STM JOURNALS

Research & Reviews: A Journal of
Life Sciences

ISSN: 2249-8656 (Online)
ISSN: 2348-9545 (Print)
Volume 14, Issue 1, 2024
DOI (Journal): 10.37591/RRJoLS

https://journals.stmjournals.com/rrjols/

Research RRJoLS

Red Cell Distribution in Pregnancy Associated with Preeclampsia Patients Worldwide: A Brief Review

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Abstract

Introduction: *Preeclampsia (PE) is a major obstetric problem contributing considerably to maternal and prenatal morbidity and mortality worldwide. Preeclampsia varies in incidence in India from 5% to 15%. The role of this hematological parameter in clinical assessment, differential diagnosis, and prognosis evaluation of PE remains unclear. Thus, the purpose of the current review was to investigate the red cell distribution width (RDW) in preeclampsia, analyze its importance for early diagnosis, severity assessment, and prognosis, and establish the RDW cutoff value.* ***Methods:*** *A total of 71 studies were initially retrieved from databases. A total of 38 studies were examined after duplicates were eliminated. Out of those, fourteen papers were eventually included in the qualitative and quantitative analysis after meeting the inclusion criteria. The specifics of the chosen publications from hospital settings across the globe between 2013 and 2023.* ***Results:*** *The review included fourteen papers that met the inclusion criteria. Each of the fourteen studies had excellent quality. Four (29%) of the eligible studies were carried out in Turkey and four (29%) from India, respectively. Each of China, Nigeria, Sudan, Japan, Iraq, and Indonesia conducted one study (7%). There were 1809 controls and 1024 cases (preeclampsia) out of a total of 2833 individuals. There were 16 to 136 cases (PE) for every research, while there were 20 to 911 controls. Three studies gave the variance and median, which were converted to the mean (SD) using the recommended procedure. When comparing women with preeclampsia to controls, the mean (SD) of the RDW level was considerably higher [15.73 (2.23) % vs. 14.03 (1.68) %, P<0.001]. 1.7 was the mean difference. Consequently, the model of continuous random effect was applied. Nine studies compared the RDW level in mild (N = 317) and severe (N = 305) instances of preeclampsia.* ***Conclusion:*** *The association between RDW and preeclampsia, particularly its diagnostic significance in severe cases, is compelling, it is important to note that RDW should not be used in isolation for diagnosis or risk stratification.*

Keywords: Preeclampsia patients, red cell, PubMed, MEDLINE, Google Scholar

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Received Date: March 06, 2024
Accepted Date: March 27, 2024
Published Date: March 30, 2024

Citation: Tarang Gupta, Sumer Singh. Red Cell Distribution in Pregnancy Associated with Preeclampsia Patients in Worldwide: A Brief Review. Research & Reviews: A Journal of Life Sciences. 2024; 14(1): 6–12p.

INTRODUCTION

Preeclampsia (PE) is a major obstetric condition that contributes considerably to maternal and prenatal morbidity and mortality worldwide. Preeclampsia is a primary cause of maternal and perinatal morbidity and mortality in expectant mothers. It is a pregnancy problem that manifests as organ damage and elevated blood pressure after 20 weeks gestation. Globally, over 70,000 maternal and 500,000 fetal deaths are attributed to it as the primary cause each year [1, 2]. The incidence of preeclampsia varies from 5% to 15% [3].

Despite decades of research on this condition, the identification of women in the early stages of

pregnancy who are at an increased risk of developing PE remains a challenge. Early detection aids in improving maternal and perinatal outcomes. Since PE is progressive and unpredictable, the only existing treatment available is well-timed delivery of pregnancy. Mild systemic inflammation is a physiological state of healthy pregnancy; however, if inflammation is dysregulated, as in the case of PE [4], it may become harmful. It has been suggested that placental diseases, including broad maternal endothelial dysfunction and insufficient cytotrophoblast invasion, cause preeclampsia [5]. Increased erythropoietic stimulation associated with underlying placental hypoxia has been observed in preeclampsia [6].

