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EFFECT OF SERUM FERRITIN LEVELS ON THE EVENT OF PREECLAMPSIA IN PREGNANT WOMEN IN FIRST TRIMESTER

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ABSTRAK PENGARUH KADAR FERRITIN SERUM TERHADAP KEJADIAN PREEKLAMPSIA PADA IBU HAMIL TRIMESTER PERTAMA

Latar Belakang Preeklamsia merupakan penyakit multisistem yang etiologinya belum diketahui, dengan manifestasi klinis yang beragam. Laporan terbaru dari WHO memperkirakan bahwa preeklamsia menyebabkan 70.000 kematian ibu setiap tahunnya di dunia. Society for the Study of Hypertension in Pregnant (ISSHP) mendefinisikan preeklamsia sebagai hipertensi de-novo dengan tekanan darah sistolik lebih tinggi dari 140 mmHg atau tekanan darah diastolik lebih tinggi dari 90 mmHg pada dua pengukuran terpisah (antara 4-6 jam). terjadi setelah usia kehamilan 20 minggu. Pemeriksaan kadar feritin serum untuk menyaring kejadian preeklamsia pada awal kehamilan sangat diperlukan karena tingginya jumlah penderita preeklamsia di Indonesia dan dampak negatif preeklamsia terhadap kehamilan.

Tujuan dari tinjauan literatur ini adalah untuk mengetahui pengaruh pemeriksaan kadar feritin serum terhadap kejadian preeklamsia pada ibu hamil trimester pertama.

Metode Beberapa database elektronik dicari untuk mengidentifikasi studi yang relevan dengan Juli 2021: Scopus, Pubmed, Google Scholar Scholar, dan PubMed. Kata kunci yang dipilih dalam pencarian mencakup 'Serum Ferritin' (dan variasinya, misalnya Ferritin dalam serum, Ferritin), dikombinasikan dengan istilah-istilah yang terkait dengan Preeklamsia termasuk 'Preeklamsia dan Kehamilan', 'Preeklamsia ibu', dan 'preeklamsia hipertensi.' Kriteria inklusi yang digunakan adalah artikel full text, menggunakan rancangan randomized controlled trial, eksperimental dan quasi eksperimen, menggunakan bahasa Indonesia dan Inggris, sampel ibu hamil dengan preeklamsia dan fokus literatur intervensi kadar feritin serum. Sebanyak 103 artikel teridentifikasi (Scopus=39; Google Scholar=23; PubMed=41).

Hasil diperoleh 19 jurnal internasional dan 11 jurnal nasional relevan. Hasil analisis menunjukkan adanya perubahan kadar feritin serum pada ibu hamil dengan preeklamsia.

Kesimpulan Kadar feritin serum yang lebih tinggi berhubungan dengan kejadian preeklamsia. Tinjauan menyeluruh ini mengkaji literatur untuk lebih memahami elemen-elemen ini, dan menggabungkan 30 artikel relevan untuk menjelaskan efektivitas pengujian serum feritin terhadap kejadian preeklamsia, serta beberapa rekomendasi untuk mengatasi masalah serius ini. Secara total, 30 artikel terkait serum feritin dan preeklamsia diidentifikasi.

Saran Perlu dikembangkan studi literatur lebih lanjut mengenai kadar feritin serum terhadap kejadian preeklamsia pada ibu hamil. Hal ini didasarkan pada beberapa temuan baru biomarker lain untuk mendeteksi kejadian preeklamsia pada ibu hamil

Kata Kunci Kadar Ferritin Serum, Preeklamsia, Ibu Hamil Trimester Pertama

ABSTRACT

Background Preeclampsia is a multisystem disease of unknown etiology, with diverse clinical manifestations. The latest report from WHO estimates that preeclampsia accounts for 70,000 maternal deaths annually in the world. The Society for the Study of Hypertension in Pregnancy (ISSHP) defines preeclampsia as de-novo hypertension with a systolic blood pressure higher than 140 mmHg or a diastolic blood pressure higher than 90 mmHg on two separate measurements (between 4-6 hours). occurs after 20 weeks of gestation. Examination of serum ferritin levels to screen for the incidence of pre-eclampsia in early pregnancy is very necessary because of the high number of patients with preeclampsia in Indonesia and the negative impact of preeclampsia on pregnancy.

The purpose of this literature review is to determine the effect of examination of serum ferritin levels on the incidence of preeclampsia in first trimester pregnant women.

Methods Several electronic databases were searched to identify studies relevant to July 2021: Scopus, Pubmed, Google Scholar, and PubMed. Keywords selected in the search included 'Serum Ferritin' (and its variations, eg Ferritin in serum, Ferritin), in combination with terms related to Preeclampsia including 'Preeclampsia and Pregnancy', 'Maternal preeclampsia,' and 'hypertension preeclampsia.' The inclusion criteria used were full text articles, using a randomized controlled trial design, experimental and quasi-experimental, using Indonesian and English, samples of pregnant women with preeclampsia and the focus of the intervention literature on serum ferritin levels. A total of 103 articles were identified (Scopus=39; Google Scholar=23; PubMed=41).

Results 19 international journals and 11 relevant national journals were obtained. The results of the analysis showed that there was a change in serum ferritin levels in pregnant women with preeclampsia.

Conclusions Higher serum ferritin levels are associated with the incidence of preeclampsia. This scoping review examines the literature to better understand these elements, and incorporates 30 relevant articles to describe the effectiveness of serum ferritin testing on the incidence of preeclampsia, as well as some recommendations to address this serious problem. In total, 30 articles related to serum ferritin and preeclampsia were identified.

Suggestion There is a need to develop further literature studies on serum ferritin levels on the incidence of preeclampsia in pregnant women. This is based on several new findings of other biomarkers for detecting the incidence of preeclampsia in pregnant women

Keyword : Serum Ferritin Levels, Preeclampsia, First Trimester Pregnant Women

INTRODUCTION

Preeclampsia is a multisystem disease of unknown etiology, with diverse clinical manifestations. Preeclampsia is a hypertensive disorder characteristic of pregnancy, the disease is characteristic of pregnant women after twenty weeks of gestation. WHO (World Health Organization) estimates that preeclampsia cases are seven times higher in developing countries than in developed countries (Osungbade, 2011). The prevalence of preeclampsia in developed countries is 1.3%-6%, while in developing countries it is 1.8%-18%. The latest report from WHO estimates that preeclampsia accounts for 70,000 maternal deaths annually in the world. In addition to maternal mortality and morbidity, preeclampsia also accounts for 500,000 infant deaths every year.

Maternal mortality rate (MMR) is one of the maternal and child health problems in the world and Indonesia. In Indonesia, the maternal mortality rate is still far from the target of the Millennium Development Goals (MDGs) in 2015, namely the MMR up to 102 per 100,000 KH, while in Indonesia it reaches 305 per 100,000 live births (Ministry of Health, 2017). Indonesia is in the 14th position out of 18 countries in the Association of Southeast Asian Nations (ASEAN) and the fifth highest ranking in the South East Asia Region (SEARO) (Sriwahyu et al., 2013). Preeclampsia is the second cause of maternal death (25.25%) after bleeding (30.32%) (Kemenkes RI, 2019).

Based on Riskesdas 2018, types of disorders or complications in pregnancy include continuous vomiting/diarrhea (20.0%), high fever (2.4%), hypertension (3.3%), immobile fetus (0.9%), bleeding in the birth canal (2.6%), amniotic fluid (2.7%), leg swelling with spasms (2.7%), prolonged cough (2.3%), chest pain/palpitations (1.6 %), and others (7.2%).³ In 2013, the reported causes of maternal death were bleeding (30.3%), hypertension (27.1%), infection (7.3%), and others. (40.8%). The 2019 Indonesian Health Profile data recorded 1,066 deaths due to Hypertension in Pregnancy (HDK).

