A Systematic Review of the Association of Low Platelet Counts and Preeclampsia

Awad-Elkareem Abass[1], Elryah I. Ali, 1Wesam Nofal[1], Husham O. Elzein[1], Mohammed Suleiman Zaroog[2], Eltigani O.M. Omer[2], Kamal Elbssir Mohammed Ali[2], Eltayeb I.O. Elmahi[2], Ayman Ali Mohammed Alameen[3]

[1]*Department of Medical Laboratory Technology, College of Applied Medical Sciences, Northern Border University, Arar, Saudi Arabia*
[2]*Department of Community Health, College of Applied Medical Sciences, Northern Border University, Arar, Saudi Arabia*
[3]*Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Jouf University, Jouf, Saudi Arabia*

KEYWORDS
Preeclampsia
Eclampsia
Platelet
Pregnancy
Hypertension

ABSTRACT
Introduction: Preeclampsia is a serious pregnancy-related disorder that affects women worldwide; representing as a main cause of feto-maternal morbidity and mortality.
Objectives: The present systematic review aims to evaluate the reported values of platelet count differences in preeclamptic women and compare them to normotensive pregnant women as controls.
Methods: Pubmed-NCBI, Web of Science and Google scholar Database were searched till November 2023 using the keywords “Preeclampsia OR eclampsia AND platelet count". Cohort, case-control, and cross-sectional studies reporting data on platelet count in preeclampsia in comparison to normotensive pregnant women were included.
Results: Ten articles were included, with a total of 870 preeclampsia cases and 1409 controls. The mean (SD) of the platelets count was significantly lower in preeclamptic women compared to normotensive pregnant women [195.2 (55.7) % vs. 249.4 (52.5) %, P < 0.001]. The mean difference was 55.18, 95% CI = 38.33–72.04. However, it was insignificantly lower in women with severe preeclampsia compared to those with mild preeclampsia [178(42.11) vs. 216 (48.69), respectively, P =0.76]. The mean difference was 40.6, 95% CI = 34.24–46.95.
Conclusions: The platelets count is low in preeclampsia and can be considered as a promising laboratory marker for the detection and follow-up of pregnant women who develop preeclampsia.

1. Introduction

Preeclampsia is a serious pregnancy-related disorder which considered as the main cause of feto-maternal morbidity and mortality. The prevalence of preeclampsia differs in various populations and multi-ethnic groups with approximately 5-8% of pregnant women affected [1-12]. Even though the exact pathogenesis of preeclampsia remains unidentified, placental vascular under-perfusion, maternal endothelial damage, and increased vascular permeability are thought to contribute to the pathophysiology of the disease [13-15]. The injured endothelium due to defective placental trophoblastic invasion leads to the activation of the platelets [16, 17]. Normal platelets are present in an inactive form in the bloodstream and can be activated when became contact with damaged endothelial wall [18- 21]. Preeclampsia is characterized by platelet activation, triggering the coagulation, and consequently fibrin deposition in small blood vessels.

It is obvious that preeclampsia is one of the causes of maternal thrombocytopenia and the platelet count increases rapidly after the delivery [22-26]. A low platelet count is suggested to be a characteristic of worsening preeclampsia [27-30]. Platelet-related parameters in pregnant women with preeclampsia are not given much thought until they exhibit a major shift, even if their platelet count is normal. Preeclamptic women may have thrombocytopenia as a result of increased platelet adhesion at the location of injured vascular endothelium, which increases platelet consumption and subsequent destruction. There is an activation of platelets along with increased degranulation leading to a decrease in platelet life span and an increase in the number of immature platelets in peripheral blood smears [31, 32].

2. Objectives

In literature, numerous studies' findings revealed a low platelet count in preeclampsia. Thus, the present review is aimed to assess and analyze if the platelet count is decreased in preeclampsia, by searching Databases in the following site: Pubmed-NCBI, Web of Science and Google scholar.

