

Original Article

Red Blood Cell Distribution Width and Transient Tachypnoea of the Newborn

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Abstract The relationship between the red blood cell distribution width (RDW) and transient tachypnoea of newborn (TTN) was evaluated. Sixty-nine neonates with TTN and 64 healthy neonates were recruited into our study. Compared with the controls, neonates with TTN had significantly higher values of RDW, mean corpuscular volume and haemoglobin but lower platelet counts. The duration of the tachypnoea would not alter the RDW.

Key words Inflammation; Red blood cell distribution width; Transient tachypnoea of newborn

Introduction

By definition, tachypnoea of newborn (TTN) refers to rapid respiration (>60 bpm), grunting and retraction occurring within six hours after birth in infants who do not show evidence of infection and the oxygen requirement seldom rise above 40%; the chest radiograph usually shows interstitial or pleural fluid accumulation, prominent

interlobar fissures, perihilar vascular markings and increased aeration. These symptoms often resolve in 48 hours, occasionally last as long as five days. The condition is more common in term infants born by elective caesarean section. The pathophysiology of TTN is not completely clarified. The probable factor is decrease in fetal lung liquid reabsorbing ability of amiloride-sensitive sodium channels as a result of increased catecholamine exposure in birth.¹⁻³

Red blood cell distribution width (RDW) indicates heterogeneity of erythrocyte volume in circulation and routinely it is reported as a component of complete blood count (CBC) without incurring additional cost. RDW is calculated by dividing standard deviation of red blood cell volume by mean corpuscular volume (MCV) and multiplying the product by 100. Higher RDW values indicate increase in variations of RBC volume. It is mainly used for the differential diagnosis of microcytic anaemia.^{4,5}

Although the mechanism of increased RDW is not known, higher RDW levels demonstrate its association with inflammatory and ischaemic processes in adult patients. Current studies have detected an association between RDW with pulmonary embolism, pneumonia, sepsis and acute myocardial infarction and RDW has been correlated with the prognosis in adult patients with acute myocardial infarction.⁵⁻¹⁰ But there are limited data about relationship between RDW and newborn population especially in TTN. Therefore, in this study, we compared RDW levels in healthy newborns and those with TTN in order to investigate the potential role of RDW in the TTN.

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Materials and Methods

Study Design

This prospective study was approved by the local Institutional Review Board. Written informed consent was obtained from all parents and the investigators complied with the ethical principles stated in the Helsinki Declaration of the World Health Organization in all stages of the study. The study was performed in the Department of Children's Health and Diseases of Manisa Merkez Efendi Government Hospital between 01/01/2013 and 30/06/2014. Summary of the study protocol was explained by one of the investigators to the parents of the new-borns using easily understandable terms and the parents were requested to participate in the study.

Study population consisted of healthy new-borns with TTN; all of them were delivered by spontaneous vaginal births. An asymptomatic group of infants of matched gestation and birth weight were also recruited as the controls. TTN subjects were recruited from our Neonatal Intensive Care Unit in the first 24 hours of postnatal age. And the control group subjects were recruited from our delivery room in the first 24 hours of postnatal age. None of the pregnant women underwent pharmacological induction or received antibiotherapy within 48 hours before the deliveries. Physical examination of all new-borns was performed by the same researcher (HC). All new-borns were of Caucasian race.

The diagnosis of TTN was made in accordance with the International Classification of Diseases, Tenth Revision code of P22.1. Inclusion criteria were the following: 1) respiratory rate higher than 60 per minute within six hours after delivery, grunting sounds with breathing, flaring of the nostrils, retractions; 2) tachypnoea lasting for at least 12 hours; 3) chest radiograph indicating at least one of the following: increased aeration on chest X-ray, flattening of the ribs, fluid accumulation in the interlober fissures and costophrenic angle, vascular congestion and depression of the diaphragmatic domes or increased anteroposterior diameter or both; 4) exclusion of either known respiratory (meconium aspiration, respiratory distress syndrome, pneumonitis, and congenital heart diseases) or nonrespiratory disorders (hypocalcaemia, persistent hypoglycaemia, and polycythaemia) likely to cause tachypnoea.^{3,11} Babies diagnosed with TTN were chosen for patient group. Respirology rates of babies in patient group were followed up hourly and improvement time of their tachypnoea was

noted down in the form.