The Health Profile of South Sulawesi Province in 2018 showed an MMR of 142 per 100,000 KH. Hypertension was ranked first with 51 cases (35.9%) (South Sulawesi Health Profile, 2018).

It was recorded that 8 mothers died from preeclampsia from 2017 to September 2019 at the Wahidin Sudirohusodo Hospital Makassar (Wahidin Sudirohusodo Hospital Makassar, 2017 - September 2019).

At RSIA ST Khadijah III Makassar during 2018 there were 57 cases of preeclampsia out of 952 pregnancies (RSIA Sitti Khadijah III Makassar, 2018).

The incidence of preeclampsia at the Sitti Khadijah I Mother and Child Hospital from January to September 2018 was 40 cases (RSIA Sitti Khadijah I Makassar, 2018).

At the Siti Fatimah Hospital for Mother and Child in Makassar for the January – December 2018 period, 54 pregnant women suffered from pre-

eclampsia (1.51%), of which 7 had mild pre-eclampsia and 47 were severe pre-eclampsia, (RSKD Siti Fatimah, 2018).

In RSKDIA Pertiwi Makassar the number of mothers in 2017 there were 3,111 pregnant women, 72 people with preeclampsia then in 2018 from January to March there were 768 pregnant women, and 36 people with preeclampsia (RSKDIA Pertiwi Makassar, 2017 - March 2018).

The American College of Obstetricians and Gynecologists (ACOG) divides the risk factors for preeclampsia into three levels, namely low, medium and high risk. Childbirth with a full-term baby before including low risk. nulliparity, Body Mass Index (BMI) >30 kg / m², family history of preeclampsia, sociodemographic characteristics, age >35 years, personal history factors (such as previous low birth weight and previous pregnancy interval of more than 10 years) were included in the risk factors currently. For high risk factors, including a history of previous preeclampsia, multiple pregnancies, chronic hypertension, type 1 or 2 diabetes, kidney disease, and autoimmune disorders. Heart disease is also a risk factor for preeclampsia.

The main cause of preeclampsia is not known. However, based on the results of this study, endothelial damage, placental ischemia and angiogenic imbalance are suggested as predisposing factors for preeclampsia. Placental ischemia occurs due to destruction of red blood cells in the placental area resulting in excessive release of heme and Fe into the circulation. This further induces the ferritin system, resulting in high levels of ferritin in the blood.

The diagnostic criteria for preeclampsia were changed by the International Society for the Study of Hypertension in Pregnancy (ISSHP) in 2014. The ISSHP defines preeclampsia as de-novo hypertension with systolic blood pressure higher than 140 mmHg or blood pressure

diastolic is higher than 90 mmHg on two separate measurements (between 4-6 hours) that occurs after 20 weeks of gestation combined with proteinuria (> 300 mg / day), in preeclampsia there is vascular spasm accompanied by water and salt retention. Proteinuria can be caused by arteriolar spasm resulting in changes in the glomerulus.

The picture of the placenta in patients with preeclampsia shows a histological picture with severe damage to blood vessels in the area of decidua cell attachment in the infarct area, this is in accordance with cell damage and Fe release. Catabolic amounts of transition metal ions, especially Fe, arise in the ischemic state of the placenta through destruction of red blood cells from thrombotic,

necrotic, and hemorrhagic areas, these substances can generate highly reactive hydroxyl radicals through Fenton chemistry. These radicals can initiate lipid peroxidation processes, which, if not controlled, can cause endothelial cell damage, as hypothesized by Hubel et al.

Serum ferritin is an acute-phase reactant, which is known to be elevated in response to many inflammatory conditions. Chronic inflammation also suppresses erythropoiesis, reduces iron/Fe usage and increases iron/Fe storage. Increased iron storage is indicated by an increase in serum ferritin level.

Ferritin is also known as a type of iron storage protein and is found extracellularly in serum. Preeclampsia can be associated with iron status through increased heme catabolism resulting from sustained mild hemolysis. Elevated serum iron and ferritin have the potential to be used diagnostically to warn of early-stage preeclampsia.

It is hoped that screening accompanied by management of early detection of serum ferritin levels and iron status can contribute to reducing the impact of preeclampsia on pregnant women and their fetuses can decrease in number.

Several studies have revealed that there is a relationship between increased ferritin levels and the incidence of preeclampsia. Rayman et al 2001 stated that median serum ferritin levels were 6 times higher in patients with preeclampsia compared to control subjects. Meanwhile, a study conducted by Entmann et al in 1983 stated that the ferritin level of preeclampsia patients was 91.8 ng/ml compared to normal pregnancy of 19.4 ng/ml.

Researchers have not found any recent studies related to the effectiveness of examination of serum ferritin levels on the incidence of preeclampsia in first trimester pregnant women. Based on this, researchers are interested in conducting research on the effectiveness of examination of serum ferritin levels on the incidence of preeclampsia in first trimester pregnant women.

RESEARCH METHODS

Identifying Relevant Studies

This type of research is a literature review with the journal year searched for the last 10 years. Several Electronic Databases Searched To Identify Relevant Studies Until July 2021: Scopus, Pubmed, Google Scholar, Google Scholar, and PubMed. Keywords selected in the search included 'Serum Ferritin' (and its variations, eg Ferritin in serum, Ferritin), in combination with terms related to

Preeclampsia including 'Preeclampsia and Pregnancy', 'Maternal preeclampsia,' and 'hypertension preeclampsia.' The search strategy is customized for the respective database thesaurus terms and field titles. A total of 103 articles were identified (Scopus=39; Google Scholar=23; PubMed=41). Removing all non-English articles and removing duplicates reduced this number to 77 articles that were eligible for title and abstract review. Of these, 61 articles were deemed relevant and underwent closer review. Articles were evaluated with the following inclusion criteria: 1) Articles must be about Examination of Serum Ferritin Levels Against the Incidence of Preeclampsia in pregnant women (eg studies involving Serum Ferritin as a Biomarker for early detection of Preeclampsia are included, but articles on Serum Ferritin as a Biomarker for early detection of anemia in pregnancy are excluded.); 2) Examination of Serum Ferritin Levels should be performed on women who experience symptoms of preeclampsia in early pregnancy; 3) Articles must identify related factors;

and 4) Articles must be written in English and available in full-text. A total of 30 articles met these criteria (Figure 1).

Mapping Data

The author undertook an extensive literature review via spreadsheet to review inclusion criteria and select articles, with any and all discrepancies resolved through discussion or input from the supervising author, KS. Articles that met the inclusion criteria were reviewed and data extracted and mapped relating to the study setting, study design, measure of Serum Ferritin Levels, study results, factors associated with Serum Ferritin Levels that influence the incidence of preeclampsia, and recommendations for treating preeclampsia. The factors that were significantly associated with Serum Ferritin Levels in the quantitative study were independently extracted by the authors and summarized in Table 1. The supervising authors reviewed all data points reported in Tables 1 and Figure 1.