3. Methods

Searching strategies:

No publication period/date or any other type of restriction were imposed. A literature search was performed on November 15, 2023. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed [33]. In brief, a literature search was done in PubMed-NCBI, Web of Science and Google scholar. The search terms based on the following keywords: "Preeclampsia OR eclampsia AND platelet count". Published studies till November 2023 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:

Cohort, case-control, and cross-sectional study, original articles published in English reporting human pregnancy, preeclampsia investigated on maternal side using the strict definition and platelet count analyzed and reported.

Exclusion criteria:

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

Quality assessment and data collection:

Modified Newcastle Ottawa quality assessment scale was used for assessing the quality of each selected study (34), with a total score of nine. A study that scored 7 and above was considered as high quality, and medium quality if scored 5. For inclusion in this review; the quality of each article was assessed by 2 reviewers independently.

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 platelets count in cases and controls(Table 1). Median (range) or median (inter-quartile) were transformed into mean (SD) as previously described [35, 36].

Statistical methods:

Meta-analyses of the variation in the values of platelets count between cases and controls were performed using Open Meta Analyst software for Windows [35, 37].

Ethical consideration:

Ethical approval was not required since the study was a systematic review. PRISMA guideline recommendations were followed [33].

4. Results

The search strategies recognized 31 articles that reduced to 26 articles after removing duplicates and identifying ineligible records. Reports not retrieved were fours, while 22 were assessed for eligibility. Report excluded either not relevant, inappropriate design, or non-English language.

Ten articles fulfilling the inclusion criteria and were eligible to be included [28, 38-46]. Among the eligible studies, three studies [38, 42, 43] were conducted in India. One study each was conducted in the Kingdom of Saudi Arabia [41], Egypt [39], Sudan [48], Ethiopia [44], China [45], Republic of Korea [28], and Brazil [40]. The total number of preeclampsia cases was 870 and the total number of controls were 1,409. The number of the cases per study ranged from 29 [40] to 163 [45], while the controls ranged from 28 [40] to 816 [28]. The median and variance were reported in three studies [28, 43, 44] and this was converted to the mean (SD) using the specific formula [35, 36]. The mean (SD) of the platelet count value was significantly lower in preeclamptic women compared to healthy pregnant women [195.2 (55.7) % vs. 249.4 (52.5) %, $P < 0.001$]. The mean difference was 55.18, 95% CI = 38.33–72.04, and Std. error of 8.59 (Fig. 2). The I2 test result revealed a high degree of heterogeneity ($I2 = 93$, $P < 0.001$). Thus, we applied the continuous random effect model (Fig. 3). Five studies compared the platelet count in the mild with severe cases of preeclampsia [28, 39, 41, 44, 45]. There were 245 and 276 women with mild and severe preeclampsia, respectively. The mean (SD) of the platelet count value was insignificantly lower in women with severe preeclampsia compared to those with mild preeclampsia [178(42.11) vs. 216 (48.69), respectively, $P = 0.76$]. The mean difference was 40.6, 95% CI = 34.24–46.95 (Fig.

4).

Table 1 Mean, SD, Mean difference (MD) per cases and controls in included studies.

Author/Year	Country	Control /No.	Control /Mean	Control /SD	Cases /No.	Cases/ Mean	Cases/ SD	MD	Lower	Upper
Yang et al	Korea	816	228	79.2	119	195	69.2	32.5	18.9	46.1
Anaam et al	India	100	218	28.2	145	143	32.3	75.2	67.6	82.8
Alkholy et al	Egypt	50	249	38.4	100	161	34.9	87.5	74.8	100.1
Freitas et al	Brazil	28	234	62.8	29	195	68.8	38.8	4.6	72.9
Alsheeha et al	KSA	60	259	39.6	60	236	37.7	22.5	8.7	36.3
Singh et al	India	42	280	89.8	108	172	71.0	108	77.7	138.3
Thalor et al	India	30	241	74.0	30	217	78.0	24.0	-14.5	62.5
Tesfay et al	Ethiopia	140	291	58.4	79	205	58.4	85.9	69.9	102.0
Duan et al	China	93	232	20.3	163	190	24.8	42.0	36.4	47.6
Abass et al	Sudan	50	261	62.7	37	236	82.3	25.2	-6.5	56.9