The role of this hematological parameter in the clinical assessment, differential diagnosis, and prognosis evaluation of PE remains unclear [7]. Very few studies have been conducted in India that could aid in the early detection of PE using easily detectable hematological markers. The present study aimed to investigate the role of red cell distribution width (RDW) as a predictor of disease and for the early diagnosis, assessment of severity, and prognosis of PE. As part of the complete blood count, the RDW is a measure that is often assessed using a fully automated hematology analyzer. Anisocytosis (red cell size change) was shown by RDW. RDW has been demonstrated to have high sensitivity for identifying anemia and can reflect early alterations in red blood cells that are associated with iron deficiency anemia [8, 9].

According to recent studies, RDW is higher in pre-hypertension and hypertension in the nonpregnant population [10]. Additionally, it has been reported that there are highly significant correlations between RDW values and stroke, acute and chronic heart failure, diabetic ketoacidosis, cardiovascular and thrombotic diseases, and cardiac mortality in patients with coronary artery disease [11, 12]. However, there is relatively limited data on RDW and preeclampsia and a great deal of evidence on RDW and hypertension in the nonpregnant population [13].

Therefore, this study aimed to investigate the association between RDW and preeclampsia. Therefore, the current review was designed to examine RDW in preeclampsia, examining its significance for early diagnosis, severity evaluation, and prognosis, and determining the RDW cutoff value.

MATERIAL AND METHODS

The study protocol followed a letter regarding its parameters. This paper is a review, it was conducted, and the heterogeneity was present within an acceptable range.

Inclusion Criteria

Original English-language articles addressing human pregnancy, rigorous definition-based investigations of preeclampsia in mothers, and RDW investigations and reports were included.

Ages 18 and under were the criteria for research that were included.

The PICOS (Population, Intervention, Comparison, Outcomes, and Study) principle served as the foundation for the inclusion criteria, which were as follows:

a. *Population:* Individuals diagnosed with preeclampsia between the ages of 18 and 40 years using the standard criteria recommended by the American College of Obstetricians and Gynecologists, which include proteinuria and a systolic blood pressure of 140 mmHg or higher or a diastolic blood pressure of 90 mmHg or higher on two separate occasions spaced at least 4 hours apart [14].
b. Exposure/RDW Intervention
c. *Control:* Healthy expecting mothers who do not use medication or have any clinical symptoms and are between the ages of 18 and 40 years
d. *Outcomes:* The diagnostic feature of RDW

e. *Research:* Studies conducted in global settings using case-control, longitudinal, retrospective, and cross-sectional methods.

Topic reviews; case reports with fewer than five cases; research conducted in vitro or on animals, posters, or conference papers; studies that only examined pregnancy-induced hypertension; and studies that did not use healthy pregnant women as controls were among the exclusion criteria.

Technique for Searching Articles

Electronic retrieval techniques were used in the literature retrieval process. Using a combination of controlled vocabulary, keywords, and Medical Subject Headings, a thorough and methodical evaluation of the literature was carried out for studies up to 2023 across several databases, including PubMed, MEDLINE, and Google Scholar. In addition, a manual search of a primary trial reference list about the chosen topics was performed, and pertinent publications were incorporated into the analysis and evaluation.

Measure of the Study's Outcome

The goal of this study was to investigate the RDW% in preeclampsia patients and the RDW cutoff value in an Indian context.

RESULTS

Table 1 presents the details of the papers selected from worldwide settings between 2013 and 2023.

When the inclusion and exclusion criteria were applied, the 71 papers that the search technique found were reduced to 38 articles.

Case-control (seven studies; [15–20, 21]), cross-sectional (two studies; [14, 22, 23]), and retrospective (five studies; [22, 24–27]) standards were the three main types of study designs that were found and subsequently included in both the qualitative and quantitative analysis [14–27]. After obtaining the entire text of the publications, five more studies were eliminated, and 22 more studies were eliminated based only on the title and/or abstract (Figure 1).