RESEARCH RESULTS

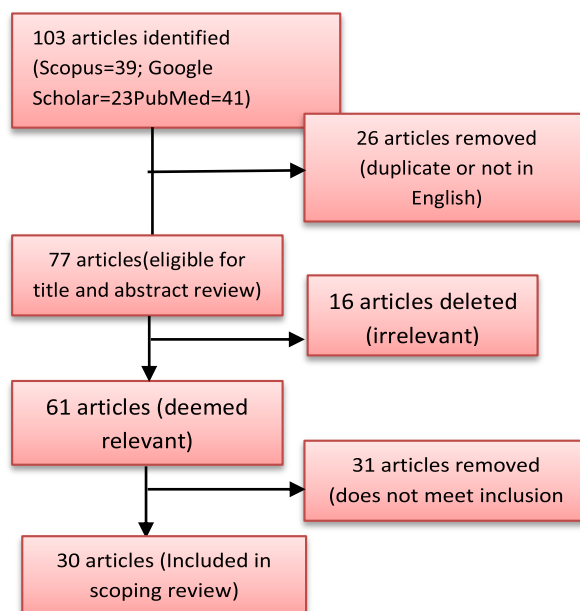


Figure 1.
Search strategy flowchart

The sample size in the 30 included studies varied. The mean serum ferritin level in the severe preeclampsia group (187.3 ± 42.8) was higher when compared to normal pregnant women (26.28 ± 6.69). In this case there was a statistically significant difference ($P < 0.05$) with a sample size of 30(1)

each. In another study 50 pre-eclamptic pregnant women as well as 30 healthy, age-adjusted pregnant women were enrolled. The study was conducted at Omdurman Midwife Hospital, Khartoum, Sudan. The results showed that serum ferritin was (76.7 ± 27.3 mg/dl) versus (62.9 ± 28.2 mg/dl) with a P value of

(0.034). Transferrin saturation percentage in pre-eclamptic women was (62.5 ± 28.7%) compared (27.5 ± 5.9%) with P value (0.034)(2).

The study was a descriptive observational study with a cross-sectional study approach with a comparative analysis of two groups of severe preeclampsia and normal pregnancy.

In relation to the research location, of the 30 research journals spread across several countries. 19 international journals and 11 relevant national journals were obtained. 11 studies were conducted in Indonesia, and two studies were from each of the following countries: 2 research studies in Sudan, 2 research studies in Iran, 2 research studies in Bangladesh, 3 research studies in Pakistan, 5 Indian research studies, each 1 research in Australia, Baghdad, Egypt, Mexico and Brazil. See Table 1 for more details on the study setting.

Serum Ferritin Levels as Biomarkers

Preeclampsia biomarkers are more directed to efforts to determine pregnant women who are at risk of suffering from preeclampsia, this is important, so that in the future, primary health care centers can determine pregnant women who have a high risk of suffering from preeclampsia, and as soon as possible make referrals to secondary health centers or even tertiary. The biomarkers found can also be used as a basis in determining the therapy and actions needed if the patient's condition worsens.(3)

Examination of serum ferritin levels was carried out by taking 2 ml of blood from the median cubital vein, then centrifuged to obtain +100 microns of serum for further examination of serum ferritin levels using the ELISA method.

Table 1.
Relevant Studies

Article Title	Country	Study Design	Research purposes	Review Method	Prevalence of Serum Ferritin Levels on the Incidence of PE	Conclusion
The Role of Serum Ferritin Levels on the Incidence of Preeclampsia	Indonesia	observational analytical research with case-control design	to determine the role of serum ferritin levels in the incidence of preeclampsia.	Serum ferritin examination was carried out using the ELISA method	The difference in mean serum ferritin levels between the preeclampsia and normal pregnancy groups was analyzed using an independent t-test. The results showed that the mean serum ferritin levels in the preeclampsia and normal pregnancy groups were 50.46+4.37 ng/ml and 17.64+1.6 ng/ml, with p value=0.004.	The conclusion of this study is that serum ferritin levels have no role in the incidence of preeclampsia.
Overview of Serum Ferritin Levels in First Trimester Pregnant Women at Hasanah Graha Afiah General Hospital Depok	Indonesia	The design used in the study was a retrospective cohort.	This study was conducted to describe the serum ferritin levels of pregnant women in the first trimester at Hasanah Graha Afiah General Hospital (RSU HGA) Depok.	The research subjects came from medical records of pregnant women in the first trimester at Hasanah Graha Afiah General Hospital, Depok, whose serum ferritin levels were checked and had met the inclusion and exclusion criteria.	Low serum ferritin levels were found in 21 study subjects, three of which were accompanied by anemia. Research subjects with low serum ferritin levels were dominated by pregnant women aged 20-35 years.	<ul style="list-style-type: none"> • Low serum ferritin levels were found in 21 study subjects, three of which were accompanied by anemia. • Subjects with low serum ferritin levels were dominated by pregnant women aged 20-35 years. Dominant research subjects do not have anemia. There were research subjects who gave birth at HGA Hospital and there were also research subjects who had abortions. The dominant birth weight

<p>Comparison of Serum Ferritin Levels in Severe Preeclampsia and Normal Pregnancy</p>	<p>Indonesia</p>	<p>This research is an observational study with a cross-sectional design approach with comparative analysis</p>	<p>This study aims to determine the difference in serum ferritin levels between severe preeclampsia and normal pregnancy.</p>	<p>Each research blood sample taken was labeled with a code name, medical record number, and date of sampling. The blood was sent to the Medan Thamrin Laboratory</p>	<p>In this study, the number of samples was 60 patients, which were divided into 2 study groups, namely 30 patients for the group with severe preeclampsia and 30 patients for the group with normal pregnancy. There were no significant differences in patient characteristics in terms of age, parity and gestational age ($p > 0.05$). Serum ferritin levels in severe preeclampsia were 187.3 ± 42.8 ng/ml and in normal pregnancy 26.28 ± 6.69 ng/ml. There is a statistically significant relationship ($p < 0.05$). The correlation between serum ferritin levels with hemoglobin and hematocrit in severe preeclampsia was negative ($p < 0.05$) and the correlation between serum ferritin levels with hemoglobin and hematocrit in normal pregnancy was found to be positive ($p < 0.05$). And the correlation between serum ferritin and blood pressure in severe preeclampsia found a positive correlation ($p < 0.05$).</p>	<p>was normal but there were also babies born weighing >4000 g. More than half of the study subjects were given multivitamins. Serum ferritin levels in severe preeclampsia showed a significant increase compared to serum ferritin levels in normal pregnancy.</p>
<p>Assessment of iron status in preeclamptic pregnant women visiting Omdurman's midwife hospital</p>	<p>Sudan</p>	<p>descriptive case control study</p>	<p>The aim of this study was to assess variations in serum iron levels, ferritin, and total iron binding capacity and percentage transferrin saturation in preeclamptic Sudanese women compared with healthy</p>	<p>Serum ferritin levels were measured using the AIA-PACK two-site immuno-enzyme-metric assay.</p>	<p>Serum iron in preeclamptic women was (140.6 ± 51.3 mg/dl), compared (71.7 ± 19.7 mg/dl) in the control group with a P value (0.008). Serum ferritin was (76.7 ± 27.3 mg/dl) versus (62.9 ± 28.2 mg/dl) with a P value (0.034). Transferrin saturation percentage in preeclamptic women was ($62.5 \pm 28.7\%$) compared ($27.5 \pm 5.9\%$) with P value</p>	<p>In Sudanese women with pre-eclampsia at Omdurman Midwife Hospital; serum ferritin and transferrin saturation percentage were significantly increased; whereas serum iron, total iron binding capacity and hemoglobin decreased significantly.</p>

