JOMBC Journal of Medical Pest Control
Immunology and Microbiology
ISSN : 10036245
FREE CONTENT

Increased Red Cell Distribution Width And An Increased Risk of Transient Tachypnea of The Newborn

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ARTICLE INFO

Article history
Received July 02, 2025
Revised July 03, 2025
Accepted Aug 08, 2025

Keywords
Red cell distribution width;
RDW;
transient tachypnea of the newborn;
TTN.

ABSTRACT

Background: Transient tachypnea of the newborn (TTN) is a common neonatal respiratory disorder resulting from a delay or incomplete removal of lung fluid following birth that impairs gas exchange. Red cell distribution width (RDW) is one of the red blood cell indices that have been found to be associated with many adverse neonatal outcomes. **Aims:** To determine the utility of an elevated RDW of predicting TTN in newborns delivered by cesarean section. **Methods:** A case–control study of 51 neonates with TTN (cases) and 67 healthy neonates (control) in Al-Zahraa Teaching Hospital in Iraq. Within 6 hours of birth, newborns whose respiratory distress had resolved were considered to be controls, and those who continued with respiratory distress were considered to be cases with TTN. Two mL of cord blood was collected from all newborns within 60 s of delivery and analyzed for complete blood count and RDW. **Results:** RDW values were significantly higher in cases than in controls ($p < 0.001$), as were hemoglobin, respiratory rate, and duration of admission. RDW was significantly correlated with respiratory rate ($r = 0.38$, $p < 0.001$) and duration of admission ($r = 0.38$, $p < 0.001$). The cutoff RDW value that significantly predicted TTN was 14% with a specificity of 65% and a sensitivity of 70%. **Conclusion:** Elevated RDW is significantly associated with the development of TTN, increased respiratory rate, prolonged duration of tachypnea and admission. RDW > 14% appears to be a predictor for the development of TTN.

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1. Introduction

Newborn respiratory distress occurs in 5%–10% of live births and is responsible for approximately 20% of neonatal mortality [1]. Tachypnea is the most common presentation in newborns with respiratory distress [2,3]. Transient tachypnea of the newborn (TTN) has an estimated frequency of 1%–2% of all instances of neonatal respiratory distress [4]. It is an early onset transient respiratory disorder that usually resolves within 48–72 h of birth. C-section remains the most commonly encountered risk factor. The likely mechanism is the lack of adrenergic stimulation resulting in the opening of lung epithelial sodium channels (ENaC) for the resorption of lung fluid with the onset of labor [5].

C-section delivery has been significantly associated with respiratory morbidity primarily consisting of TTN. Several studies have evaluated the effect of mode of delivery on the neonatal hematological profile including complete blood count (CBC) and red blood cell (RBC) indices. Red cell distribution width (RDW) is an index of the variation in RBC size or anisocytosis. It is calculated by dividing the standard deviation (SD) of RBC volume by the mean corpuscular volume and then multiplying the result by 100 [6]. Several factors have been found to influence RDW, such as age, black ethnicity, physical exercise, poor oral intake resulting in anemia (iron, vitamin B12, or folate deficiency), chronic disorders, or critical illness [7]. RBC nitric oxide release due to tissue hypoxia in conditions such as sepsis results in hemoglobin (Hb) auto-oxidation that has an important influence on RBC indices and the microcirculation [8, 9]. An elevated RDW has been found to be associated with a higher risk of death with the mortality rate increasing by 23% for every 1% increase in RDW [10]. RDW has been found to have prognostic ability for many health issues. Many articles have evaluated the effect of mode of delivery on neonatal outcomes with C-section being associated with undesirable respiratory or hematological changes.

2. Aim of the study

To evaluate the association of an elevated RDW as an early predictor of TTN in term and near-term newborns delivered by elective C-section.

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3. Patient and method

This was a case–control study performed in the neonatal care unit of Al-Zahraa Teaching Hospital in the Al-Najaf Al-Ashraf Governorate of Iraq from 3/1/2019 to 9/25/2019. A total of 118 newborns were recruited into the study. There were 51 cases who were delivered at ≥36 weeks' gestational age (GA) by elective C-section whose mothers had no medical history and developed respiratory distress or tachypnea during the first 4–6 h of life. A total of 67 newborns were included as controls that were born under the same circumstances but without respiratory distress or tachypnea.

Newborns were excluded if they were <36 weeks' gestation and had respiratory distress syndrome, any malpresentation, malposition, or perinatal complications (meconium-stained amniotic fluid, asphyxia, hypocalcemia, hypoglycemia, polycythemia), congenital heart disease, congenital anomalies, birth weight < 2,500 g, or any maternal disease. Maternal age, parity, and type of anesthesia were recorded. The GA was determined based on an ultrasound obtained during the first trimester of pregnancy, the first day of the last menstrual period, or a Ballard scoring system assessment. The Apgar score at 1 and 5 min, birth weight, and gender were recorded.