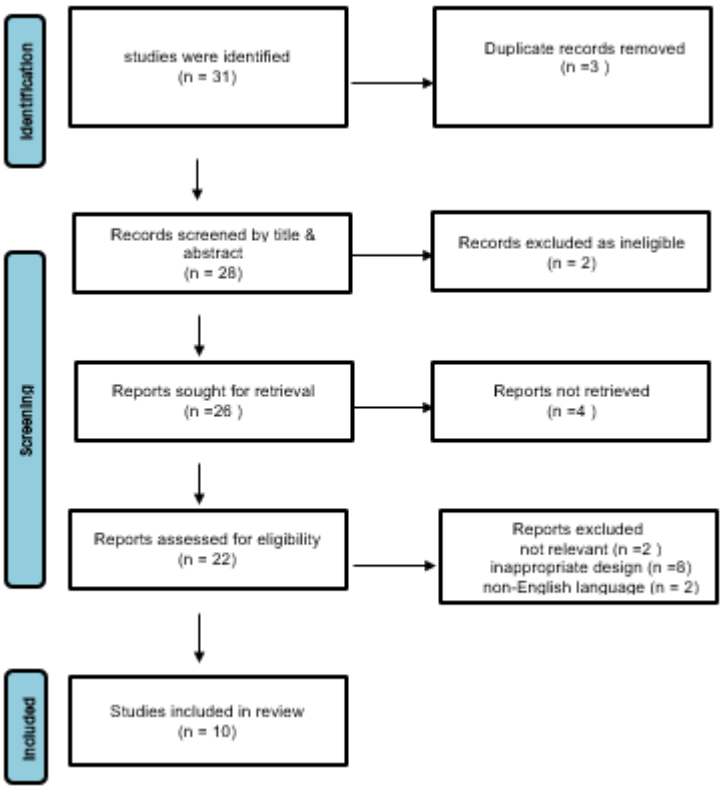

Fig 1: PRISMA flow diagram for systematic review

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

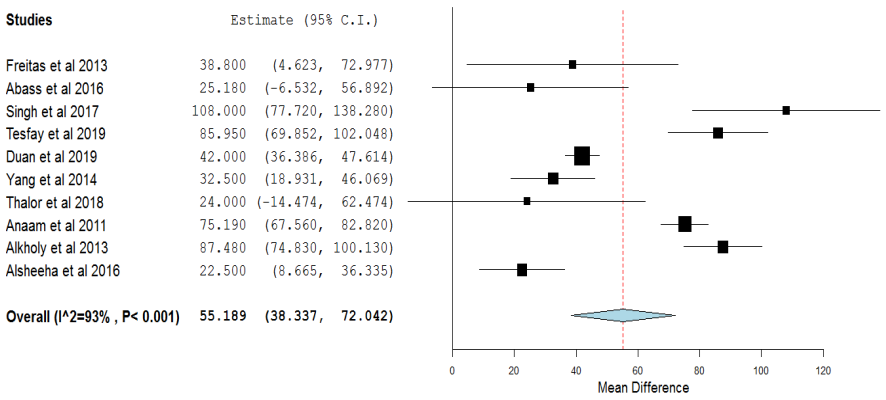

Fig 2: Platelets counts in preeclamptic and normotensive pregnant women.