			pregnant women.		(0.034). The total iron binding capacity in pre-eclamptic women was (247.6 ± 57.7mg/dl) versus (270.0 ± 33.9mg/dl) with a P-value (0.047). Hemoglobin was (11.5 ± 0.84g/dl) versus (12.5 ± 0.62g/dl) with a P-value (0.000). No significant variation in mean age, BMI or urinary protein between the two groups was found.	
Evaluation of Serum Biomarkers and Other Diagnostic Modalities for Early Diagnosis of Preeclampsia	Indonesia	Randomized Controlled Trial (RCT) or Cohort study design	This systematic review aims to evaluate the potential of the various serum biomarkers and diagnostic modalities (uterine artery Doppler, MAP, and maternal history) available for early prediction of PE	An early detection of PE would allow a chance to plan the appropriate monitoring and for clinical management to be immediately done following early detection thus making prophylactic strategies much more effective.	Ninety-five articles were found that fulfilled all of our inclusion criteria. Placental growth factor (PIGF), pregnancy associated plasma protein A (PAPP-A), soluble fms-like tyrosine kinase (sFLT) and placental protein 13 (PP-13) were the most commonly studied biomarkers. Whereas uterine Doppler scanning and Mean Arterial Pressure (MAP) were the most commonly studied out of other modalities.	Current evidence shows serum biomarkers such as PIGF, PP-13 and sFlt yielded the best results for a single biomarker with others having conflicting results. However, a combination model with other diagnostic modalities performed better than a single biomarker. In the future, new techniques will hopefully provide sets of multiple markers, which will lead to a screening program with clinically relevant performance. However further studies are required to improve current methods. ¹
Levels of Heme Oxygenase-1 (Hmox-1) and Serum Ferritin in Patients with Preeclampsia and Normal Pregnancy	Indonesia	This study is an observational analytic with a cross-sectional design.	To determine the ratio of Hmox1 levels to serum ferritin in preeclampsia and normal pregnancy patients.	examination of Hmox1 levels and ferritin levels with the ELISA Kit as well as physical and laboratory examinations, then statistical calculations were carried out	From the study, the mean levels of Hmox-1 in normal pregnancy and preeclampsia were 1.2 (NB 1.6) ng/ml and 0.3 (NB 0.2) ng/ml, showing a significant difference (p<0.05). The mean ferritin levels in normal pregnancy and preeclampsia were 32.9 (NB 56.0) ng/ml and 43.0 (NB 45.2) ng/ml with a significant difference (p<0.05). Meanwhile, the correlation between Hmox-1 and serum ferritin levels for normal pregnancy and preeclampsia was r=-0.131 and r=0.174 with no significant difference (p>0.05).	Hmox-1 levels in patients with preeclampsia were lower than in normal pregnancies, while ferritin levels in patients with preeclampsia were higher than in normal pregnancies. Hmox-1 and serum ferritin levels were not significantly correlated.

<p>Comparison of serum ferritin levels in pregnant women with preterm and term delivery</p>	<p>Iran</p>	<p>cross-sectional study</p>	<p>Since ferritin is an acute-phase reactant, this study aimed to evaluate serum ferritin levels in women with preterm and term labor.</p>	<p>Serum ferritin levels are measured by a particle-enhanced immunoturbidimetric method with a fully automated analyzer</p>	<p>The mean ferritin levels in all preterm groups were significantly higher than in the term group, but there was no difference between the preterm groups. In addition, ferritin levels in each preterm group were significantly higher than in the normal pregnancy group at the same gestational age. In preterm labor, ferritin levels were significantly higher in cases with premature rupture of membranes (PROM) or with prolonged leakage (more than 12 hours). In addition, in patients with PROM or prolonged leakage, ferritin levels were significantly higher in preterm labor than in term labor. A ferritin level of 37.5 ng/mL was recognized as the best limit for preterm labor, compared with term delivery, and the sensitivity, specificity, and diagnostic accuracy were 78.7%, 68.7%, and 73.6%, respectively.</p>	<p>The findings of this study suggest that serum ferritin levels can be used to identify patients at risk of preterm delivery.</p>
<p>Serum Ferritin in Preeclampsia and Eclampsia: A Case Control Study</p>	<p>Bangladesh</p>	<p>It was a case control study and was conducted during the period of January 2010 - December 2010 in the department of Obs & Gynae DMCH and dept</p>	<p>The main objective of the study was to evaluate the association of serum ferritin and iron in preeclampsia & eclampsia</p>	<p>Microparticle Enzyme Immunoassay (MEIA) technology</p>	<p>A total 100 pregnant women were included in this study. Of them 50 preeclamptic or eclamptic, nonanaemic patients not in labour (26-40weeks) were taken as case and 50 normotensive pregnant women were taken as control. Mean Serum ferritin level in case and control group was 100.03 ± 123.52 $\mu\text{g}/\text{mL}$ and 31.53 ± 20.86 $\mu\text{g}/\text{mL}$ respectively which is highly significant ($P < 0.001$). Out of 50 cases ferritin level was raised in 10 cases (20%). In 80% cases ferritin level was below the cut-off value that is normal or below normal but in 100% of controls had ferritin</p>	<p>In this study it was observed that serum ferritin level were significantly higher in preeclampsia and eclampsia patients than the normal pregnancy. So, it may be concluded that increased level of serum ferritin may play a role in pathogenesis of preeclampsia and eclampsia.²</p>

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Evaluation of coagulation factors and serum ferritin in preeclamptic Pakistani women	Pakistan	Prolonged aPTT, PT and INR were recorded in both PE groups with a decrease in platelets and fibrinogen levels, compared to the control groups.	The study aimed to determine the role of coagulation factors and ferritin in relation to PE susceptibility in Pakistani women	APTT, PT, INR, fibrinogen levels and PLT were checked by automated coagulation analyser (poch-100i, Japan). Ferritin levels were determined by ferritin ELISA kit	level below the cut off value. Ferritin levels were not significantly ($p=0.23$) different in any of the groups.	In conclusion, coagulopathic disorder should be clinically suspected and the coagulating factors in PE patients should be examined for early detection, effective antenatal care and for the proper management of this disorder to decrease maternofoetal mortality, morbidity and perinatal mortality. ³
Correlation of Hepcidin Levels and Ferritin Levels in Pregnant Women	Indonesia	This study is an analytic observational study with a cross-sectional design	This study aims to determine the correlation between hepcidin and ferritin levels in pregnant women.	Hepcidin levels were checked by ELISA method, and ferritin levels by immunochemiluminescent method	The median value of hemoglobin levels in pregnant women was 11.75 (9.3-14.6) g/dl. Hepcidin level 6.37 (1.01-90.18) ng/ml. Ferritin level 16.3 (2.9-102.25) ng/ml. Hepcidin levels with ferritin were weakly correlated and not significant in pregnant women ($r=0.025$; $p=0.849$).	This study showed that there was no correlation between hepcidin levels and ferritin levels in pregnant women.
Iron Status In Preeclampsia	Pakistan	Design: Coefficient correlation study	To evaluate iron status in pregnancy induced hypertension and role of iron in the etiology and pathogenesis of pre-eclampsia	Ten ml of blood was collected from all the selected subjects of which two ml of blood was transferred to a bottle, containing EDTA and was used for hemoglobin and haematocrit estimation	Results depicts that mean age of pre-eclamptic group was significantly low ($P<0.001$) as compared to control. Both parameters, Hemoglobin and Haematocrit were significantly higher ($P<0.05$) in pre-eclamptic as compared to controls. Serum iron, serum ferritin and transferrin saturation were significantly higher ($P<0.001$) in pre-eclamptic in comparison with control group. Total iron binding capacity and unsaturated iron binding capacity were significantly lower ($P<0.001$) in pre-eclamptic group when compared to control group. Correlation coefficient between serum iron, total iron binding capacity (TIBC), serum ferritin, unsaturated iron binding capacity (UIBC) and systolic and diastolic blood	It is concluded that hemoglobin, haematocrit, serum iron, serum ferritin and transferrin saturation are significantly increased in pregnant women that later develops pre-eclampsia. Excess iron is postulated as casual factor in the oxidative stress ie; in its radical form, which may be involved in the pathogenesis of pre-eclampsia. Therefore, iron status of pregnant women should be assessed before giving iron supplements as these may cause more harm than benefit. ⁴

