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ORIGINAL ARTICLE

Platelet Distribution Width and Preeclampsia: A Meta-Analysis

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ABSTRACT

Many research findings have determined the platelet distribution width (PDW) in preeclampsia; no published meta-analysis existed.

The aim of this review is to evaluate the reported PDW differences in preeclamptic women compared to healthy pregnant women. A Scopus, Pubmed-NCBI, ScienceDirect-open access and Google scholar Database were searched for a period of Jan 2010 to Apr 2020. OpenMeta Analyst software was used to compute the pooled Meta-logistic regression.

A 13 study were included; with a total of 1143 preeclampsia and 1725 normal pregnant women control. The mean (SD) of the PDW level was significantly higher in preeclampsia compared to controls [14.52 (2.61) % vs. 13.0 (2.55) %, P < 0.001]. Seven studies compared the PDW level in the mild with severe preeclampsia. It was significantly higher in severe compared to mild preeclampsia [16.38(2.45) % vs. 14.55 (2.57) %, P < 0.001].

Finding of this meta-analysis suggests that PDW represents a promising biomarker for the detection of patients with preeclampsia.

INTRODUCTION

Preeclampsia (PE) is a serious pregnancy-related disorder which considered as the main cause of feto-maternal morbidity and mortality. The prevalence of PE differs in various populations and multi-ethnic groups with approximately 5-8% of pregnant women affected worldwide (1).

Despite the exact pathogenesis of PE remains unknown, changes in placental perfusion, maternal endothelial injury, and increased vascular permeability are believed to contribute to its pathophysiology (2). Other factors have been also attributed to PE which includes, platelet activation, changes in the coagulation, and fibrin deposition (3).

Normal platelets are present in an inactive form in the bloodstream and can be activated when became contact with exposed endothelial wall (4). Hemostatic active platelets are involved in the pathogenesis of many thrombophilic diseases like PE (5). Platelet activity is correlated with change in platelet volume or size, the larger platelets are abnormally more active and thrombogenic than smaller ones (6). The parameter of mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and plateletcrit (PCT) are volume measuring platelet indices; which increase if the platelet becomes activated. Platelet indices have been recently used in the prediction, diagnosis, and prognosis of many diseases (7), being reported as clinically useful biomarkers.

As one of the platelets indices; the PDW reflects the variability in the size of the platelets (8) and it's therefore increased in the presence of platelets anisocytosis. It is calculated in femtoliters (fL) by measuring the width of the size distribution curve at

the 20% level when the peak distribution curve is taken as 80% or 100% (9). Therefore, it can be a practical marker to assess the activation of platelets or thrombophilic disease and ideal indicators for PE (10).

In the literature, numerous studies' findings revealed a high level of PDW in PE. A recent study has shown that PDW was an ideal indicator for PE; it increased as the disease progresses. They stated that among platelet indices, the PDW is significantly higher in women with severe PE than in women with mild PE, and is positively correlated with the mean arterial pressure. Also, they concluded that the PDW can serve as a candidate marker for predicting the severity of PE (11). However, the present meta-analysis is aimed to assess the PDW values in preeclampsia as reported in the literature.

MATERIALS AND METHODS

Searching strategies: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed (12). In brief, a literature search was done in the following databases sites: Scopus, Pubmed-NCBI, ScienceDirect-open access, and Google scholar. The search terms based on the following words: "Preeclampsia OR eclampsia AND platelet indices OR PDW". Published studies from a period of Jan/2010 to Apr/2020 were retrieved and evaluated if eligible based on this systematic review inclusion/exclusion criterion. Titles and abstracts of eligible papers were checked: not relevant, inappropriate design, non-English language, and duplicates studies were removed.

Inclusion criteria: Case-control study or cross-sectional, original articles published in English reporting human pregnancy, preeclampsia investigated on maternal side using the strict definition and PDW analyzed and reported.

Exclusion criteria: Review articles, case reports, in vitro based studies, posters, conference abstracts, and studies without controls (healthy pregnant women).

Quality assessment and data collection: Included articles were assessed using the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (13). Modified Newcastle Ottawa quality assessment scale for assessing the quality of each selected study (14).

Data extraction: The most useful relevant data that was extracted was recorded into a table requiring the authors' name, year of publication, study location, and number of cases and controls, values of PDW in cases and controls. Median (range) or median (inter-quartile) were transformed into mean (SD) as previously described (15).

Statistical methods: Meta-analyses of the variation in the values of PDW between cases and controls were performed using Open Meta Analyst software for Windows (16).

Ethical considerations: The present study was a systematic meta-analysis, for this ethical approval was not required.

RESULTS

The search strategies recognized 58 (articles that reduced to 56 articles after applying the criteria of inclusion and exclusion. Based on the title and/or abstract; additional 41 articles were excluded, and another 2 excluded after retrieval of the full-text of rest articles (Fig. 1). A 13 articles (10 case-control study and 3 cross-sectional study) fulfilling the inclusion criteria and were eligible to be used in the meta-analysis (11, 17-28). Of the eligible studies, five (17-19, 26, 28) studies were conducted in India, two (23, 27) were in Ethiopia, and one study each was conducted in the Republic of Korea (11), Saudi Arabia (20), Egypt (21), Sudan (22), China (24), and Brazil (25).

The total number of preeclampsia cases were 1143 and the total number of controls were1725. The number of the cases per study ranged from 29 (25) to 163 (24), while the controls ranged from 28 (25) and 816 (11). The median and variance were reported in 3 studies (11, 15, 21) and this was converted to the mean (SD) using the specific formula (15).