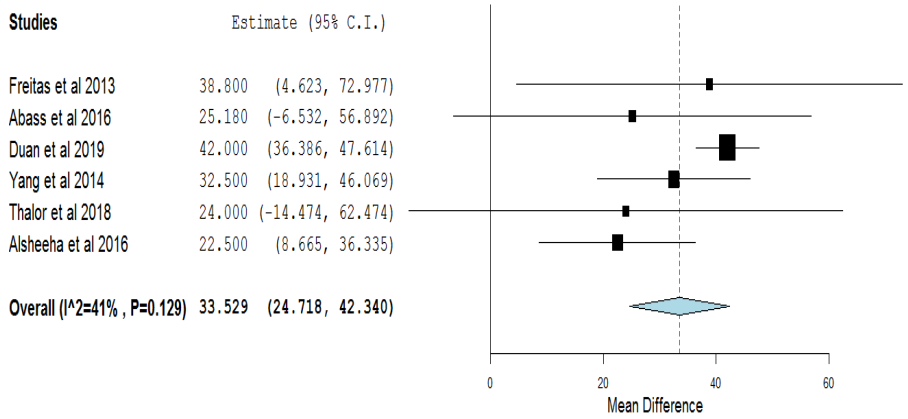

Fig 3: Platelets counts in preeclamptic and normotensive pregnant women after removing the outliers.

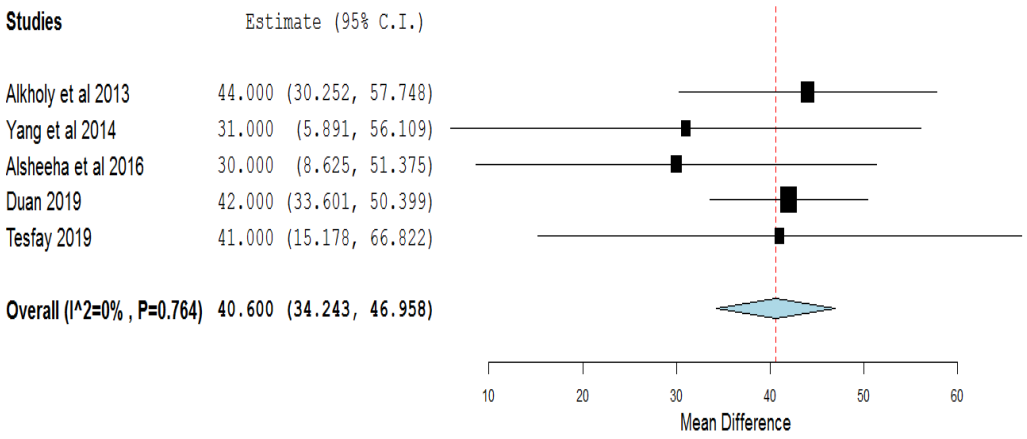

Fig 4: Platelets counts in severe and mild preeclampsia.

5. Discussion

The main result of the current systematic review was a reduced value of platelet count in preeclamptic pregnant women compared to normotensive pregnant women. Normal platelets are circulated in the blood streem in an inactive form; they become activated when contact the exposed endothelial wall [18, 19]. Abnormally active platelets are involved in the pathogenesis of many thrombophilic diseases like preeclampsia [47]. There are several studies which suggest platelet may play a major role in the pathogenesis of preeclampsia. Abnormal coagulation in established preeclampsia are well recognized [48]. The degree of thrombocytopenia increases with the disease severity. Lower the platelet count, greater are feto-maternal mortality and morbidity [49]. Thrombocytopenia is a well-documented procedure in preeclampsia. Preeclampsia and thereby maternal mortality might be reduced through serial monitoring of platelet count as a part of antenatal follow-up. The pathogenesis of thrombocytopenia in preeclampsia is not obvious. Although it is suggested that low platelet count in preeclampsia are linked to abnormal activation of coagulation system and faster platelet consumption [50]. Several studies evaluated the platelet count in preeclamptic women and healthy pregnant women as controls, their findings revealed that platelet counts of these patients were lower than the platelet counts of controls [28, 38-46]. A systemetic review and meta-analysis concluded by Walle and his colleagues revealed a significant decrease in platelet count during the development of preeclampsia among pregnant women [51].

