Review

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Hypertensive Disorder in Pregnancy and Pre-eclampsia

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اضطرابات ضغط الدم في النساء الحوامل وتسمم الحمل

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Abstract

Background: Frequently, hypertension (high blood pressure) or its disorder occurs during pregnancy, and it remains one of the major causes of maternal and fetal mortality and morbidity associated with pregnancy, as well as the risk of pregnant women with hypertension during pregnancy to cardiovascular disease later in life. However, contrary to the general hypertension guidelines, the reasons for this report include the benefit of normalizing treatment of high blood pressure in pregnant women and potential risks related to decreased prenatal chorionic perfusion, and exposure of the uterus to antihypertensive drugs. This approach is based on a review of previous reports and literature and includes a taxonomic review of the types of blood pressure during pregnancy, the physiological changes in pregnancy that affect blood pressure disorders, the immediate and long-term consequences of hypertension, and the pathophysiology of pre-eclampsia that are related to the disturbance of proteinuria in the body, and the goals of hypertension treatment may reduce meternal severe effects without increased risk of pregnancy loss or neonatal care at a high level. The critical need to investigate the social and economic variables that contribute to the inequities in maternal health care is discussed in our final discussion on the field's research future.

so it is necessary to know the pressure and treat it immediately. Failure to treat high blood pressure can lead to maternal morbidity and mortality, especially during childbirth, or the loss of the fetus significantly.

Therefore, in this mini review, we will try to discuss high blood pressure in pregnant women and determine the goals of treatment and preeclampsia caused by high blood pressure.

The aim of the review is a quick scientific summary of this disorder that has become common at the present time.

Conclusions : Medical consultation should be done in order to improve the health of the mother, as well as the use of optimal medication and pre-pregnancy management in women with or threatened with high blood pressure, and we consider it necessary to inform them of the increased risks to her health and the health of the fetus.

Strategies must be in place to predict those most at risk and to determine optimal drug therapies to minimize adverse pregnancy outcomes

Key words : Disorder , Hypertensive , Pre-eclampsia , Pregnancy.

الخلاصة

المقدمة : في كثير من الأحيان يحدث ارتفاع ضغط الدم أو اضطرابه أثناء الحمل ، ويظل أحد الأسباب الرئيسية لوفيات الأم والجنين والمراضة المرتبطة بالحمل، فضلاً عن خطر إصابة المرأة الحامل بارتفاع ضغط الدم أثناء الحمل اصابتها بأمراض القلب والأوعية الدموية في وقت لاحق في الحياة. ومع ذلك ، على عكس الإرشادات العامة لارتفاع ضغط الدم، فإن أسباب هذا التقرير تشمل فائدة علاج ضغط الدم الطبيعي للنساء الحوامل ، والمخاوف النظرية بشأن انخفاض التروية المشيمية الرحمية، وتعرض الرحم للأدوية الخافضة للضغط.

اعتمد هذا النهج على مراجعة التقارير والأدبيات السابقة ويتضمن مراجعة تصنيفية لأنواع ضغط الدم أثناء الحمل، والتغيرات الفسيولوجية في الحمل التي تؤثر على اضطراب ضغط الدم ، والعواقب الفورية والطويلة الأجل لارتفاع ضغط الدم ، والفيزيولوجيا المرضية من مقدمات الارتعاج المرتبطة باضطراب البروتينية في الجسم ، وقد تقلل أهداف علاج ارتفاع ضغط الدم من الآثار الشديدة دون زيادة خطر فقدان الحمل أو رعاية الأطفال حديثي الولادة على مستوى عالٍ. وأخيراً نناقش مستقبل البحث في هذا المجال والحاجة الملحة لدراسة العوامل الاجتماعية والاقتصادية التي تساهم في التفاوتات في رعاية صحة الأم. لذلك من الضروري معرفة الضغط ومعالجته على الفور.

يمكن أن يؤدي الفشل في علاج ارتفاع ضغط الدم إلى أمراض ووفيات الأمهات ، خاصة أثناء الولادة ، أو فقدان الجنين بشكل كبير . في هذه المراجعة المصغرة ، سنحاول مناقشة ارتفاع ضغط الدم لدى النساء الحوامل وتحديد أهداف العلاج وتسمم الحمل الناجم عن ارتفاع ضغط الدم . الهدف من المراجعة هو ملخص علمي سريع عن هذا الاضطراب الذي أصبح شائعًا في الوقت الحاضر.

الاستنتاجات : يجب عمل الاستشارة الطبية من أجل تحسين صحة الأم، وكذلك استخدام الأدوية المثلى وإدارة ما قبل الحمل للنساء المصابات أو المهددة بارتفاع ضغط الدم ، ونرى أنه من الضروري إبلاغهن بالمخاطر المتزايدة على صحتها وصحة الجنين.

كما يجب وضع استراتيجيات للتنبؤ بالأشخاص الأكثر عرضة للخطر ولتحديد العلاجات الدوائية المثلى لتقليل نتائج الحمل السلبية

الكلمات المفتاحية: اضطراب ارتفاع ضغط الدم ، الحمل ، تسمم الحمل

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Introduction

High blood pressure during pregnancy or hypertensive disorders of pregnancy (HDP) in general is considered one of the main causes of maternal death and fetal loss in developing countries [1]. Blood pressure disorders during pregnancy include chronic hypertension, gestational hypertension, and preeclampsia , Diagnostic criteria and side effects of blood pressure disorders in pregnant women have developed during the last five decades, so the latest definition of high blood pressure was established by obstetricians and gynecologists in the United States of America in 2013 [2].