High maternal serum ferritin in early pregnancy and risk of spontaneous preterm birth	Australia	the majority of randomised trials have not shown a significant reduction in preterm births following maternal administration of antibiotics	The aim of the present study was to examine the association between Fe biomarkers, including serum ferritin concentrations, and the risk of total (.37 weeks), early (.34 weeks) and moderate-to-late (34–36 weeks) sPTB.	Serum ferritin level was measured using a solid-phase direct sandwich ELISA method (Calbiotech, Inc.)	pressure in pre-eclamptic group showed no significant positive correlation in any parameter The multivariate analysis found increased odds of sPTB for women with elevated ferritin levels defined as .75th percentile (\$43mg/l) (OR 1.49, 95% CI 1.06, 2.10) and .90th percentile (\$68mg/l) (OR 1.92, 95% CI 1.25, 2.96). Increased odds of early and moderate-to-late sPTB were associated with ferritin levels .90th percentile (OR 2.50, 95% CI 1.32, 4.73) and .75th percentile (OR 1.56, 95% CI 1.03, 2.37), respectively. No association was found between the risk of sPTB and elevated sTfR levels or Fe deficiency	In conclusion, elevated maternal serum ferritin levels in early pregnancy are associated with an increased risk of sPTB from 34 weeks of gestation. The usefulness of early pregnancy ferritin levels in identifying women at risk of sPTB warrants further investigation. ⁵
Total Iron Binding Capacity (TIBC), free iron, ceruloplasmin, transferrin and ferritin concentrations, in pregnant women with preeclampsia	Baghdad	Analytical case-control studies	The aim of this study was to compare Total Iron Binding Capacity (TIBC), Iron, ceruloplasmin, transferrin and ferritin concentrations, in preeclamptic and healthy pregnant women, and to investigate the association between these factors and preeclampsia.	The supernatant was used to measure Serum TIBC and iron content by the spectrophotometer method provided by Biolabo, France	The mean serum iron in the preeclampsia group was 97.0 ± 7.83 , while it was 94.35 ± 11.81 in the normal group ($p \leq 0.01$). Similarly, the mean serum TIBC concentrations in normal pregnant and preeclamptic women were 319.65 ± 32.35 and 292.3 ± 30.86 , respectively ($p = 0.01$). The mean serum ferritin was 0.33 ± 0.056 in preeclamptic women and in normal pregnant women was 0.29 ± 0.039 , a significant difference between the ceruloplasmin concentrations in the two groups, while the mean transferrin in preeclampsia and normal pregnant women was 204.61 ± 21.60584 and 223.75 ± 22.64877 , respectively.	Ischemic placental tissue may be a major source of potentially toxic iron in preeclampsia and the released iron species may contribute to endothelial cell etiology and injury, which can be reduced by antioxidant supplementation. Keywords: preeclampsia, iron, ferritin, ceruloplasmin, total iron binding capacity.
Ferritin Levels Decrease Between	Indonesia	This study is a cohort study.	To determine changes in ferritin levels in	The data were processed and	The number of samples obtained and met the inclusion	Conclusion: There is a significant decrease in ferritin levels in

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Second and Third Trimester of Pregnancy			the second and third trimesters of pregnancy	analyzed statistically.	criteria in this study were 30 people. From the results of this study, it was found that there was a decrease in ferritin levels from second trimester to third trimester pregnant women as many as 28 mothers (93.3%) and there were 2 mothers (6.7%) who experienced an increase. These results indicated that serum ferritin levels in the second and third trimesters were significantly different ($p < 0.001$). This difference can be seen in the median value of serum ferritin levels in the second trimester which is higher than in the third trimester (31.10 ng/ml > 22.20 ng/ml).	pregnant women from the second to third trimesters caused by the increased need for iron in pregnancy, which is due to hemodilution which peaks at 28 - 32 weeks of gestation and the iron transfer process. to the fetus but it can also be caused by factors of poor diet composition.
A Prospective Study of Evaluation of Changes in Biochemical and Urine Parameters in Pre-eclampsia	Iran	This study was targeted singleton pregnant women as the case group (50 patients of preeclampsia) or the control group (50 healthy parturients)	The purpose of this study was investigated that whether the measure of the biochemical and urine parameters in pregnant women has correlation relationship with preeclampsia	In order to survey of serum iron, ferritin, creatinine, platelet and liver enzymes, blood samples of case and control groups were taken before delivery and analyzed	it was found significant differences in the mean level of serum ferritin of the preeclamptic patients who have ELLP syndrome (EL: Elevated liver enzyme, LP: Low platelet count) in comparison with preeclampsia women with high level of liver enzymes. However, this relation meaningful was not shown among mean serum iron and EELP syndrome with preeclampsia. The correlation coefficients between iron and creatinine/proteinuria/a lbuminuria as well as ferritin and creatinine/proteinuria/a lbuminuria concentrations in group of preeclampsia were not significantly different	Present results revealed that a correlation relationship between the concentration of serum ferritin and iron and ELLP syndrome and preeclampsia may in fact exist ⁶
Clinical Pathology And Medical Laboratory	Indonesia	Literature Review	To determine the body's iron reserves can be checked serum iron levels (SI), total iron binding capacity (TIBC), serum ferritin	Examinations that can be carried out by the method of immunoradiometric assay (IRMA) and enzyme linked immunosorbent assay (ELISA)	Serum transferrin receptors were measured by enzyme immunoassay and immunoturbidimetric assay.	Examination of serum ferritin levels proved to be the earliest indicator, which was decreased in a state of decreased body iron reserves.

Hubungan antara Serum Ferritin dan Preeklampsia	Bangladesh	Research design: This is a case-control study with laboratory methods	The aim of the study is to explore the association between serum ferritin and Preeclampsia and to do a comparison of serum ferritin to assess risk of development preeclampsia between case and control	Collection of blood sample: Maintaining all aseptic precautions, 6 ml of venous blood was drawn from the antecubital vein of each pregnant woman in the sitting position 2 ml of that blood was taken in EDTA tube for Hb% and peripheral blood film. 4 ml of blood was immediately transferred into a clean, dry test tube and was centrifuged with 1 hour of collection. The serum thus obtained was stored at — 70' C until assessed.	In the present study, the mean serum Ferritin level of PE group was almost 10 times higher (167.11 ± 10.43 ngm/ml) than that of controls (17.0 ± 3.03 ngm/ml) than that of control (431.0 ± 10.93 gm/dl). More than one-third of the cases showed serum ferritin >210 ngm/ml, compared to none of the control group.	Serum Ferritin level is significantly higher in preeclamptic patients than the control group. ⁷
Iron Status in Preeclampsia – A Study from South India	South India	This was a case control study which was a part of a larger study done to know the levels of various elements in women with preeclampsia	The aim of this study was to find out iron status parameters in preeclamptics and their comparison to normotensive pregnancies. This	Hemoglobin was estimated by Cyanmet Hemoglobin method, serum ferritin and iron were estimated by kit method.	Pregnancy outcome in both groups were compared. Data were expressed as Mean \pm Standard Deviation. Comparison of serum levels of the elements was performed by Independent t test and Chi square test and P value of < 0.05 was considered as statistically significant. Mean serum iron and ferritin levels in preeclamptics were significantly higher compared to normotensives whereas hemoglobin levels did not show much difference. A statistical test was performed using a logistic regression test. Based on 30 samples of pregnant women, the results showed that 16 pregnant women had hemoglobin levels of >13 gr/dl (53.3%), and 14 pregnant women (46.7%) had a positive predictive value of ROT. The	Also preeclamptic women were older, with higher BMI and lower birth weight compared to normotensives. The higher serum iron and ferritin levels might play an important role in the etiopathogenesis of preeclampsia. Therefore, pregnant women with higher serum iron and ferritin levels should be investigated for preeclampsia. Iron status of pregnant women should be assessed before giving iron supplements as these may cause more harm than benefit. ⁸ The effect test analysis results showed a positive relationship between hemoglobin levels and the predictive value for preeclampsia ($p=0.04$, $B=1.299$). Thus, pregnant women who experienced an increase in the hemoglobin levels of 1 g/dl had a potential of
Effect Of Hemoglobin Levels Pregnant Women On The Predictive Value For Preeclampsia Of Rot (Roll-Over Test)	Indonesia	This was an analytic observational study with a cross-sectional design.	This study aims to analyze the effect of hemoglobin levels on the predictive value for preeclampsia of ROT (Roll Over Test) among pregnant women.	Data on hemoglobin levels were obtained from secondary data derived from the MCH Booklet and ROT values obtained by directly checking the supine and left	A statistical test was performed using a logistic regression test. Based on 30 samples of pregnant women, the results showed that 16 pregnant women had hemoglobin levels of >13 gr/dl (53.3%), and 14 pregnant women (46.7%) had a positive predictive value of ROT. The	The effect test analysis results showed a positive relationship between hemoglobin levels and the predictive value for preeclampsia ($p=0.04$, $B=1.299$). Thus, pregnant women who experienced an increase in the hemoglobin levels of 1 g/dl had a potential of

