).

The RDS has an overall incidence of 2–3%. However, it occurs at greater incidence in preterm infants (50% in infants born between 26 and 28 weeks). Additionally, the incidence decreases with advanced gestational age (< 20–30% of infants at 30–31 weeks) (1). Surfactant deficiency causes RDS. Other pathophysiologic processes included fibrin deposition in the alveolar spaces (2). Platelets play a significant role in fibrin deposits, and decreased platelet count manifests in infants with RDS (3). Platelet size was investigated in patients with platelet-related disorders with no data about mean platelet volume (MPV) and preterm infants with RDS (3, 4).

Adiponectin (APN) is a hormone with pleiotropic effects on pulmonary cells (5). It has an anti-inflammatory effect and vascular protective function in the lung (6). The role of APN in RDS development in humans is not properly investigated; however, animal studies reported an association between hypoadiponectinemia and

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RDS (5). Accordingly, the present study evaluated the association between MPV and APN levels and RDS development in preterm infants.

Methods

A prospective cohort study was conducted in the neonatal intensive care unit at a tertiary hospital from May 2019 to May 2021. The target population was preterm neonates whose gestational age was ≤ 34 weeks assessed by the new Ballard score (7) admitted to the incubators and diagnosed with RDS according to the following inclusion and exclusion criteria. Inclusion criteria were: a) preterm neonates ≤ 34 weeks, and b) diagnosed with RDS. The presence of clinical (tachypnea, grunting, cyanosis on the first day of life, requiring mechanical ventilation including oxygen, continuous positive airway pressure, and mechanical ventilation) and radiological (ground glass opacification, increasing hypoaeriation, and air bronchograms) signs confirmed the diagnosis of RDS (1). Exclusion criteria consisted of a) neonates of mothers with severe preeclampsia, diabetes mellitus, or infections as chorioamnionitis, b) women taking anti-epileptic drugs, c) women receiving any medication affecting platelet production, and d) premature infants with significant perinatal hypoxia, and sepsis. A control group was recruited and composed of age-matched neonates who needed no admission or ventilatory support.

Blood samples were withdrawn on days 1 and 7 of life. Samples were withdrawn for complete blood count and APN level measurement (by enzyme-linked immunosorbent assay).

Sample size

- The sample size was calculated using the following formula (8):

$$n = \left[\frac{Z_{\propto/2}}{\mathrm{E}}\right]^2 * \mathrm{P}(1-\mathrm{P})$$

where:
n = sample size
$\mathbf{Z_{\alpha/2}}$ = 1.96 (The critical value that divides the central 95% of the Z distribution from the 5% in the tail)
E = Margin of error/Width of confidence interval = 5.1%
P = Prevalence/proportion in the study group = 3% (9)
Therefore, by calculation, the sample size was equal to 46 patients. This number was divided equally into two groups (23 patients in each group) after adding 10% dropout.

Ethical approval

This study was conducted after obtaining the approval of the Research Ethics Committee at the Faculty of Medicine, Suez Canal University, on 24/6/2019, with a reference number of 3882#.

Statistical analysis

The data was collected, coded, and entered into the computer via Microsoft Excel 2013 program. Statistical Package for Social Sciences (SPSS) for Windows version 20.0 (SPSS, Chicago, IL, USA) was used for data analysis. Data were analyzed and presented as numbers and percentages using tables and graphs with the CI at 95%, a *P*-value of less than 0.05 was considered statistically significant. Kruskal-Wallis, Mann-Whitney U, and Spearman's correlation tests in measuring non-parametric data were used. While t-test, Chi-square, and ANOVA tests were used in analyzing parametric data. A receiver operating characteristic (ROC) curve was developed.

Results

Table 1 shows the demographic data of both groups. According to the demographic data, no statistical difference was observed between both groups.

Table 2 demonstrates the MPV and APN levels between the control and study groups. The MPV on Day 1 and Day 7: a statistically significant difference was found between the two groups. The study group showed a higher mean MPV on day 1 and day 7 than the control group (P<0.001). The APN on day 1 and day 7: there was a statistically significant difference between the two groups. The study group showed a lower mean APN on day 1 and day 7 than the control group (P<0.001).