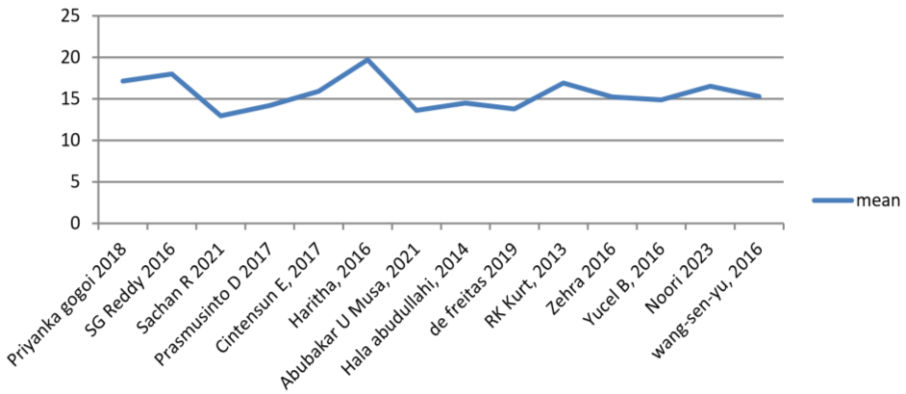

Figure 1. Mean RDW levels in different studies in preeclampsia patients.

The review included fourteen papers that met the inclusion criteria [14, 27]. Each of the 14 included studies was of excellent quality (Table 1). Four (29%) [15, 19, 26, 27] and four (29%) [17, 18, 20, 24] of the eligible studies were conducted in Turkey and India, respectively. Each of China, Nigeria, Sudan, Japan, Iraq, and Indonesia conducted one study (7%).

There were 1809 controls and 1024 cases (preeclampsia) out of a total of 2833 individuals. There were 16 [23] to 136 [22] cases in every study, while there were 20 [23] to 911 [24] controls. Three studies [22, 15, 26] gave the variance and median, which were converted to the mean (SD) using the recommended procedure.

When comparing women with preeclampsia to controls, the mean (SD) RDW level was considerably higher [15.73 (2.23) % vs. 14.03 (1.68) %, P < 0.001]. 1.7 was) the mean difference (Figure 1). Consequently, a continuous random effect model was applied.

Nine studies [14, 15, 17, 19, 20, 24, 25, 26] compared RDW levels in mild (N = 317) and severe (N = 305) preeclampsia. There were 317 and 305 women with mild and severe preeclampsia, respectively.

Compared with women with moderate preeclampsia, those with severe preeclampsia had considerably higher RDW levels.

ROC: Table 1 shows the details of the selected articles for ROC to obtain cutoff values from 2016 to 2023 in hospital settings. This was a retrospective study. A study was performed to predict preeclampsia; the RDW sample was taken after diagnosis of PE; therefore, their analysis by ROC showed that the cutoff value of RDW was 14.1%, sensitivity was 72%, and specificity was 77% (24). In another retrospective study, the ROC cutoff value for RDW was 14.1%, sensitivity was 50%, and specificity was 71% (15). Another prospective study was conducted, and the RDW sample took–13-20 weeks of gestation. Therefore, they analyzed the cutoff value of RDW as 12.08, sensitivity of 50%, and specificity of 66% (22). A cohort study was done, so they analyzed by ROC the cutoff value of RDW is 15.9%, sensitivity 71%, and specificity 65% [24].

Table 1. Characteristics of the included studies.

S.N.	First author	Year of publication	Study setting and design	Study period	Study population	Sample size	PE RDW	Control RDW	P-value	ROC analysis	Cutoff of RDW	AUC	Sensitivity, specificity, p-value
1	Wang-sen-yu, China	2016	Retrospective		149	SPE=24 MPE=39 HP=70	15.3±4.01	13.1±2.3	0.001		>14.1	0.773	Sp=72% Sen=77.9% P<0.001
2	Abubakar U. Musa, Nigeria	2021	Cross-sectional	Oct. 2019–Sept. 2020	93	PE=31 Eclampsia= 31 Control= 31	13.61±1.07	14.23±6.67	<0.001	NO			
3	Hala Abdullahi, Sudan	2014	Case-control	June–Aug 2014	130	PE-65 Control= 65	14.5±1.8	14.4±1.4	0.710	No			
4	Marcia Aries Rodrigues de	2019	Cross-sectional	Dec 2014-June 2017	36	PE=16 Control= 20	13.80±2.10	13.67±1.48	0.603	No			
	Freitas, Japan												
5	R.K. Kurt, Turkey	2013	Case-control		102	SPE=17 MPE=35 Control=	16.9±1.7	14.1±1.1	<0.001	No			