However, the finding of this systemic review and meta-analysis revealed no significant variation when comparing platelets count in mild and severe preeclampsia. Woldeamanuel and his colleagues in their systemetic review and meta-analysis concluded that the platelet count was significantly lower in preeclamptic women, irrespective of severity and presence or absence of associated complications, even before the onset of preeclampsia and in the second trimester of pregnancy [52]. Based on this systematic review, there were significantly lower values of platelets count in preeclamptic women compared to normotensive pregnant women.

Platelet count can be a useful parameter for the detection and follow-up pregnant women with preeclampsia.

Acknowledgement

Not applicable

Funding sources

This research received no specific grant from any funding agency in the public, commercial, or not-for profit sectors.

Conflict of Interest

The Authors have no conflict of interest.

Reference

[1] Sibai B, Dekker G, Kupferminc M. Preeclampsia. Lancet. 2005; 365: 785–799.

[2] http://dx.doi.org/10.1016/S0140-6736(05)17987-2

[3] Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look P. WHO analysis of causes of maternal death:a systemic review. Lancet. 2006; 367: 1066-1074. http://dx.doi.org/10.1016/S0140-6736(06)68397-9

[4] Stekkinger E, Zandstra M, Peeters LL, Spaandernen ME. Early-onset preeclampsia and the prevalence of postpartum metabolic syndrome. Obstet Gynaecol. 2009; 114(5):1076-108. http://dx.doi.org/10.1097/AOG.0b013e3181b7b242

[5] Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol. 2009; 33:130–137. http://dx.doi.org/10.1053/j.semperi.2009.02.010

[6] Trogstad L, Magnus P, Stoltenberg C. Pre-eclampsia: risk factors and causal models. Best Pract Res Clin Obstet Gynaecol. 2011; 30: 1–14. http://dx.doi.org/10.1016/j.bpobgyn.2011.01.007

[7] Chang KJ, Seow KM, Chen KH. Preeclampsia: Recent Advances in Predicting, Preventing, and Managing the Maternal and Fetal Life-Threatening Condition. Int J Environ Res Public Health. 2023; 20(4): 2994. http://dx.doi.org/10.3390/ijerph20042994

[8] Karrar SA, Martingano DJ, Hong PL. Preeclampsia. [Updated 2024 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. https://www.ncbi.nlm.nih.gov/books/NBK570611/

[9] Yang Y, Le Ray I, Zhu J, Zhang J, Hua J, Reilly M. Preeclampsia Prevalence, Risk Factors, and Pregnancy Outcomes in Sweden and China. JAMA Netw Open. 2021; 4(5):e218401. http://dx.doi.org/10.1001/jamanetworkopen.2021.8401

[10] Phyllis August, Baha M Sibai. Preeclampsia: Clinical features and diagnosis. Last updated June 2024. https://www.uptodate.com/contents/preeclampsia-clinical-features-and-diagnosis

[11] ACOG Practice Bulletin Committee.Diagnosis and management of preeclampsia and eclampsia. Obstet Gynecol. 2002;99:159-167. http://dx.doi.org/ 10.1016/s0029-7844(01)01747-1

[12] Berg CJ, Mackay AP, Qin C, Callaghan WM. Overview of maternal morbidity during hospitalization for labor and delivery in the United States: 1993–1997 and 2001–2005. Obstet Gynecol. 2009;113:1075–1081. http://dx.doi.org/ 10.1097/AOG.0b013e3181a09fc0

[13] MacKay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. Obstet Gynecol. 2001;97:533–538. http://dx.doi.org/ 10.1016/s0029-7844(00)01223-0

[14] Staff AC, Benton SJ, von Dadelszen P, Roberts JM, Taylor RN, Powers RW, Charnock-Jones DS, Redman CW. Redefining preeclampsia using placenta-derived biomarkers. Hypertension. 2013; 61(5): 932-42. http://dx.doi.org/10.1161/HYPERTENSIONAHA.111.00250