Exclusion criteria for both the TTN and control groups included those born before 36 weeks or those with low birth weight of <2,500 g. Neonates older than 24 hours and those with perinatal asphyxia, meconium aspiration syndrome, congenital malformations, suspected early-onset neonatal sepsis (EONS), congenital infections associated with the TORCH complex or metabolic disease were excluded. Infants whose parents refused to give their written consent were also not included. Suspected EONS criteria were positive clinical signs of sepsis (feeding intolerance, vomiting, abdominal distension, temperature instability, jaundice, sclerema, lethargy, irritability convulsion, tachycardia >160 bpm, bradycardia <100 bpm, hypotension and impaired peripheral perfusion) and/or a history of factors associated with a raised risk of infection (maternal fever ($\geq 38^{\circ}\text{C}$), prolonged rupture of membranes >18 h and clinical chorioamnionitis). In addition, C-reactive protein (CRP) >10 mg/L, metabolic acidosis, thrombocytopenia and signs of pneumonia on chest X-ray was considered suspected EONS also.

Laboratory Analyses

Peripheral blood samples of the study participants in the TTN and the control groups were obtained during their first hospital visits and CBC and CRP were determined. CBC was calculated by the automated haematology analyser XE-1200 (Sysmex, Japan). Serum CRP concentrations were measured using nephelometry technique and an appropriate kit (Mindray, People's Republic of China). The interrun coefficient of variation of the RDW assay was found to be <1 percent. Biochemical workups were performed to exclude other clinical situations in which tachypnoea could be carried out. Blood samples were attained and bilateral chest radiography was taken and evaluated.

Statistical Analyses

Data were analysed using the Statistical Package for Social Sciences 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. Independent-samples t-test was used to compare independent groups. Data were expressed as mean \pm SD. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

Results

Sixty-nine new-borns with the diagnosis of TTN and 64 healthy new-borns were analysed prospectively. Baseline demographic characteristics and laboratory data of the study population are shown in Table 1. The gestational age of the control group was found to be significantly higher (38.83 ± 1.17 weeks vs 38.33 ± 1.22 weeks; $p=0.019$) than the TTN group. No other intergroup differences were detected regarding gender (male/female), maternal age, gestational diabetes mellitus, preeclampsia, birth weight, white blood cell (WBC), band count, red blood cell (RBC), haematocrit (Htc), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and CRP values ($p>0.05$). In new-borns in the TTN group, RDW ($20.44 \pm 3.12\%$ vs $15.69 \pm 0.96\%$; $p<0.001$), MCV (103.22 ± 5.36 fL vs 87.18 ± 4.59 fL; $p<0.001$) and haemoglobin levels (16.20 ± 1.83 gr/dL vs 15.08 ± 1.36 gr/dL; $p<0.001$) were significantly higher, whereas platelet counts were significantly lower ($248.25 \pm 62.53 \times 10^3/\text{mm}^3$ vs $286.44 \pm 64.73 \times 10^3/\text{mm}^3$; $p=0.001$).

TTN group was divided into two subgroups; one subgroup with the tachypnoea duration less than 48 hours ($n=36$), the

other subgroup with the tachypnoea duration more than 48 hours ($n=33$). No significant intersubgroups difference was detected regarding maternal age, gestational diabetes mellitus, preeclampsia, gestational age, birth weight, WBC, band count, RBC, haemoglobin, Htc, MCV, MCH, MCHC, platelet counts CRP and RDW value ($p>0.05$) (Table 1).

Discussion

Our study is the first to look into the relationship between TTN and RDW values. RDW is estimated from CBC which does not incur additional cost. In the current study, we found RDW value in TTN higher compared to that of control group ($p<0.001$) (Table 1). No significant differences were found between the two TTN sub-groups, whether the duration of tachypnoea was longer or shorter than 48 hours ($p=0.071$) (Table 1). It was found out that high RDW value was associated with TTN, however, it was not related to TTN duration.

In a study which investigated reference ranges of RDW for new-borns, the authors detected lower limits and upper limits of normal at birth, for term and late-preterm infants as 15.5% and 20%, respectively. However, in premature

Table 1 Baseline demographic characteristics and laboratory data of the study population