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Iron Status In Preeclampsia	Abbottabad/Pakistan	Coefficient correlation study	To evaluate iron status in pregnancy induced hypertension and role of iron in the etiology and pathogenesis of pre-eclampsia	lateral maternal blood pressure. Serum ferritin was estimated by Enzyme-immunoassay Kit method.	Results depicts that mean age of pre-eclamptic group was significantly low (P<0.001) as compared to control. Both parameters, Hemoglobin and Haematocrit were significantly higher (P<0.05) in pre-eclamptic as compared to controls. Serum iron, serum ferritin and transferrin saturation were significantly higher (P<0.001) in pre-eclamptic in comparison with control group. Total iron binding capacity and unsaturated iron binding capacity were significantly lower (P<0.001) in pre-eclamptic group when compared to control group. Correlation coefficient between serum iron, total iron binding capacity (TIBC), serum ferritin, unsaturated iron binding capacity (UIBC) and systolic and diastolic blood pressure in pre-eclamptic group showed no significant positive correlation in any parameter.	1.299 times to have a positive ROT value. ⁹ It is concluded that hemoglobin, haematocrit, serum iron, serum ferritin and transferrin saturation are significantly increased in pregnant women that later develops pre-eclampsia. Excess iron is postulated as casual factor in the oxidative stress ie; in its radical form, which may be involved in the pathogenesis of pre-eclampsia. Therefore, iron status of pregnant women should be assessed before giving iron supplements as these may cause more harm than benefit. ⁴
Increased serum ferritin levels in women with preeclampsia	Egypt, Cairo	This was a case-control study conducted in the emergency ward of Obstetrics and Gynecology Department of Suez Canal University Hospitals	To study the correlation between serum ferritin level and the severity of preeclampsia	Serum ferritin (ng/dl) was assayed using a quantitative test system. This is a solid phase enzyme-linked immunosorbent assay (ELISA) kit purchased from Immunospec Corporation. Serum	The mean serum ferritin was significantly higher in mild and severe preeclampsia groups vs. the control group (33.27 ± 6.9 and 69.47 ± 20.1 ng/ml versus 16.9 ± 20.9ng ng/ml, respectively, p-value < 0.001). Regarding, the mean serum iron level in the mild, severe preeclampsia and control groups, it was 201.87 ± 58.13, 219.4 ± 53.1 µg/dl and 173.9 ± 56.58 µg/dl respectively (p-value < 0.05). There was a highly significant correlation between ferritin and each of systolic and diastolic	The level of serum ferritin was high in patients with preeclampsia, and it correlates well with the severity of the disease. ¹⁰

Comparative analysis of iron status and other hematological parameters in preeclampsia	Mexico	Prospective, comparative, observational pilot study	To compare serum ferritin (SF) concentrations and other hematological parameters between patients with preeclampsia (PE) and normal pregnant women of the same gestational period who received supplemental iron during pregnancy.	an Sysmex XT-4000i hematology analyzer (Sysmex Corporation, Hyogo, Japan), and 5 ml were placed in a tube without anticoagulant to determine the concentrations of ferritin and serum iron in a COBAS INTEGRA® processor 400 PLUS (Roche Diagnostics GmbH, Mannheim, Germany).	blood pressures ($r=0.8$, $p<0.001$ and $r=0.7$, $p<0.001$ respectively) In comparison with controls, preeclamptic patients had a higher weight, body mass index, and arterial pressure. Serum ferritin and serum iron were higher in patients with PE (median: 36.5 $\mu\text{g/l}$ vs. 20.9 $\mu\text{g/l}$ and 103.9 $\mu\text{g/dl}$ vs. 90.8 $\mu\text{g/dl}$) with a significant difference ($P = 0.019$ and $P = 0.345$). SF values $>40 \mu\text{g/l}$ correlated with PE ($r = 0.281$; $P = 0.032$). A platelet count less than $100 \times 10^9/\text{l}$ was higher in the PE group than in the control group (13% vs. 3%, $P = 0.354$)	Higher SF levels, despite being within normal range, were associated with PE. The incidence of thrombocytopenia was higher in preeclamptic women, however, the remaining hematological parameters were similar in both groups. ¹¹
Dynamic Of Serum Ferritin Level In First Trimester Pregnancy	Indonesia	The design was retrospective cohort.	Objective of this study was to overlook serum ferritin levels in trimester 1 pregnancy.	Data were presented in percentages for categorical data. Numerical data presented in medians and ranges for abnormal data distribution; and mean and standard intersections for normal data distribution	Median serum ferritin levels in this study were still in the normal range of 40.82 (6.97 - 172.66) $\mu\text{g} / \text{L}$. Twenty one subjects (69.1%) had normal serum ferritin level ($\geq 30 \mu\text{g/L}$) and 47 (30.9%) had low ferritin level.	Median serum ferritin in this study was within normal range. Low level of serum ferritin found in 21 subjects, three among them also suffered from anemia. ¹²
Assessment of Iron Status in Pregnant Ladies with Preeclampsia	Sudan	Methodology This case control study	The objective of this was estimated Iron status (Iron, Ferritin, TIBC, Transferrin) in pregnant women and preeclamptic women.	Collection of blood samples for the study about 5ml of venous blood was collected under aseptic precaution in a sterile bulb from selected subjects. Then the serum is separated by centrifugation which is used for estimation of Iron, Ferritin and TIBC. In the subjects serum concentrations of iron and TIBC were estimated using ferrozine	The approximate doubling of transferrin saturation in pre-delivery sera of women with preeclampsia relative to controls result from combined effect of increased serum iron and decreased total serum transferrin concentration(9). Mean ferritin levels were significantly elevated in both pregnancy induced hypertension and eclampsia as compared to controls(10).Maternal ferritin concentration is primarily a reflection of maternal, iron status, and a high level is associated with unfavorable	From this study, all iron profile (Iron, Ferritin, and Transferrin) were significant higher while, TIBC was significant lower. ¹³

