Elevated maternal serum iron concentrations and decreased platelet count in women with pregnancy induced hypertension: A systematic review of observational studies.

Bhaktraj Singh[1], Roopa Satyanarayan Basutkar[*]

First Author: [1]Bhaktraj Singh, Intern student, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, The Nilgiris-643001, Tamil Nadu, India

Correspondence Author: Roopa Satyanarayan Basutkar*, Assistant Professor, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, The Nilgiris-643001, Tamil Nadu, India

ABSTRACT

Increase in level of maternal serum iron and decreased platelet count will damage of the vascular endothelium and increase the level of blood pressure. From Cochrane CENTRAL, PubMed, Google scholar and Scopus, eight observational studies were identified. Joanna Briggs Institute (JBI) data extraction form and Quality Assessment Tool (NHLBI) was used. In the study conducted by Rayman MP et al and Gutirerrez-Aguirre CH et al there was 1.7-fold increase in serum iron in preeclampsia group. In the studies conducted by Alkholy EA et al, Shetty J et al and Damani Z et al revealed the platelet count was significantly lower in pregnancy induced hypertension group. Based on the findings, this review has highlighted that pregnancy induced hypertension is significantly associated with increased in maternal serum iron concentrations and the reduced platelet indices. A protocol to be established during the antenatal care to check the serum iron concentrations and platelet indices.

INTRODUCTION

Pregnancy induced hypertension (PIH) globally affects 5-10% of pregnant women and responsible for the maternal deaths [1,2] The prevalence of gestational hypertension in nulliparas women is 6-15% & 2-4% in multiparas [3]. PIH is estimated to affect 7% to 10% of all pregnancies in the United States [4]. The incidence of PIH in India ranges from 5% to 15% [5]. The initiating event in PIH is because of reduced uteroplacental perfusion of abnormal cytotrophoblast invasion of spiral arterioles. Placental ischemia is thought to lead to widespread activation or dysfunction of the maternal vascular endothelium that results in enhanced formation of endothelin and thromboxane, increased vascular sensitivity to angiotensin II, and decreased formation of vasodilators such as nitric oxide and prostacyclin [6-8]. The women with PIH conditions have high risks of preeclampsia, C-section delivery and renal diseases. The PIH conditions also affect the foetus in many ways such as intrauterine growth restriction, delaying or pre-delivery conditions and inappropriate body weight [9]. As PIH's aetiology is still unknown therefore preeclampsia's pathogenesis includes developmental abnormalities, placental prefusion and thus leading to impaired maternal organ function [10-12]. The concentration of serum iron levels is usually elevated in PIH conditions as it will act as better distinguisher between PIH and other types of hypertensions. The elevated iron levels are the end phase of destruction of blood cells [13]. Iron acts as an important element having various actions involving such as a carrier in oxygen transport (by binding to the hemoglobin), adenosine triphosphate production in the nucleic acid synthesis, maintenance, and protection of cellular structures from oxidative damage [14].

It is also involved in the pathway of hypoxia-inducible factor (HIF) which helps in the development of the placenta. While being a transition element, iron acts as a catalyst for the Fenton and Haber-Weiss reactions and promotes oxidative stress and damage to endothelial

cells when found in the excess [6]. The Haber–Weiss reaction generates •OH (hydroxyl radicals) from H_2O_2 (hydrogen peroxide) and superoxide ($•O_2^-$) catalysed by iron ions. Fe^{3+} + $•O_2^- \rightarrow Fe^{2+}$ + O. The second step is the Fenton reaction: $Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^- + •OH$ [6,14]. Although, oxidative stress is a recognized factor of the pathogenesis of pregnancy-induced hypertension. Thus, this leads to insufficient re-modelling which thereby cause utero-placental high-resistance circulation, hypoxia, and increased production of reactive oxygen species (ROS), affecting apoptosis and the immune system, and intensification of inflammatory response. These processes activate the maternal circulation system and damage of the vascular endothelium. The endothelial homeostasis may get disturbed which eventually results in the increased levels of blood pressure [9]. Several studies have also suggested that platelet may play a major role in the etiopathogenesis of preeclampsia. Out of all hematological changes that occur in preeclampsia thrombocytopenia is the most common. The degree of thrombocytopenia increases with the severity of the disease. Abnormal vascular response associated with increased systemic vascular resistance, enhanced platelet aggregation, activation and alteration of the coagulation system, and endothelial cell dysfunction are believed to play an important role in the pathogenesis of pregnancy induced hypertension [15,16]. As pregnancy induced hypertension has huge impact worldwide, the aim of this review is to gather evidence from the published observational studies to determine the relationship of elevated maternal serum iron concentrations and decreased platelet indices as a risk biomarker in detection of PIH during early pregnancy.