The mean (SD) of the PDW level was significantly higher in preeclamptic women compared to healthy pregnant women [14.52 (2.61) % vs. 13.0 (2.55) %, P < 0.001]. The mean difference was 2.14, 95% CI = 1.05–3.22 (Fig. 1). The I2 test result revealed a high degree of heterogeneity (I2 = 97%, P < 0.001). Therefore, we applied the continuous random effect model (Fig. 3).

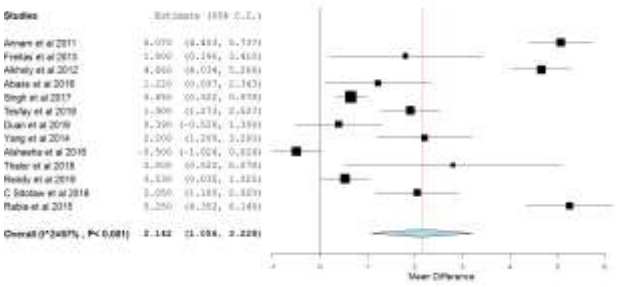

Fig. 1: Forest plot: comparison of PDW in preeclamptic and healthy pregnant women

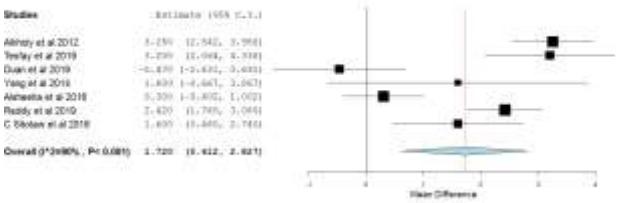

Fig. 2: Forest plot: comparison of PDW in mild preeclampsia and severe preeclampsia.

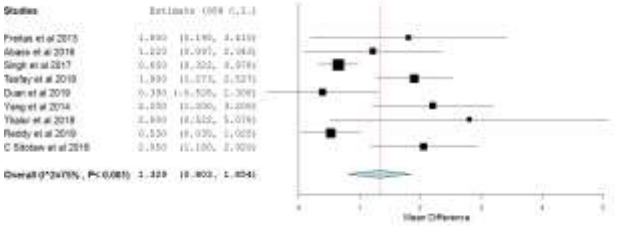

Fig. 3: Forest plot: comparison of PDW in preeclamptic and healthy pregnant women after removing the outliers

Seven studies compared PDW level in the mild with severe cases of preeclampsia (11, 20, 31, 23, 24, 26, 27). There were 393 and 426 women with mild and severe preeclampsia, respectively. The mean (SD) of PDW was significantly higher in women with severe preeclampsia compared to those with mild preeclampsia [16.38(2.45) % vs. 14.55 (2.57) %, P < 0.001]. The mean difference was 1.72, 95% CI = 0.61-2.82 (Fig. 2).

DISCUSSION

Although the exact cause of PE is not fully understood, the diagnosis depends mainly on finding of hypertension and proteinuria after 20 weeks of pregnancy (29).

Normal platelets are circulated in vascular-bed in an inactive form; they become activated when contacting the exposed endothelial wall (30). Active Platelet is correlated with change in platelet volume or size, the larger platelets are thrombogenic and more active than smaller ones (6). Abnormally active platelets are involved in the pathogenesis of many thrombophilic diseases like PE (13).

The platelet indices are volume or size measuring indices increase if the platelet becomes activated. Recently, platelet indices have been used in the prediction, diagnosis, and prognosis of many diseases, being reported as clinically useful biomarkers (31). PDW as one of the platelet volume measuring indices represents the heterogeneity in platelet morphology and is clinically related to platelet activation (32). Thus, it can be a practical tool to evaluate the platelet activation in PE.

The main result of the current review meta-analyses was a high level of PDW in preeclamptic women compared to healthy pregnant women. The mechanism of the platelet activation in PE is due to triggering the coagulation by damaged endothelial cells that lead to adhesion, activation, and aggregation of the platelets. Basic research has revealed that the level of thrombopoietin in plasma increases in patients with PE as a main parameter of platelet activity (33). However, finding of this review revealed that the PDW-as marker of the platelet activation- increased in PE more than in normal pregnancy. Yang et al (11), declared that PDW was an ideal indicator for PE, and is positively correlated with the mean arterial pressure– a well-known severity marker of PE (11). A more recent study has shown that PDW varied significantly between PE and normal pregnancy. They concluded that changes in such parameter can provide a cue towards early diagnosis or potential worsening of pre-eclampsia/eclampsia status, evaluating the PDW can also be beneficial as an indicator of pre-eclampsia and eclampsia (34).

Some clinical information has stated the potentially severe outcomes of PE. PE involves a multi-organ system; therefore, it is challenging to establish an accurate marker for the severity of PE development. However, no more studies evaluated the parameters of the platelet volume indices in the prediction of PE severity. Another finding of this meta-analysis, the greater increase in the PDW was in severe PE than in mild PE. Yang et al, (11) concluded that among other platelet indices, the PDW is significantly higher in women with severe PE than in women with mild PE. Consequently, the PDW can serve as a candidate marker for predicting the severity of PE; they declared. Atilla et al (35) also revealed that PDW level was associated with both, the presence and severity of preeclampsia.

CONCLUSION

Based on this systematic meta-analysis, there were significantly higher values of PDW in comparing PE with normal pregnancy and severe PE with mild PE. Therefore, PDW can be used as a simple laboratory marker for the detection and follow-up of patients that develop preeclampsia.

Conflict of Interest: No conflict of interest is declared by the author.

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