	Control group (n=64)	TTN group (n=69)	p value	TTN group (n=69)		p value
				Tachypnoea time ≤ 48 h (n=36)	Tachypnoea time >48 h (n=33)	
Gestational age (weeks)	38.83 ± 1.17	38.33 ± 1.22	0.019	38.44 ± 1.15	38.21 ± 1.29	0.434
Birth weight (gr.)	3276.09 ± 405.66	3193.91 ± 474.49	0.287	3256.67 ± 459.93	3125.45 ± 487.64	0.254
Gender (male/female)(n)	33/31	39/30	0.566	20/16	19/14	0.866
Maternal age (years)	26.69 ± 4.85	28.04 ± 5.03	0.117	27.78 ± 5.09	28.33 ± 5.02	0.650
Gestational diabetes mellitus	2	3	0.711	1	2	0.504
Preeclampsia (n)	3	5	0.535	3	2	0.716
White blood cell ($10^3/\text{mm}^3$)	16.31 ± 4.54	17.87 ± 5.35	0.074	18.75 ± 5.78	16.90 ± 4.74	0.154
Band count ($10^3/\text{mm}^3$)	7.99 ± 2.30	8.47 ± 2.49	0.246	8.91 ± 2.71	8.00 ± 2.17	0.133
Red blood cell (million/ mm^3)	4.56 ± 0.45	4.63 ± 0.53	0.420	4.72 ± 0.58	4.53 ± 0.47	0.144
Haemoglobin (gr/dL)	15.08 ± 1.36	16.20 ± 1.83	0.000	16.53 ± 1.95	15.84 ± 1.65	0.120
Haematocrit (%)	47.51 ± 4.57	48.57 ± 4.93	0.200	49.20 ± 5.35	47.90 ± 4.39	0.276
Mean corpuscular volume (fL)	87.18 ± 4.59	103.22 ± 5.36	0.000	104.25 ± 4.50	102.09 ± 6.03	0.096
Platelet count ($10^3/\text{mm}^3$)	286.44 ± 64.73	248.25 ± 62.53	0.001	248.19 ± 67.02	248.30 ± 58.28	0.994
MCH (pg)	35.43 ± 2.11	35.26 ± 2.00	0.628	35.26 ± 1.73	35.26 ± 2.29	0.996
MCHC (gr/dL)	33.95 ± 1.10	34.26 ± 1.10	0.111	34.06 ± 1.03	34.47 ± 1.14	0.122
RDW (%)	15.69 ± 0.96	20.44 ± 3.12	0.000	19.86 ± 3.29	21.07 ± 2.85	0.110
C-reactive protein (mg/L)	1.40 ± 1.22	1.71 ± 1.69	0.230	1.72 ± 1.85	1.70 ± 1.52	0.966

Results are given in mean \pm SD. Independent samples t-test was used.

$p<0.05$ (significant difference)

MCH=mean corpuscular haemoglobin; MCHC=mean corpuscular haemoglobin concentration; RDW=Red blood cell distribution width

infants, upper limit of RDW was higher (23%).¹² In our study, mean (\pm SD) value of RDW (15.69 \pm 1.08%) measured in the control group within the first day of the postnatal period was similar to the lower limit of normal reference range of term and late-term infants in the mentioned study above.

Limited number of studies have compared some clinical conditions in new-borns and RDW values. In a retrospective study, mean (\pm SD) RDW values measured within the first 3 days after birth, were 15.65 \pm 1.18% in full-term new-borns, 17.7 \pm 2.06% in preterms; and 17.45 \pm 1.81% in cases with IUGR. A negative correlation was observed between RDW and gestational age ($r=-0.51$; $p<0.001$). In premature infants who had higher RDW values within the first 3 days of their life-time, increased rates of mortality ($p<0.0001$) and late-onset sepsis (LOS) ($p<0.005$) were found. In addition, in the premature group RDW value of prematures with bronchopulmonary dysplasia (BDP) in their first month was found to be higher compared to prematures without BPD ($p<0.005$). The authors indicated the need for further studies to reveal the value of RDW as potential risk indicator in new-borns with critical diseases.¹³ In our study, mean (\pm SD) RDW value (15.69 \pm 1.08%) estimated in the control group within the first day was compared to the mean (\pm SD) RDW value (15.65 \pm 1.18%) of term and near-term infants determined within the first 3 postnatal days of the cited study. In another study where RDW indices were evaluated in 46 very-low-birth weight (VLBW) infants (birth weight <1,000 g) with EONS, 16 (35%) infants had died during the evaluation period and the authors suggested that RDW did not predict mortality in VLBW infants.¹⁴

Although patients with similar gestational weeks and birth weights of control and patient groups were tried to be chosen, control group of gestational age was determined significantly higher (38.83 \pm 1.17 weeks vs 38.33 \pm 1.22 weeks; $p=0.019$) than TTN group. In addition, it was surprising that haemoglobin value in TTN group (16.20 \pm 1.83 gr/dL vs 15.08 \pm 1.36 gr/dL; $p<0.001$) was high and platelet value (248.25 \pm 62.53 $\times 10^3$ /mm³ vs 286.44 \pm 64.73 $\times 10^3$ /mm³; $p=0.001$) was low.

The main limitation of our study was relatively scarce number of new-borns included in the study. Secondly, evaluation in patient group for once led to inadequate determination of probable changes in RDW levels during and after tachypnoea duration and consequently, RDW relation and TTN duration.

RDW is an arithmetic index which requires no additional cost and checked from complete blood count. As a result, it was established that RDW value was high in term and near-term new-borns diagnosed with TTN. However, we saw that

RDW value was similar in those whose TTN lasts longer and shorter than 48 hours. We thought that RDW value can be used in the early diagnosis of TTN. Nevertheless, a large number of new studies performed with patient groups are needed to examine RDW and TTN connection and evaluate RDW availability in estimating TTN duration.

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