MATERIALS AND METHODS

The criteria's for considering studies for this review.

Inclusion criteria

The search involved observational studies (cross-sectional), with an increase in maternal serum iron concentration and decrease platelet count indices among the pregnant women who experienced the condition of pregnancy induced hypertension. The observational studies included in this review consists of population involving the pregnant women with maternal age of 18–35 years at conception. And studies that mentioned a diastolic blood pressure of at least 90 mm Hg recorded in the left lateral decubitus position on two occasions at least after 6 hours were considered among the PIH women. Studies in which subjects suffering from any medical complications, such as diabetes mellitus or inflammatory diseases, pregnant women who never received a blood transfusion were not considered eligible to be included in this review. Before the month of enrollment into the study none of the study participants received vitamin or iron supplements or aspirin.

Control group studies (a) were primigravida's and multigravidas; (b) were normotensive throughout their prenatal course (c) had trace or less proteinuria on a dean-catch specimen.

Exclusion criteria

Randomized controlled trials (RCTs) and interventional studies were not part for review. And the papers of foreign languages, unrelated studies, wrong study design and wrong population were also excluded.

Types of outcome measures

Primary outcome

Primary outcome measure involves all those studies have elevated serum iron levels and ferritin levels, platelet count in pregnant women with pregnancy induced hypertension.

Secondary outcomes:

Red blood cells count, hemoglobin concentration, hematocrit, red cell width, RBC indices [mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) in some studies serum haptoglobin was also mentioned as secondary outcomes.

Search techniques used in identification of studies.

Search strategy

The different search indexes such as PubMed, Scopus, Google Scholar and The Cochrane CENTRAL were searched. All articles were uploaded into Zotero and then screened in Rayyan for the inclusion and exclusion of studies in this review. The articles which fulfilled the eligibility criteria were included in this review.

Keywords

The keywords used to search papers, includes pregnancy-induced hypertension, serum iron, eclampsia, pre-eclampsia, hypertensive disorders, pregnancy aggravated hypertension, gestational hypertension, percent transferrin and ferritin.

Collection of data

Study selection

The search was conducted between 4th September 2019 to 8th March 2020. The studies published from last thirty years were screened to include in the review writeup. The screening of the studies which fulfil the eligibility criteria was performed by two independent reviewers BRS and RSB. The screening was performed based on the inclusion and exclusion criteria using the Rayyan online portal. There were no restrictions considered for the trimesters of pregnancy, study duration and the country settings. All the duplicates were assessed and then the full text articles were independently reviewed by two reviewers. All the disagreements and conclusions were discussed.

Data extraction

The two independent reviewers used Joanna Briggs Institute (JBI) data extraction form which was specific for observational/experimental studies. This include study tittle, name of author, different country settings, design of study, sample size, intervention type, data source and population, domain tested, measurement of iron levels, serum ferritin levels, platelet count, RBC count, Hb concentration, hematocrit, red cell width, RBC indices, mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) in some studies serum haptoglobin was also mentioned as secondary outcomes results and conclusions.

Appraisal and quality assessment of included studies:

Quality Assessment Tool (NHLBI) which is specific for cohort and cross- sectional studies was used to select & appraise the papers of included studies in the review. NHLBI is a tool created by National Institute of Health (NIH) for cross- sectional and observation. Two independent reviewers assessed the internal validity of included studies using QAT. The assessment tool NHLBI use the parameter as "yes", "no" and others (cannot determine/not applicable/not reported) for the checklist is provided.