						50							
6	Zehra Vahul, Turkey	2016	Retrospective	Jan 2013Jan 2015	238	PE=118 Control=12 0	15.23±1.96	14.48±1.70	<0.005	No			
7.	Yucel B., Turkey	2016	Retrospective cohort	Mar2016 July 2016	219	SPE=82 MPE=27 Control=110	14.89±1.85	13.59±2.2	0.011	No			
8	Wassan Nori, Iraq	2023	Case-control		120	SPE=30 MPE-30 Control=60	16.53±2.1	13.06±0.8	<0.001	No			
9	Priyanka Gogoi, India	2016	Case-control	Jan-July 2017	134	PE=67 Control=67	17.14±2.7	16.19±2.0	0.025	No			
10	Reka Sachan, India	2021	Prospective case-control		101	SPE=16 MPE=34 Control=51	18.01±3.4	12.8±2.1	<0.001	Yes	>12.08	0.520	Sen=50% Sp=66%
11	Damar Prasmusinto, Indonesia	2017	Retrospective study		254	PE=136 Control=118	14.5±2.3	13.89±1.59	<0.001	yes	>14.17	0.618	Sen=50.7% Sp=71.2%
12	Eris Cintensun Turkey	2017	Retrospective case-control		128	SPE=13 MPE=51 Control=64	15.9±3.4	16.0±2.9	0.774	No			
13	Haritha Mannem, India	2016	Case-control	Mar 2014 Mar 2016	75	SPE=25 MPE=25 Control=5	19.72±5.38	14.06±1.57	<0.001	no			
14	Shilpa Gopal Reddy, India	2016			1054	SPE=67 MPE=76 Control=911	18.01±3.4	12.8±2.1	<0.001	Yes	>15.9%	0.766	Sen=71.3% Sp=65%

DISCUSSION

Preeclampsia is a multifaceted condition with intricate underlying mechanisms. The hallmarks are hypertension and proteinuria after the 20th week of pregnancy. Among the many pathophysiological mechanisms involved are endothelial dysfunction, oxidative stress, and systemic inflammation [28]. It is well-recognized that inflammation affects several physiological functions, including the synthesis and operation of blood cells. This could affect red blood cell characteristics in preeclampsia when an underlying inflammatory state is frequently present. Iron is used to produce hemoglobin, an oxygen-carrying molecule found in red blood cells. Any disturbance in iron metabolism may have an impact on hemoglobin synthesis and, in turn, on the properties of red blood cells. Inefficient use of iron can lead to variations in red blood cell size, which manifests as higher RDW [25]. Another defining feature of preeclampsia is oxidative stress, which affects red blood cell (RBC) turnover and endothelial dysfunction. This stress may lead to hemolysis or breakdown of RBCs, which could increase the RDW. Research conducted in the Indian context indicates that RDW values are greater in preeclamptic patients than in normotensive pregnant women. Furthermore, preeclamptic women with severe features tend to have higher RDW levels than women with mild preeclampsia. This implies that RDW may function as a biomarker of preeclampsia severity [19]. The onset of severe preeclampsia may be predicted by elevated RDW levels. Healthcare practitioners could reduce difficulties by identifying pregnant women who are more likely to experience severe outcomes, implementing early interventions, and tighter monitoring. Healthcare practitioners could reduce difficulties by identifying pregnant women who are more likely to experience severe outcomes, implementing early interventions, and tighter monitoring.

The ability to diagnose severe preeclampsia in pregnant women may be improved by incorporating RDW into the clinical assessment process. As RDW is already included in the standard CBC, it offers a readily available marker that can be used in conjunction with other preeclampsia diagnostic criteria and risk assessment instruments.

CONCLUSION

Although the association between RDW and preeclampsia, particularly its diagnostic significance in severe cases, is compelling, it is important to note that RDW should not be used in isolation for diagnosis or risk stratification. Preeclampsia is a complex condition with a multifactorial etiology, and the diagnostic process typically involves a combination of clinical findings and laboratory tests, including blood pressure measurements, proteinuria assessment, and other blood markers.

Future research should aim to further elucidate the mechanisms linking RDW with preeclampsia and validate the clinical utility of RDW as a diagnostic and prognostic tool. Longitudinal studies exploring how RDW changes throughout pregnancy in women who develop preeclampsia, as compared to those who do not, could provide deeper insights into its potential role in the early detection and monitoring of the disease.

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