[15] Tomimatsu T, Mimura K, Matsuzaki S, Endo M, Kumasawa K, Kimura T. Preeclampsia: Maternal Systemic Vascular Disorder Caused by Generalized Endothelial Dysfunction Due to Placental Antiangiogenic Factors. Int J Mol Sci. 2019; 20(17): 4246. http://dx.doi.org/10.3390/ijms20174246

[16] McElwain CJ, Tuboly E, McCarthy FP, McCarthy CM. Mechanisms of Endothelial Dysfunction in Pre-eclampsia and Gestational Diabetes Mellitus: Windows Into Future Cardiometabolic Health? Front Endocrinol (Lausanne). 2020;11:655. http://dx.doi.org/10.3389/fendo.2020.00655

[17] Vinodhini R and Lavanya K. Evaluation of platelet count as a prognostic index in eclampsia and preeclampsia. Int J Modn Res Revs. 2014; 2(10): 447–452. https://journalijmrr.com/wp-content/uploads/2014/10/IJMRR-112.pdf

[18] Moser, G.; Guettler, J.; Forstner, D.; Gauster, M. Maternal Platelets—Friend or Foe of the Human Placenta? Int. J. Mol. Sci. 2019, 20, 5639. http://dx.doi.org/10.3390/ijms20225639

[19] Holthe MR, Staff AC, Berge LN, Lyberg T. Different levels of platelet activation in preeclamptic, normotensive pregnant,

and nonpregnant women. Am J Obstet Gynecol. 2004; 190:1128-1134. http://dx.doi.org/10.1016/j.ajog.2003.10.699

[20] Vladareanu AM, Andrei C, Onisai M, et al. The endothelial-platelet dysfunction in preeclampsia. Maedica- J of Clin Med. 2007; 3: 214-22. https://www.maedica.ro/articles/2007/2007_Vol2(5)_No3/2007_Vol2(5)_No3_pg214-221.pdf

[21] Becker RC, Sexton T, Smyth SS. Translational Implications of Platelets as Vascular First Responders. Circ Res. 2018;122(3):506-522. http://dx.doi.org/10.1161/CIRCRESAHA.117.310939

[22] Hamilos M, Petousis S, Parthenakis F. Interaction between platelets and endothelium: from pathophysiology to new therapeutic options. Cardiovasc Diagn Ther 2018;8(5):568-580. http://dx.doi.org/10.21037/cdt.2018.07.01

[23] Mohapatra S, Pradhan BB, Satpathy UK, Mohanty A, Pattnaik JR. Platelet estimation: its prognostic value in pregnancy induced hypertension. Ind J Physiol Pharmacol. 2007; 51(2):160-164. https://europepmc.org/article/med/18175660

[24] Habas E, Rayani A, Ganterie R. Thrombocytopenia in hypertensive disease of pregnancy. J Obstet Gynaecol India. 2013; 63(2):96-100. http://dx.doi.org/10.1007/s13224-012-0257-2

[25] Rupakala BM, Gupta R, Shetty VH, Sailakshmi MPA. Thrombocytopenia in hypertensive disorders of pregnancy. Int J Reprod Contracept Obstet Gynecol 2018;7:848-54. http://dx.doi.org/10.18203/2320-1770.ijrcog20180409

[26] Mayama, M., Morikawa, M., Yamada, T. et al. Mild thrombocytopenia indicating maternal organ damage in preeclampsia: a cross-sectional study. BMC Pregnancy Childbirth. 2021; 21: 91. https://doi.org/10.1186/s12884-021-03564-4

[27] Biva Rani Mondal, Debatosh Paul, Tuhin Sultana, Quddusur Rahman, Sharmeen Ahmed, Kaniz Fatema, Waqar AhmedKhan, Bilquis Banu, Mesbah Uddin Ahmed, A.N. Nashimuddin Ahmed. Assessment of platelet count and platelet indices in pre-eclampsiaand eclampsia. The American Journal of Innovative Research and Applied Sciences. 2015; 1(3): 80-84

[28] https://www.researchgate.net/publication/350062099_ASSESSMENT_OF_PLATELET_COUNT_AND_PLATELET_INDICES_IN_PRE-ECLAMPSIA_AND_ECLAMPSIA#fullTextFileContent.