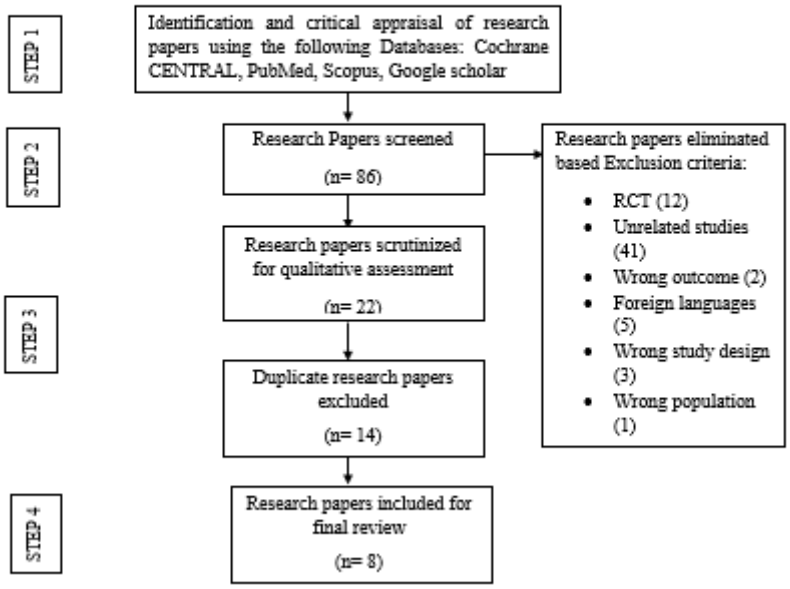
The studies which were included in the review and the quality of the study was rated as poor/ fair/ good. Studies by Rayman MP *et al.*, Gutierrez-Aguirre CH *et al*., Alkholy EA *et al*. were rated as good; however, the study by Siddiqui IA *et al*., Serdar Z *et al*., Samuel *et al*., Shetty J *et al*., Damani Z *et al*. were fair in quality. All disputes were resolved.

RESULTS

From Cochrane CENTRAL, PubMed, Google scholar and Scopus 94 studies were found. Further 8 articles were duplicates and removed from the study. 78 articles were excluded as the studies did not qualify the eligibility criteria, of which 12 were randomised controlled trials

(RCT), 41 were unrelated studies (no relation with serum iron or pregnancy induced hypertension), 5 were foreign language. Out of the remaining 22 articles 14 were excluded due to duplication. The review was performed on the conclusions of the seven articles which are selected after the literature search. The whole process is represented as a flowchart in **Figure 1**.

Figure 1: Flow diagram of screening process of studies.



Association between pregnancy induced hypertension and serum iron

All studies included in this review investigated the association between pregnancy induced hypertension and elevated serum iron levels. The systolic and diastolic blood pressure levels were used to diagnose pregnancy induced hypertension and serum iron as a risk biomarker for pregnancy induced hypertension. Rayman MP *et al* [17] conducted a case control study in women during their late pregnancy. The median serum iron concentration was around 1.7-fold higher in patients with preeclampsia than in pregnant controls (p= 0.001). In study by Gutierrez -Aguirre CH et al [18]. Serum iron was higher in patients with pre-eclampsia than in control group (103.9 vs. 90.8 μg/dl) (p = 0.345). The median serum ferritin was around 6-fold higher

in the preeclamptic patients than in the control subjects (53.1 vs 9.4 µg/L, p < .001). A positive correlation between elevated iron levels and higher serum ferritin levels was observed (r = 0.297; p = 0.024) in both groups. No significant difference was found in age (p=0.576), height (p=0.931), days receiving iron or iron dose received in either group. Both studies have shown mean increase in serum iron levels in pregnancy induced hypertension. In another study by Serdar Z *et al* [19]. age and body mass index were found non-significant. Serum iron and copper levels were significantly elevated and total iron binding capacity as significantly decreased in preeclamptic patients compared with those of healthy pregnancies. The transferrin levels were low in preeclampsia patients compared with normotensive patients. A study by Siddiqui IA *et al* [20] shows no significance difference between the age (p=0.95), BMI (p=0.38). Mean serum iron concentrations in preeclamptic and control normal pregnant women were 23.48 ± 9.05 µmol/l and 12.2 ± 5.21 µmol/l, respectively. Similarly, mean serum ferritin concentration was 32.56 ± 11.72 g/l in preeclamptic was and in normal pregnant women it was found to be19.89 ± 8.86 g/l.