All newborns were resuscitated by trained resident physicians according to the Neonatal Resuscitation Program 2016 edition. All newborns were assessed for respiratory rate within the first 4–6 h of life. Two mL of cord blood was collected from all included newborns within the first 30–60 s after delivery following sterilization of the cord with povidone iodine. Umbilical cord blood was collected in an EDTA tube, and the CBC was determined using a Sysmex blood counter. The samples were obtained following verbal consent from the families. Physical examination of all newborns was performed, and the respiratory rate during the first 4–6 h of life was monitored. Any associated findings indicative of distress such as grunting, cyanosis, intercostal or subcostal retractions, or flaring of the alae nasi were documented. At 6 h of age, any newborn that had improved and had no respiratory distress was regarded as a control, and those who continued to have respiratory distress were deemed to have TTN. TTN was diagnosed when the newborn's respiratory rate was >60 breaths/min (tachypnea) for at least 12 h, and there was still a need for O2. The chest radiograph could be either normal or have at least one of the following radiological findings of TTN: widening of the intercostal spaces, flattening of the diaphragm, hyperinflation, or fluid accumulating in the interlobar fissures and costophrenic angles. Cases were admitted to the neonatal care unit and followed throughout the duration of their admission. The duration of admission, treatment during admission, and outcome were recorded.

4. Statistical analysis

Statistical analyses were performed using Statistical Package for Social Sciences (version 23; SPSS Inc., Chicago, IL, USA). Categorical variables were represented by numbers and percentages, whereas continuous variables were represented by means and SD.

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The independent t test was used to compare continuous variables, whereas the Chi-square test was used to compare categorical variables. Pearson's correlation coefficient was used to assess the correlation among variables. The difference was considered statistically significant if $p \leq 0.05$.

4. Results

There were 51 (43.2%) cases diagnosed with TTN and 67 (56.8%) control infants who were healthy. The mean GA of the total study population was 37.6 ± 0.87 weeks. A total of 69 (58.5%) patients were male and 49 (41.5%) female, and 26 (22%) were delivered with general anesthesia and 92 (78%) with spinal anesthesia (Table 1).

Table.1 Demographic characteristics of the total population of the study.

variables		**Mean**	**Stander Deviation**
mother age(years)		29.25	±5.691
Weight (kg)		3.2568	±0.37083
apgar-1 min.		5.75	±0.997
apgar-5 min.		8.13	±0.661
Gestational age (week)		37.609	±0.8670
RDW (%)		14.0559	±1.11137
Hb (g\dl)		14.8458	±1.70678
RR(breath\min.)		59.1186	±11.24336
Duration (hr.)		32.45	±49.176
variables		**No.**	**Percentage**
Gender	male	69	58.5%
	female	49	41.5%
Anesthesia	GA.	26	22%
	spinal	92	78%
GA; gestational age, Hb; hemoglobin, RDW; Red cell distribution width, RR; respiratory rate			

The RDW was significantly higher in cases than in controls ($p < 0.001$). Hb, respiratory rate, and duration of admission were also significantly different between the groups (Table 2).

Table 2: comparisons between variables of the cases and control groups.

Variables	**Cases**	**Controls**	**P -values**
	(mean± SD)	**(mean±SD)**	
Mother age (years)	29.39±(5.5)	29.13±(5.8)	0.8
Baby weight (kg)	3.28±(0.3)	3.23±(0.3)	0.4
Apgar 1 min.	5.57±(1.1)	5.88±(0.8)	0.09
Apgar 5 min.	7.78±(0.5)	8.39±(0.6)	<0.001
Gestational age (week)	37.6±(0.9)	37.5±(0.8)	0.7
RDW (%)	14.56±(0.9)	13.6±(1.08)	<0.001
Hb (g\dl)	15.4±(2.03)	14.4±(1.2)	0.001
RR(breath\min.)	69.6±(7.8)	51.1± (5.2)	<0.001

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Duration(hr)		69.7±(54.4)	67±(4.03)	<0.001
variables		**cases**	**controls**	**p-values**
Anaesthesia	GA.	15(57.4%)	11(42.6%)	0.1
	spinal	36 (39%)	56 (60%)	
Gender	male	33 (47%)	36(52.7%)	0.2
	female	18 (36.3%)	31 (63%)	
GA; gestational age, Hb; hemoglobin, RDW; Red cell distribution width, RR; respiratory rate, SD; standard deviation				

RDW correlated significantly with the respiratory rate ($r = 0.38$, $p < 0.001$), as well as the length of admission ($r = 0.38$, $p < 0.001$) (Figure 1A, B). An RDW cutoff value of 14% predicted TTN with a specificity of 65% and a sensitivity of 70% (Figure 2).