Hyperferritinemia worsens the perinatal outcomes of conceptions of pregnancies with preeclampsia	Brazil	A cross-sectional study carried out in 2017 with a convenience sample of pregnant women with preeclampsia attended at a high-risk maternity hospital in Alagoas, Brazil.	To analyze the prevalence of hyperferritinemia in pregnant women with preeclampsia and its association with adverse perinatal outcomes.	method using Bio-System and ferritin was estimated using immuno enzymometric Assay (TOSOH-A1A-360). Transferrin saturation was calculated by the following formula. Women were dichotomized according to the serum ferritin level (150 ng/mL).	outcome(6). Mean value of serum iron is significantly Except for ferritin level, there were no differences in C-reactive protein (CRP), hemoglobin, Glutamate Oxaloacetate Transaminase (GOT) and Pyruvic Glutamic Transaminase (PGT) levels between women with or without hyperferritinemia. After adjusting for potential confounders, hyperferritinemia was associated with low birth weight (2.19 [2.13–3.89 95%CI]), low birth length (7.76 [2.52–23.8 95% CI]) and being born small for gestational age (3.14 [1.36–7.28 95% CI]).	In the presence of hyperferritinemia, preeclampsia patients were associated with a higher rate of unfavorable neonatal outcomes. ¹⁴
Comparative study of copper, zinc, iron, ferritin, calcium and magnesium levels in pregnancy induced hypertension and normotensive primigravida mothers	India	METHODS: It was a comparative cross sectional study of one year, September 2013 to August 2014, conducted in the Dept. of Biochemistry, Dept. of Gynaecology and Obstetrics, R. G. Kar Medical College & Hospital, Kolkata.	Several studies in this context have conflicting reports. So, a comparative study of serum levels of copper (Cu), zinc (Zn), iron (Fe), ferritin, calcium (Ca) and magnesium (Mg), in PIH and normotensive primipara mothers was conducted.	Fasting blood samples (10 ml) were collected at 8-9 a.m. into polypropylene tubes. Serum was separated within 2 hours and aliquots were kept frozen at -20°C until trace element analysis. All laboratory wares including pipette tips and autosampler cups were cleaned thoroughly with detergent and tap water, rinsed with distilled water, soaked in dilute nitric acid and then rinsed thoroughly	Serum Ca, Mg, Cu and Zn levels were found to be significantly reduced (<0.05) in the PIH group compared to the normal pregnant group. Serum ferritin was markedly increased in the cases (mean 90.41±47.39, p<0.00001). No significant correlation was found in serum Fe levels	Alteration of serum Cu, Zn, Ca, Mg and ferritin levels can be considered to have a role in the etiopathogenesis and severity of PIH. ¹⁵

Association of first trimester maternal vitamin D, ferritin and hemoglobin level with third trimester fetal biometry: result from cohort study on vitamin D status and its impact during pregnancy and childhood in Indonesia	Indonesian	From July 2016 a prospective cohort study of pregnant women had begun in four cities in West Java, Indonesia. Data	The aim of this study was to explore the association between maternal vitamin D level in the first trimester and fetal biometry in the later stage of pregnancy with adjusted OR for other determinants like hemoglobin and ferritin level. Methods:	Serum vitamin D and ferritin analysis was performed by ELISA.	Among 203 recruited women, 195 (96.06%) had hypovitaminosis D. One hundred fifty two (75%) were in deficient state and 43 women (21%) were in insufficient state. Women with insufficient vitamin D had the highest proportion of anemia, while women with normal vitamin D level had the highest proportion of low ferritin level. Maternal serum vitamin D showed significant associations with biparietal diameter ($\beta = 0.141$, $p = 0.042$) and abdominal circumference ($\beta = 0.819$, $p = 0.001$) after adjustment with maternal age, pre-pregnancy body mass index, parity, serum ferritin level, and hemoglobin level.	Our study suggested that sufficient maternal vitamin D level was an important factor to improve fetal growth and development. ¹⁶
Role of maternal serum ferritin as a predictive marker in intrauterine growth restriction	India	This was a longitudinal prospective study conducted in the department of obstetrics and gynaecology in our hospital between January 2011 and December 2012.	Measurement of maternal serum ferritin has also been used as a predictive marker of increase risk of IUGR	Maternal serum samples of all women were taken at 25th week and again at 30-32 weeks in trace free mineral evacuated tubes for assessment of serum ferritin by chemiluminescence. Mean of both values was calculated.	Mean ferritin value of women with average for gestational age neonates was 15.49 ng/ml and women with growth restricted neonates was 19.71 ng/ml. The women with mean serum ferritin above 20 ng/ml, were 6.26 times more likely to have asymmetrically growth restricted baby and 4.47 times more likely to have a symmetrically growth restricted baby when compared to women with serum ferritin value less than <20 ng/ml.	In our study negative correlation was found between the value of serum ferritin and neonatal birth weight. In future large randomized control trial is needed to found association between maternal serum ferritin and IUGR. ¹⁷
HFE Gene Polymorphism and Iron Status in Preeclampsia	India	This is a hospital-based case-control study.	This study attempts to determine the association if any between C282Y allele of HFE gene with preeclampsia, and evaluate the serum iron status in women with pre-eclampsia and third trimester	8 ml of venous blood sample was collected after overnight fasting and 24 hours urine sample was collected and analysed. All the estimations were done by standard methods as given below. Serum ferritin -	There is no significant association between preeclampsia and HFE gene and C282Y allele polymorphism. 92% of the cases and 98% of the controls do not show mutation in the C282Y allele. Odds ratio for wild type is 1.065 and that of heterozygote is 4.261. 95% confidence interval is large (0.021-54.76), indicating a low	There are increased iron indices in preeclampsia when compared to the controls. Haemoglobin concentration and Haematocrit are raised in preeclampsia. There is no association of C282Y mutation of HFE gene with preeclampsia. Therefore, C282Y allele cannot be used as a

			healthy pregnant women, as this polymorphism is closely associated with haemochromatosis, a hereditary disorder in which serum iron is elevated, which is also seen in pre-eclampsia.	Enzyme immuno assay (ELISA).	level of precision in wild type. Z value for wild type is 0.031 and that of heterozygote is 1.275, p-value for both is not significant. Serum iron, ferritin and %age of transferrin saturation were significantly higher (p=0.001) in preeclamptic women, in comparison with the control group. Unsaturated Iron Binding Capacity (UIBC) and TIBC were significantly lower (p=0.001) in preeclamptic group.	molecular marker for preeclampsia. ¹⁸
Increased Serum Ferritin and Iron Levels in Preeclampsia	India	This case control study was	The aim of the study was to assess the status of serum ferritin and iron in preeclampsia.	Estimation of serum ferritin and serum iron concentration was done by fully automated random access chemistry analyzer Cobas Integra,Roche make,	The mean serum ferritin concentration in cases and controls were 55.35µg/l and 17.19µg/l respectively. Mean serum iron concentration in cases was 190.88 µg/dl and that in controls was 83.66µg/dl.	This study showed significantly higher level of serum ferritin and serum iron in preeclamptic group as compared to the normotensive control group. ¹⁹

Prevalence of Serum Ferritin Levels on the Incidence of Preeclampsia

A total of 100 pregnant women were included in the study at the Obs & Gynae DMCH department and the dept. BSMMU Bangladesh Biochemistry period January 2010-De. Of those 50 preeclampsia or eclampsia, nonanemic patients not in labor (26-40weeks) were taken as cases and 50 normotensive pregnant women were taken as controls. The mean serum ferritin levels in the case and control groups were 100.03 ± 123.52 gm/L and 31.53 ± 20.86 gm/L, respectively, which were very significant ($P < 0.001$). Of the 50 cases, ferritin levels increased in 10 cases (20%).

In a study conducted in Indonesia with the title the role of serum ferritin levels on the incidence of preeclampsia, the results of the difference in mean serum ferritin levels between the preeclampsia and normal pregnancy groups were analyzed using an independent t-test. The results showed that the mean serum ferritin levels in the preeclampsia and normal pregnancy groups were 50.46 ± 4.37 ng/ml and 17.64 ± 1.6 ng/ml, with p value=0.004.

In a study conducted in Pakistan under the title Evaluation of coagulation factors and serum ferritin in preeclampsia in Pakistani women, the mean and statistical significance of the coagulation parameters were observed and tabulated in Table 2. Prolonged aPTT, PT and INR were observed in both

groups of PE, especially in the group with PE. severe with decreased PLT and fibrinogen. A non-significant decrease ($p = 0.23$) was observed in ferritin levels in the PE group compared to the control group. Statistical significance was checked for each parameter in the mild and severe preeclampsia group versus the control group.