There was no significant differences in red blood cell count (p=0.26), hemoglobin (p=0.71), and hematocrit (p=0.96) concentrations among the preeclamptic and normal pregnant women. A study by Samuels *et al* [21]. found that patients with pregnancy-induced hypertension have a higher serum iron concentration (111 ± 26 J.g/dl) when compared with normal control pregnancies (69 ± 17 J.g/dl) (p < 0.0001).

Association between pregnancy induced hypertension and platelet count:

All the studies selected in this review have similar outcomes. All the studies are showing decrease in platelet count indices. A study by Moneim Alkholy *et al* [15] found that platelet count was significantly lower in women with PIH compared to normal pregnant women groups (139.340 ± 32.610,183.940 ± 37.380 and 249.120 ± 38.350with P < 0.001) respectively.

Another study conducted by Shetty J *et al* [5] discovered that out of the sample size of 200 subjects, platelet count was found low i.e., >100000 in 42 subjects. A study by Damani *et al* **[**16] found the platelet count of subjects was higher in the third trimester (158.7±68.4) compared to the second trimester (100.9±62) and the first trimester (108±62).

Pregnancy induced hypertension and complications in mothers.

Three studies were identified which explained the complications experienced by mothers who had pregnancy induced hypertension. Hemolysis and disseminated intravascular coagulation have long been recognized as complications of severe pregnancy-induced hypertension. Samuels P *et al* [21], demonstrates that mild hemolysis is part of the constellation of signs and symptoms constituting pregnancy-induced hypertension and is not limited to severe disease.

Although laboratory evidence of hemolysis correlated well with serum iron levels, these parameters often remained within the normal limits. Therefore, we believe that these laboratory values cannot be used alone to establish a diagnosis of pregnancy-induced hypertension. The regression value (r) was found to be 0.84 in participants who had pregnancy induced hypertension**.** Rayman MP *et al* [17]**,** found that ten participants had AST levels >42 IU/L, suggesting a component of liver damage, whereas 13 had a low platelet count (<175*10 ^{3}cells/L), also indicative of disease severity, although 2 control subjects also had a platelet count in this range. Seven of the pregnancies were complicated by the HELLP (hemolysis, elevated liver enzymes, low platelets) or HELLP (elevated liver enzymes, low platelets) syndromes. Serdar Z *et al* [19]**,** postulated the significantly increased odds ratios for the higher tertiles of oxidation markers and iron and increased significances in severe preeclampsia indicates an association of these increased iron can further promote oxidative stress by decreasing serum antioxidant capacity. Most of the abnormalities are neglected in developing countries thereby the conduct of such studies would be beneficial for the clinicians for early

recognition and treatment of pregnancy induced hypertension. The summary of the studies reviewed and mentioned in **Table 1** and **Table 2**.

Table 1: An overview of the methodology and outcomes of various included studies.

Author, Year	Country	Study design	Sample size	Domain tested	Outcome	Limitations
Rayman MP et al, 2002	United Kingdom	Case control	40	Serum iron	Serum iron levels (21.7 µmol/L in PIH and 12.9 µmol/L control, P < .001)	Sample size was not adequate.
Samuels P et al, 1987	Philadelphia, USA	Case control	54	Serum iron	Increased serum iron (111 ± 26 µg/dl) in PIH (69 ± 17 µg/dl) in control, (p < 0.0001)	Although laboratory evidence of hemolysis correlated well with serum iron levels, these parameters often remained within the normal limits for our clinical laboratory.
Siddiqui IA et al, 2011	Saudi Arabia	Case control	120	Serum iron	Increased serum iron (23.48 ± 9.05µmol/l in PIH) (12.2 ± 5.21 µmol/l in control), (p=0.05)	Absence of the information on other parameters of body iron status like (TIBC), transferring saturation and apo transferrin.
Gutierrez-Aguirre et al, 2017	Mexico	Pilot observational study	61	Serum iron	Increased serum iron (103.9 µg/dl PIH and 90.8µg/dl control) (p= 0.345)	The clinical significance of statically significant difference in serum ferritin concentration