[29] De Vivo A, Baviera G, Giordano D, et al. Endoglin, PlGF and sFlt-1 as markers for predicting pre-eclampsia. Acta Obstet Gynecol Scand. 2008; 87: 837–842. http://dx.doi.org/10.1080/00016340802253759

[30] Yang Seung Woo, Soo Hyun Cho, Han Sung Kwon, In Sook Sohn, Han Sung Hwang. Significance of the platelet distribution width as a severity marker for the development of preeclampsia. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2014; 175: 107–111. http://dx.doi.org/10.1016/j.ejogrb.2013.12.036

[31] Walle M, Gelaw Y, Getu F, Asrie F, Getaneh Z. Preeclampsia has an association with both platelet count and mean platelet volume: A systematic review and meta-analysis. PLoS One. 2022;17(9):e0274398. http://dx.doi.org/10.1371/journal.pone.0274398

[32] Gashaw Garedew Woldeamanuel, Kenean Getaneh Tlaye, Ling Wu, Liona C. Poon, Chi Chiu Wang.Platelet count in preeclampsia: a systematic review and meta-analysis. American Journal of Obstetrics & Gynecology. 2023; 5(7):100979. http://dx.doi.org/10.1016/j.ajogmf.2023.100979

[33] Sameer MA, Meshram DP, Deshpande SA, et al. Role of platelet count as important prognostic marker in pregnancy induced hypertension. J Dent Med Sci (IOSR-JDMS). 2014; 13(4): 39–43. http://dx.doi.org/10.9790/0853-13433943

[34] Nirmala T, Vani BR, Murthy Srinivasa V, et al. Study of platelet indices in pregnancy induced hypertension. Indian J Pathol Oncol. 2015; 2(1): 25–30. https://www.ijpo.co.in/article-details/306

[35] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71. http://dx.doi.org/10.1136/bmj.n71

[36] Munn Z, Moola S, Lisy K, Rittano D. The systematic review of prevalence and incidence data. Joanna Briggs Inst Rev Man. 2014; 2014(Suppl):1–37. http://joannabriggs.org/assets/docs/ sumari/ReviewersManual_2014-The-Systematic-Review-of-Prevalence-and- Incidence-Data_v2.pdf.

[37] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005; 5, 13. http://dx.doi.org/10.1186/1471-2288-5-13

[38] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014; 14, 135. http://dx.doi.org/10.1186/1471-2288-14-135

[39] Meta-Analyst O. Open Meta-Analyst - the tool | evidence synthesis in health. https://www.brown.edu/academics/public-health/research/

[40] Annam Vamseedhar, Srinivasa K , Santhosh K Yatnatti , Suresh DR. Evaluation of platelet indices and platelet counts and their significance in Pre eclampsia and eclampsia. Int J Biol Med Res. 2011; 2(1): 425-42. https://www.researchgate.net/publication/48347108_Evaluation_of_platelet_indices_and_platelet_counts_and_their_significance_in_pre-eclampsia_and_eclampsia

[41] Alkholy Eman Abdel-Moneim, Elsayed Ali Farag, Mohammed Atef Behery and Mervat Mohammed Ibrahim. The significance of platelet count, mean platelet volume and platelet distribution width in preeclampsia. AAMJ. 2013; 11(1): 200-214.

https://www.researchgate.net/publication/320559016_THE_SIGNIFICANCE_OF_PLATELET_COUNT_MEAN_PLATELET_VOLUME_AND_PLATELET_WIDTH_DISTRIBUTION_INPREECLAMPSIA#fullTextFileContent

[42] Freitas Letícia Gonçalves, Patrícia Nessralla Alpoim, Flávia Komatsuzaki, Maria das Graças Carvalho & Luci Maria S. Preeclampsia: Are platelet count and indices useful for its prognostic? Hematology. 2013; 18(6): 360-36. http://dx.doi.org/10.1179/1607845413Y.0000000098