Table 1. Demographic information of the control and the study groups

Variable		Control Group (N=23)	Study Group (N=23)	*P*-value
Gender	Male	11 (47.8%)	12 (52.2%)	0.768
	Female	12 (52.2%)	11 (47.8%)	
Mode of Delivery (MOD)	Vaginal Delivery	5%).10 (43	6 (26.1%)	0.2
	Cesearian Section(CS)	13(56.5%)	17 (73.9%)	
Multiple Pregnancies		1 (4.35%)	1 (4.35%)	0.38
Gestational Age		33.0 ± 0.59	33.3 ± 0.57	0.092
Birth Weight (gm)		1806 ± 135	1532 ± 234	0.165

Table 2. Comparison between control and study groups in Mean Platelet Volume and Adiponectin level

Variable		Control Group (N=23)	Study Group (N=23)	*P*-value
Mean Platelet Volume	D1	7.2 ±0.2	8.4 ± 0.8	< 0.001
	D7	7.4 ± 0.6	9.4 ± 2.5	0.001
Adiponectin Level	D1	44.8 ± 17.7	26.6 ± 12.6	< 0.001
	D7	32.4 ± 18	17.6 ± 7	0.001

Figure 1. The MPV on day 1 at a cut-off level of more than 7.7 had a sensitivity of 86.96% and specificity of 100%, meanwhile on day 7, a cut-off level of more than 8.15 had a sensitivity of 78.26% and specificity of 91.3% to predict RDS.The APN on day 1 at a cut-off level less than or equal to 37 had a sensitivity of 86.96% and specificity of 60.87%; meanwhile, on day 7, a cut-off level less than or equal 22.4 had a sensitivity of 82.61% and specificity of 69.57% to predict RDS.

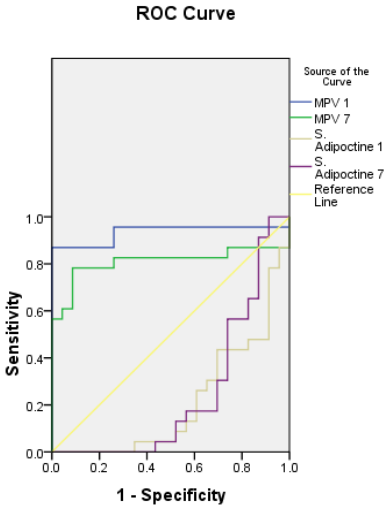

Figure 1. Receiver operating characteristic curve for MPV and APN levels to predict RDS

Discussion

A significant difference in the MPV was observed between neonates with RDS and the control group. Neonates with RDS reported increased MPV than their counter peers. This finding is in agreement with previous studies reporting significantly higher MPV in RDS patients (10-12). Additionally, another study reported increased MPV in neonates with transient tachypnea and those requiring mechanical ventilation (13). This effect has been attributed to RDS-related hypoxia and oxidative stress, affecting young platelets' bone marrow production (10). Moreover, MPV was considered a reflection of platelet production, explaining its association with some disease affecting the bone marrow as perinatal hypoxia, inflammation, or infections (12).

The MPV cut-off levels of more than 7.7 and 8.15 on days 1 and 7 predicted the development of RDS significantly. Another study reported a level of 8.11 to predict RDS-related mortality (14). Another research reported slightly lower levels (15) which would be rendered to different study populations as they reported on extremely preterm neonates with bronchopulmonary dysplasia. This highlighted the predictive role of MPV in developing RDS in the first 48 h (16).

The mean APN levels in RDS patients on days 1 and 7 were statistically lower than those of patients without RDS. Another study reported increased levels of APN during RDS as patients improved (17). These results contradicted previously reported ones where APN levels were higher in those with RDS than those without (18). While animal studies reported low APN levels associated with significant lung injury (5, 19), conflicting results were reported concerning humans (20). This difference may be due to the recruitment of critically ill patients and those with sepsis admitted to the intensive care unit (ICU).

The current study reported that a level of ≤ 37 predicted significant occurrence of RDS. Another study showed that lower serum APN levels were associated with lower lung function in young adults (21).

Strengths and limitations

the current study assessed the validity of APN and MPV in predicting RDS. Furthermore, serial

measurements of APN and MPV in this study added more precision. The present study had some limitations. Firstly, the sample size was relatively small and may not be representative. Secondly, this study was carried out in a single tertiary center, limiting the generalizability of the results. We did not recruit critically ill neonates with sepsis or septic shock.

Conclusion

According to the results obtained from the present research, the MPV was significantly increased while APN levels were lower in preterm neonates with RDS. Both markers predicted the development of RDS significantly.

Acknowledgments

None.

Conflicts of interest

The authors do not have any conflict of interest.

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