						between the groups is unclear
Serdar Z et al ,2006	Turkey	Case control	90	Serum iron	increased serum iron 98±48 preeclampsia mg/dl & 73±31 control group.	Nil
Alkholy EA et al, 2013	Egypt	Cross sectional	150	Platelet count	Decreased platelet count there is a significant gradual decrease in platelet count from normotensive pregnant women (249,120 ± 38,350/ mm3) to mild PE group (183,940 ± 37,380/ mm3) and severe PE group (139,340 ±32,610/ mm3)	Nil
Shetty J et al, 2016	India	N/a	200	Platelet count	Decreased platelet count. Out of 200 subjects, the platelet count for 42 subjects were decreased.	Nil
Damani Z et al, 2016	Albania	Case control	40	Platelet count	Decreased platelet count in PIH group 217050±50780.7 as compared to control group 235500±38448	Nil

Table 2: Summary of the studies related to pregnancy induced hypertension & platelet count with serum iron concentrations.

Author, Year	Parameters measured	p-value	R-value and/or Odds ratio, 95% CI	Findings

Rayman MP et al, 2002	Serum total iron, unsaturated iron-binding capacity (UIBC), Percent transferrin saturation, TIBC, Serum ferritin	p=0.001	Not mentioned	Raised serum iron and ferritin may have the potential to be used diagnostically to warn of incipient preeclampsia.
Samuels P et al, 1987	Serum iron, TIBC, serum ferritin	p= 0.000	R=0.848	Mild hemolysis is part of the constellation of signs and symptoms constituting pregnancy-induced hypertension. Elevated serum iron levels observed in many patients with this disorder are derived in large part from hemolysis.
Siddhiqui IA et al, 2011	Serum iron, serum ferritin, RBC count, Hb concentration, haematocrit, (MCV) and (MCHC)	p= <0.05	Not mentioned	Antenatal IDA and congenital muscular dystrophy have an adverse effect on child's cognitive development.
Gtierrez Aguuirre CH et al, 2017	Serum iron	p= 0.345	R=0.297	In this pilot study it is found that a higher serum ferritin level, despite being within normal range, was associated with PE in pregnant women receiving prophylactic iron.
Serdar Z et al, 2006	Serum iron, serum copper	p=0.001	OR=3	The significantly increased odds ratios for the higher tertiles of oxidation markers and iron and increased significances in severe preeclampsia indicates an association of the increased iron can further promote oxidative stress by decreasing serum antioxidant capacity
Alkholy EA et al, 2013	Platelet count and platelet indices	p=0.001	Not mentioned	The estimation of platelet indices may be considered as an easy, reliable, economic and rapid method for detection of preeclampsia and assessment of its severity.
Shetty J et al, 2016	Platelet count and platelet indices, D-dimer, erythrocyte sedimentation rate, hemoglobin (Hb), red cell indices,	n/a	n/a	The samples size of 200 subjects, platelet count was found low i.e., >100000 in 42 subjects.

	packed cell volume, total count prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT)			
Damani Z et al, 2016	Platelet count	p= 0.003	n/a	Pregnancy induced hypertension (PIH) is associated significantly with low platelet count.

n/a- Not available, r-regression coefficient, OR- odds ratio, CI- confidence interval, Hb-hemoglobin, MCV- Mean corpuscular volume, Hct-Hematocrit.

Assessment of bias in the included studies

Being a prospective study, all the confounding variables were examined in the study by Rayman MP et al [17] and no reasons for missing data is given. Heterogeneity was not found in this study as patients were from similar socio-economic status. In the study the confounding was adjusted by not giving iron supplements to preeclamptic or control group. Siddiqui IA *et al* [20] did measure potential factors that can influence the outcome and missing of data was not reported.