In a study in Baghdad with the research title Total Iron Binding Capacity (TIBC), free iron, ceruloplasmin, transferrin and ferritin concentrations, in pregnant women with preeclampsia were obtained. The mean serum iron in the preeclampsia group was 97.0 ± 7.83 , while 94.35 ± 11.81 in the normal group ($p \leq 0.01$). Similarly, the mean serum TIBC concentrations in normal pregnant and preeclamptic women were 319.65 ± 32.35 and 292.3 ± 30.86 , respectively ($p < 0.01$). The mean serum ferritin was 0.33 ± 0.056 in preeclamptic women and in normal pregnant women was 0.29 ± 0.039 , a significant difference between the ceruloplasmin concentrations in the two groups, while the mean transferrin in preeclampsia and normal pregnant women was 204.61 ± 21.60584 and 223.75 ± 22.64877 , respectively.

Recommendation

Most of the molecular researchers offer recommendations for the development of biomarkers in an effort to detect the incidence of preeclampsia in

pregnant women early. One of them is a serum biomarker, namely serum ferritin. Examination of serum ferritin levels to screen for the incidence of preeclampsia in early pregnancy is very necessary because of the high number of patients with preeclampsia in Indonesia and the negative impact of preeclampsia on pregnancy. It is hoped that screening accompanied by management of early detection of serum ferritin levels and iron status can contribute to reducing the impact of preeclampsia on pregnant women and their fetuses can decrease in number.

DISCUSSION

The purpose of this article is to present up-to-date information and a comprehensive review of the existing literature on the Effectiveness of Serum Ferritin Levels on the Incidence of Preeclampsia in First Trimester Pregnant Women. In total, we included 30 peer-reviewed articles that met the inclusion criteria listed below. we state. The findings of this scoping review give some credence to previous literature studies, which describe serum ferritin as a biomarker that can be used as a reference in screening the incidence of preeclampsia in pregnant women.

With the broad coverage and diversity of the literature across geographies, sizes, models of practice, and sample size and composition, our review noted that all included studies featured both qualitative and quantitative research methods, most often cross-sectional study designs. While this methodology is certainly valuable for generating data that can easily be compared between groups and countries, it does little to address the 'why' or 'how' questions that could explain the extent of the effect of screening for preeclampsia in early pregnancy using biomarkers of serum ferritin levels. Without underestimating the value and importance of existing research in expanding our understanding of serum ferritin as a biomarker that can be considered in the early detection of preeclampsia in obstetrics. The cross-sectional design, which allowed the investigators to explore the relationship between variables, prevented us from identifying causal and temporal effects between serum ferritin levels and the incidence of preeclampsia. The case control study design will allow us to determine whether there are differences in serum ferritin levels in pregnant women with preeclampsia and in normotensive women. Design Correlation analysis is a statistical method used to determine a quantity that states how strong the relationship between serum ferritin levels and the incidence of preeclampsia is. In addition, there is also a retrospective cohort study design,

which is a retrospective study using secondary data, to see whether there is a relationship between serum ferritin levels and the incidence of preeclampsia in pregnant women.

Globally an estimated 2.87,000 women died in childbirth in 2010, of which India accounted for around 19%. The greatest impact of preeclampsia is in developing countries where it accounts for 20 – 80% of the marked increase in maternal mortality.

Preeclampsia is a disease of many theories. Among them, genetic factors, immunology, circulation, utero vascular changes and endothelial dysfunction are important concerns. Despite extensive research, the underlying mechanism of preeclampsia is not yet defined. Because the pathogenesis is not clear, preventive and curative measures are efforts that can help in handling cases of preeclampsia.

Several independent investigators have demonstrated through research that the vascular endothelium provides the single target organ system involved in preeclampsia. The relatively new endothelial injury theory explains many of the clinical findings in preeclampsia. Placental ischemia is a common cause of endothelial cell damage leading to the sudden symptoms of hypertension, proteinuria, and edema that are characteristic of this condition. It has been suggested that lipid peroxidation may play a role in the pathology of preeclampsia. The high level of these lipid hydroperoxides believed to be present in preeclampsia is one of the candidate agents capable of causing such damage to the vascular endothelium.

Prenatal serum ferritin concentrations were significantly higher in patients with eclampsia than in healthy pregnant women. Serum ferritin is the best sensitive marker of iron status parameters reflecting preeclampsia and the results can support the role of iron as a catalyst for oxidative stress and lipid peroxidation in the pathophysiology of preeclampsia.

Based on these conditions, it is very important to emphasize preventive measures by detecting preeclampsia as early as possible using predictors of preeclampsia. This study analyzed serum ferritin levels on the incidence of preeclampsia in pregnant women.

Serum Ferritin Check

The study was conducted at the Department of Obstetrics and Gynecology, College of Medicine and Sir Salimullah Hospital. Serum Ferritin was tested at the Department of Biochemistry, BSMMU/Bangladesh. Blood sampling: Maintaining all aseptic precautions, 6 ml of venous blood was drawn from the antecubital vein of each pregnant

woman in a sitting position 2 ml of that blood was drawn in an EDTA tube for Hb% and peripheral blood IIm. 4 ml of blood was immediately transferred into a clean and dry test tube and centrifuged with collection for 1 hour. The obtained serum was stored at -70°C until assessed.

Study population: There were 40 cases of preeclampsia and 40 normotensive pregnant women enrolled from Sir Salimullah Medical College and Hospital, Dhaka. Normotensive pregnant women were taken as controls

Laboratory method

- Estimation of serum ferritin by MEIA.
- Estimation of Hb% by Colorimetric Method
- Estimation of blood urea, serum creatinine, serum electrolytes, random blood sugar, serum bilirubin, SGPO, SGOT by analyzer.

Another study entitled Comparison of serum ferritin levels in pregnant women with preterm and term deliveries by Tayebah Jahedbozorgan, Minoos Yaghmaei and Maryam Naserieh at Shahid Beheshti University of Medical Sciences, Tehran, Iran described that blood samples were collected from participants/sample under sterile conditions and stored in an iron-free tube at room temperature. Serum samples were separated within two hours and stored at minus 20°C. Serum ferritin levels were measured by a particle-enhanced immunoturbidimetric method with a fully automated analyzer. In addition, hemoglobin levels were measured using a fully automatic spectrophotometer.

In addition the research was carried out at the Pakistan Institute of Medical Sciences (PIMS) Islamabad, Quaid-e-Azam International Hospital, Islamabad and Quaid-i-Azam University, Islamabad after receiving approval from the ethics committees of the three institutes. Two hundred blood samples of pregnant women aged less than 35 years and in the third trimester were included for the study conducted from September 2015 to July. 2017. APTT, PT, INR, fibrinogen and PLT levels were checked with an automatic coagulation analyzer while ferritin levels were determined with a ferritin ELISA kit.

Limitations

This scoping review is not without its limitations. First, remember that serum ferritin is a biomarker of preeclampsia, which has just been introduced in Indonesia. The small sample size is also one of the limitations in this study so that further studies are needed on a larger population including other parameters/biomarkers such as serum AST, LDH, hemopexin, total bilirubin, transferrin and percent transferrin saturation that can affect serum

iron levels in children. preeclampsia. Lack of funds and resources is the main problem of this research.

Our review is also limited by filtering out articles that are not available in English, or articles that are not accessible to the database subscriptions maintained by the University of British Columbia. Furthermore, there may be publication bias as a consequence of studies with significant findings preferentially selected by journals for publication and between health professions.

CONCLUSION

Higher serum ferritin levels are associated with the incidence of preeclampsia. This scoping review examines the literature to better understand these elements, and incorporates 30 relevant articles to describe the effectiveness of serum ferritin testing on the incidence of preeclampsia, as well as some recommendations to address this serious problem. In total, 30 articles related to serum ferritin and preeclampsia were identified. Among the several articles in the review, biomarkers that have the potential to be the basis for screening the incidence of preeclampsia in pregnant women are also reviewed.

SUGGESTION

There is a need to develop further literature studies on serum ferritin levels on the incidence of preeclampsia in pregnant women. This is based on several new findings of other biomarkers for detecting the incidence of preeclampsia in pregnant women

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