[43] AlSheeha Muneera A, Rafi S Alaboudi, Mohammad A Alghasham, Javed Iqbal, Ishag Adam. Platelet count and platelet indices in women with preeclampsia. Vascular Health and Risk Management. 2016; 12: 477–480. http://dx.doi.org/10.2147/VHRM.S120944

[44] Singh Abha, Ruchi Varma. Role of Platelet Distribution Width (PDW) and Plateletcrit in the Assessment of Nonthrombocytopenic Preeclampsia and Eclampsia. The Journal of Obstetrics and Gynecology of India. 2018; 68(4): 289–293. http://dx.doi.org/10.1007/s13224-017-1036-x

[45] Thalor Nitesh, Kanika Singh∗, Mukta Pujani, Varsha Chauhan, Charu Agarwal, Rashmi Ahuja. A correlation between platelet indices and preeclampsia. hematol transfus cell ther. 2019; 41(2): 129–133. http://dx.doi.org/10.1016/j.htct.2018.08.008

[46] Tesfay Feven, Mikias Negash, Jemal Alemu, Mohammedtahir Yahya, Gebre Teklu1, Meseret Yibrah, Tsegay Asfaw, Aster Tsegaye. Role of platelet parameters in early detection and prediction of severity of preeclampsia: A comparative cross-sectional study at Ayder comprehensive specialized and Mekelle general hospitals, Mekelle, Tigray, Ethiopia. PLoS ONE. 2019; 14(11): e0225536. http://dx.doi.org/10.1371/journal.pone.0225536

[47] Duan Zhongliang,Cui Li, Wing Ting Leung, Jiangnan Wu , Mingyan Wang, Chunmei Ying , and Ling Wang. Alterations of Several Serum Parameters Are Associated with Preeclampsia and May Be Potential Markers for the Assessment of PE Severity. Hindawi Disease Markers. 2020; Article ID 7815214, 7 pages. http://dx.doi.org/10.1155/2020/7815214

[48] Awad-Elkareem Abass, Remaz Abdalla, Isra Omer, Salma Ahmed, Ahoud Khalid, Husham Elzein. Evaluation of Platelets Count and Indices in Pre-Eclampsia Compared to Normal Pregnancies. IOSR Journal of Dental and Medical Sciences. 2016; 15(7): 05-08. http://dx.doi.org/10.9790/0853-150750508

[49] Goshal M K , M Bhattecharyya. Overview of Platelet Physiology: Its Hemostatic and Nonhemostatic Role in Disease Pathogenesis. The Scien World J. 2014; Article ID 781857, 16 pages. http://dx.doi.org/10.1155/2014/781857

[50] Piazze J, Gioia S, Maranghi L, Anceschi M. Mean platelet and red blood cell volume measurements to estimate the severity of hypertension in pregnancy. J Perinat Med. 2006; 34(3):246-7. http://dx.doi.org/10.1515/JPM.2006.044

[51] Kulkarini RD, Sutaria UD. Platelt counts in toxaemia of pregnancy. Ind J Obstet Gynecol.1983;33:32-325. https://jogi.co.in/storage/articles/files/filebase/Archives/1983/jun/1983_321_325_Jun.pdf

[52] Redman CWG, Bonnar J, Beilin L. Early platelet consumption in preeclampsia. BMJ. 1987; 1: 467 – 469. http://dx.doi.org/10.1136/bmj.1.6111.467

[53] Walle M, Gelaw Y, Getu F, Asrie F, Getaneh Z. Preeclampsia has an association with both platelet count and mean platelet volume: A systematic review and meta-analysis. PLOS ONE. 2022; 17(9): e0274398. http://dx.doi.org/10.1371/journal.pone.0274398

[54] Woldeamanuel GG, Tlaye KG, Wu L, Poon LC, Wang CC. Platelet count in preeclampsia: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2023; 5(7):100979. http://dx.doi.org/10.1016/j.ajogmf.2023.100979