In study by Serdar Z et al [19]-aspartate aminotransferase (AST) activity (an indicator of liver damage) was not calculated, and this might lead to confounding bias. Gutierrez-Aguiree CH et al., [8]conducted a pilot study for each variable but did not use an appropriate analysis method or design that adjusted for all the important confounding variables. In the study the participants were interviewed, and detailed medical history and medication history was taken, thus there might be chances for response bias. We found that outcome assessors were aware about the exposure status of participants in case and control all the 7 studies. We used the assistance of Conducting Systematic Reviews and Meta-Analysis of Observational Studies of Etiology

(COSMOS-E) for assessing the risk of bias in the included studies and it has been illustrated in **Table 3. DISCUSSION**

Table 3: Risk of bias assessment of the included studies by COSMOS-E scale.

Rayman MP et al, 2002		
Methods **Participants** **Outcome**	Case control 40 Serum iron	
Bias	**Author's judgement**	**Support for judgement**
Causal relationship (Confounding bias) Selective sampling (Selection bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Low risk Unclear risk Low risk	Aspartate aminotransferase (AST) activity (an indicator of liver damage) was determined. Forty obstetric patients at the John Radcliffe Hospital, Oxford were recruited and hence is not applicable for generalised pregnant population. Outcome assessors took cases and controls by medical records.
Samuels P et al, 1987		
Methods **Participants** **Outcome**	Case Control 54 Serum iron	
Bias	**Author's judgement**	**Support for judgement**
Causal relationship (Confounding bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Low risk Unclear risk	Multiple linear regression to determine the proportion of the serum iron in patients with pregnancy-induced hypertension that could be attributed to haemolysis, hepatocellular damage, and volume contraction. Outcome assessors should have been unaware of the exposure status of the study participants.
Serdar Z et al, 2006		
Methods **Participants** **Outcome**	Case control 90 Serum iron	
Bias	**Author's judgement**	**Support for judgement**
Incomplete covariates (Confounding bias) Sampling (Selection bias)	High risk Unclear risk	Aspartate aminotransferase (AST) activity (an indicator of liver damage) was not determined. Severe preeclampsia in the third trimester who were admitted to the Obstetrics Department of Uludag ˘ University Medical Faculty Clinics were recurited.
Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Unclear risk	Outcome assessors should have been unaware of the exposure status of the study participants.

Siddiqui IA et al, 2010		
Methods **Participants** **Outcome**	Case control 120 Serum iron	
Bias	**Author's judgement**	**Support for judgement**
Incomplete covariates (Confounding bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Low risk Unclear risk	Several potential factors that can influence the outcome were measured. Outcome assessors should have been unaware of the exposure status of the study participants.
Causal relationship (Confounding bias) Selective sampling (Selection bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Low risk Unclear risk Low risk	Aspartate aminotransferase (AST) activity (an indicator of liver damage) was determined. Forty obstetric patients at the John Radcliffe Hospital, Oxford and hence is not applicable for generalised pregnant population. Outcome assessors took cases and controls by medical records.
Alkholy EA et al 2013		
Methods **Participants** **Outcome**	Cross sectional 150 Platelet count	
Bias	**Author's judgement**	**Support for judgement**
Causal relationship (Confounding bias) Missing data (attrition bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Unclear risk Unclear risk Low risk	Design is not adjusted for all the important confounding variables. No information on missing data was given. Outcome assessors took cases and controls by medical records.
Shetty J et al, 2016		
Methods **Participants** **Outcome**	Case control 200 Platelet count	
Bias	**Author's judgement**	**Support for judgement**
Causal relationship (Confounding bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Unclear risk Unclear risk	Design is not adjusted for all the important confounding variables. Outcome assessors should have been unaware of the exposure status of the study participants.
Gtierrez Aguuirre CH et al, 2017		
Methods **Participants** **Outcome**	Pilot Observational study 61 Serum iron	
Bias	**Author's judgement**	**Support for judgement**
Causal relationship (Confounding bias)	Unclear risk	Design is not adjusted for all the important confounding variables.

Missing data (attrition bias) */++0 Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Unclear risk Low risk	No information on missing data was given. Outcome assessors took cases and controls by medical records.
Damani Z et al, 2016		
Methods **Participants** **Outcome**	Case Control 40 Platelet	
Bias	**Author's judgement**	**Support for judgement**
Causal relationship (Confounding bias) Outcome assessors were aware of the exposure status of the study participants (Information Bias)	Unclear risk Unclear risk	Design is not adjusted for all the important confounding variables. Outcome assessors should have been unaware of the exposure status of the study participants.