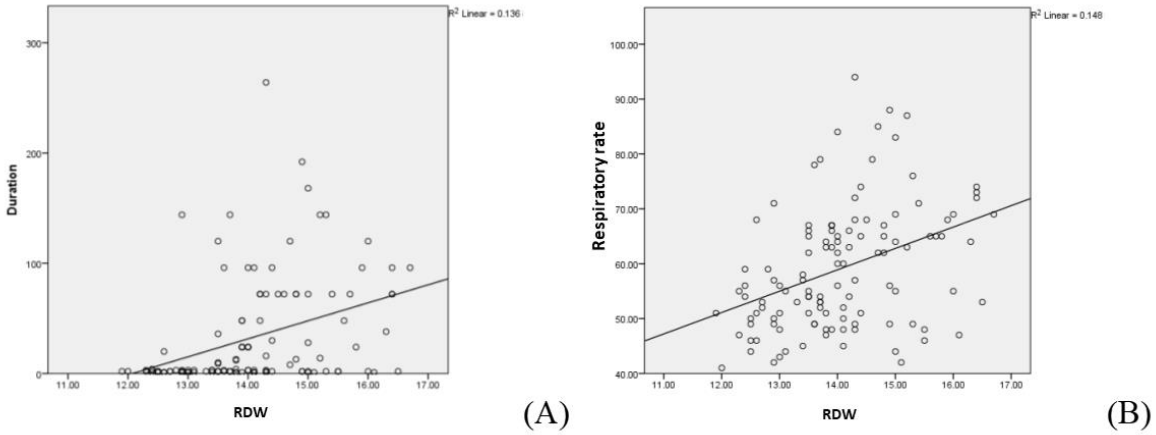

Figure-1 Correlation of RDW and duration of admission (A) and RR (B) for the total 118 neonates.

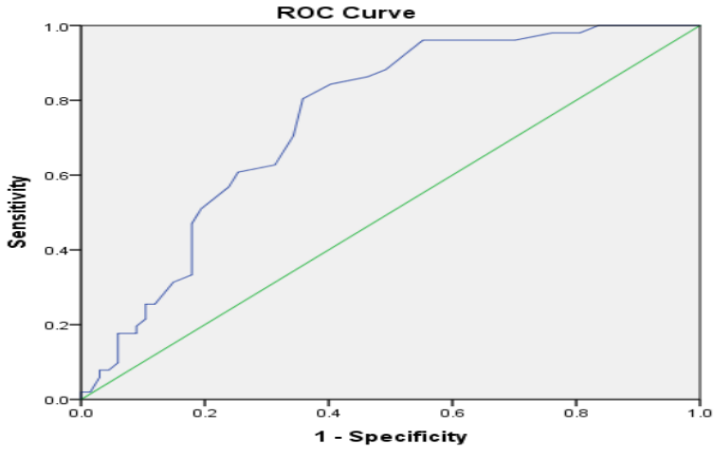

Figure-2 ROC curve for specificity and sensitivity of RDW to predict TTN.

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6. Discussion

There have only been a limited number of studies comparing various clinical conditions in newborns and RDW. These studies have evaluated its association with inflammatory and cardiac conditions, the risk for sepsis, and the differential diagnosis of anemia. However, to the best of our knowledge, its association with an increased risk for TTN has only been evaluated once [11], and that previous study evaluated the relationship between increased RDW and an increased risk for TTN in normal, vaginally delivered neonates. An association of RDW with an increase in TTN, the type of anesthesia, and C-section utilizing cord blood for the study has yet to be performed. In the present study, a significant difference in RDW values was found between the TTN and control groups. The RDW in the TTN group was significantly higher than that in the control group ($p < 0.001$), which was consistent with the results by Cosar et al [11]. For neonates delivered by normal vaginal delivery. In the current study, there was a significant correlation between an elevated RDW on the duration of admission and respiratory rate for the total study population ($p < 0.001$), which differed from the study by Cosar et al.15 that found no significant association between TTN and length of admission or RDW ($p = 0.1$). In the present study, there was no significant effect of GA on RDW. This was different from the study by Alparslan et al [12] to determine normative RDW data, as well as the study by Garofoli et al [13]. Both of those studies found a significant effect of GA on RDW [12, 13]. Our study found a significant difference in Hb ($p = 0.001$) between cases and controls, which differs from Cosar et al [11], but is in agreement with Oztekin et al [14], who noted a significantly lower hematocrit in infants with tachypnea of longer duration than in their control group. This study also found no significant effect of the type of anesthesia used for C-section on RDW ($p = 0.9$), which may be attributed to the brief period of anesthesia during a C-section and its proximity to the time of blood collection. In the present study, the RDW cutoff value that was associated with an increased risk of TTN and prolonged admission was 14% with a sensitivity of 70%. No previous study, to the best of our knowledge, had determined such a value as a predictor for neonatal illness.

The mechanism of transepithelial movement of lung fluid through ENaC is activated by adrenergic stimulation with the onset of birth. This mechanism is responsible for approximately 35% of lung fluid resorption. This period can provide enough time to induce hematological changes in RBC indices that does not occur with a C-section performed prior to the onset of labor.

In conclusion, there is a significant association between an elevated RDW and the development of TTN. This elevated RDW is also associated with a prolonged duration of tachypnea and length of admission. An RDW > 14% may be a predictor for the development of TTN. Larger studies are necessary to further elucidate the role of RDW as a predictor for both neonatal respiratory and other disorders.

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