This review is performed to investigate the association of pregnancy induced hypertension with elevated serum iron concentration and decreased platelet count during 20-28 weeks of gestation. Overall, 8 studies were examined to investigate the prevalence of PIH in women with increased serum iron and decreased platelet count. The review also consists different ethnic groups and studies were performed at different location, thereby providing the assurance of heterogeneity. Out of 8 studies 3 studies focused on the decrease level of platelet count and remaining 5 studies concluded about increased levels of serum iron in pregnancy induced hypertension. 4 out of 8 studies focused on increased serum iron and reduced platelet count, one study investigated the elevation of serum ferritin as primary objective, one study emphasized on cause of elevation of serum iron is due to hemolysis, hepatocellular damage, and hem concentration, and the remaining two explained about the risk factors and complication associated with pregnancy induced hypertension.

The study conducted by Rayman MP *et al* [17] highlighted a significant deficit in the antioxidant capacity of serum by decreased serum iron. This study gives new idea about the etiological pathways that can lead to increase in oxidative stress. The study explained the origin of increased serum iron levels and the involvement of iron in the aetiology of preeclampsia.

Similarly, the study conducted by Gutirez-Aguirre CH *et al* [18]focused on the elevation of serum ferritin levels as primary objective and observed higher levels of serum ferritin (despite being within normal range) in the preeclamptic group. The study also highlighted the incidence of thrombocytopenia in the preeclamptic group. However, the drawback of the study is having limited sample size and no justification regarding sample size, power, variance, or effect size was given.

In the study conducted by Siddiqui IA *et al* [20]. it was found that serum iron and ferritin concentrations were elevated and associated to cause preeclampsia. The study emphasized the role of confounding factors like AST, and it ruled out the acute phase which cause the increase ferritin levels in preeclamptic group. One limitation of this study is, the recruited participants were less with preeclampsia and has effect on the power of the study, whereas the study recruited twice than the cases in the control group who were normal pregnant women. Another limitation in the study was the absence of the information on parameters of body iron status like total iron binding capacity (TIBC), transferring saturation and Apo transferrin which might be more helpful in corroborating the findings.

Serdar Z *et al* [19] conducted a study to investigate parameters of iron and copper status and oxidative stress and antioxidant function in women with healthy pregnancy, mild and severe preeclampsia with a view to exploring the possible contribution of these parameters to the aetiology. They observed a significant increase in serum iron levels in mild and severe preeclampsia when compared to normotensive healthy pregnant women. The study also

emphasized on the role of vitamin E and -carotene in preventing free radical damage. The study has not provided the knowledge regarding the confounding factors which can influence the levels.

Alkholy EA *et al* [15] performed the study to evaluate the relationship between platelet count and platelet indices; mean platelet volume (MPV) and platelet distribution width (PDW) and severity of preeclampsia and to evaluate their role in prediction of preeclampsia. The study used ROC curve to establish the effect of platelet count on preeclampsia with sensitivity and specificity of 90%, 92% respectively.

Shetty J *et al* [5] conducted the study in Indian population to evaluate the nature of these special hematological abnormalities in PIH. The study showed the sample size of 200 subjects, platelet count was found low in 42 subjects.

Damani Z *et al* [16] conducted the study to investigate the relationship between platelet count and pregnancy induced hypertension. Significant lower platelet count was observed among pregnant women with PIH compared to individuals from control group. The study also indicates that low platelet count is more apparent during 3rd trimester of pregnancy and is focused more on pathophysiological role of decreased platelet count in PIH.

The strengths of this review include that it is first review to evaluate the relationship between elevated maternal serum iron concentrations and decrease platelet count among the PIH population. Its postulates that the further research is required to identify the elevated serum iron concentration and decreased platelet count as a risk marker to diagnose the PIH in early pregnancy. The results from this review are generalizable.

CONCLUSIONS

This review has highlighted that PIH is significantly associated with increased in maternal serum iron concentrations and the reduced platelet indices. Thus, the routine antenatal check-

up management protocol should include to routinely monitor the serum iron levels and platelet count during the early stage of pregnancy. This is one of the reliable and economical rapid method of detection of PIH and asses the severity.

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