Most medical reports agree on the definition of blood pressure during pregnancy as blood pressure (BP) ≥140/90 mmHg [3] . Most of the medical reports issued by the World Health Organization indicate a continuous increase in disorders resulting from high blood pressure during pregnancy due to advanced maternal age at the time of the first pregnancy, rising rates of obesity and other cardiac risk factors, such as cerebrovascular disease and cardiomyopathy, which now account for half of all maternal deaths. [4].

There is variability at the beginning of antihypertensive therapy due to the uncertainty about the effect of these antihypertensive drugs on the mother or the fetal risks in the uteroplacental circulation due to exposure of the uterus to antihypertensive drugs [5].

All health care providers in maternity care health centers should be able to promptly recognize the signs, symptoms, and laboratory findings of high blood pressure during pregnancy with or without proteinuria.

We must fully appreciate the danger of high blood pressure during pregnancy and the possibility of its involvement in the disorder of many organs and the risks of the perinatal period.

Healthcare providers may face emergency cases of pregnant women with high blood pressure, so the roles of healthcare providers in rural areas are different depending on the availability of resources.

A summary of scientific evidence is provided in this scientific statement. related to diagnostic and treatment strategies for HDP, given that recent trends indicate an increase in HDP.

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Classification

Classification of hypertension in pregnant women according to the International Society for the Study of Hypertension (ISSHP) during pregnancy into four categories:

1-Chronic high blood pressure is diagnosed 20 weeks before conception or before implantation : Essential or Secondary.

2-High blood pressure after 20 weeks of pregnancy, this is called gestational hypertension :

-without proteinuria (pregnancy-induced hypertension, transient hypertension, non-proteinuric gestational hypertension)

-With poor circumstances (severe preeclampsia, eclampsia)

-With proteinuria (pregnancy-induced hypertension, preeclampsia, toxemia) - without harmful circumstances - in unfavorable circumstances (severe preeclampsia, eclampsia)

3-Preeclampsia is also diagnosed after 20 weeks of pregnancy, and it was found that 25% of pregnant women with high blood pressure lead to preeclampsia

4- Another type of hypertension known as "masked hypertension" is more difficult to diagnose and is characterized by blood pressure that is normal during a clinic or doctor's appointment but elevated at other times. It is most commonly detected by automated home blood pressure monitoring or 24-hour ambulatory blood pressure monitoring (ABPM).

5-Transient gestational hypertension .

6- Over 500 000 fetal and neonatal deaths and over 70.000 maternal deaths worldwide occur each year as a result of preeclampsia, either de novo or secondary to chronic hypertension. Since preeclampsia can become more severe quickly and without notice, we do not advise dividing it into mild or severe forms [6;7] .

Definitions

Mild to moderate hypertension is defined as two or more elevations in blood pressure (BP) recorded at least four hours apart [8]. Diastolic blood pressure (dBP) is greater than or equal to 90 mmHg and/or systolic blood pressure (sBP) is larger than or equal to 140 mmHg (but less than 160 mmHg) (but less than 110 mmHg).

When sBP is more than or equal to 170 mmHg, with or without dBP larger than or equal to 110 mmHg, it is a medical emergency and needs immediate treatment. Severe hypertension is defined as sBP greater than or equal to 160 mmHg and/or dBP greater than or equal to 110 mmHg. [9].

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Epidimology

Hypertension is the leading cause of maternal death globally after 12 hours of maternal haemorrhage, and is a major cause of short- and long-term maternal and fetal morbidity [10]. A higher risk of preterm birth and low birth weight of baby is also linked to high systolic blood pressure during pregnancy [11]. In order to assist forecast pregnancy-related issues, high blood pressure has traditionally been reported before conception (both maternal and fetal). According to statistics, 15.3% of women globally are at risk of having cardiovascular disease, and 7.5% of women have excessive blood pressure. the upcoming In previous studies, including [12] , high pressure develops rapidly in women and can be diagnosed 10 years before, and this increases the chances of predicting heart disease and cardiovascular diseases, in addition to that studies confirmed the idea that women with a history of high blood pressure during pregnancy and reproduction age more quickly [12 ; 13] .

Goal of treatment

The goal of treating high blood pressure in pregnant women is different from those who suffer from high pressure in general .the benefit of treatment to maintain BP in the range of 110-140/80-85 mm Hg according to what he mentioned in the American College of Obstetrician and Gynecologists (ACOG) Practice Bulletin (2019) [14] .

The choice of antihypertensive drugs is limited due to concerns about the safety of the fetus, In addition, the medication should be gradual in reducing pressure so as not to affect the uterine blood flow to the fetus [15].

The Working Group of the National High Blood Pressure Education Program (NHBPEP) states that oral methyldopa is the first line of treatment for high blood pressure., where clinical studies, by following up on children who were exposed to the drug in the womb, have shown that methyldopa is a safe drug, while the second line is intravenous using to treat severe cases of hypertension or when it is not possible to use methyldopa by use hydralazine [16] . β- blockers have been shown to be safe when used to treat acute hypertension, as they have shown equivalent efficacy to hydralazine such us Labetalol But a study showed that Labetalol may cause delayed growth and low placental weight(7). Also, nifedipine has been studied extensively and has been shown to lower blood pressure, improve kidney function, and not affect blood flow in the umbilical artery [17)] . As for the use of ACE inhibitors or angiotensin II receptor blockers, it has been shown that it negatively affects the renal system of the fetus and causes low amniotic fluid and may cause deformities of the limbs and bones of the skull [16] .

Finally, attention should be paid to direct vasodilators, which can cause excessive hypotension (both sodium nitroprusside and diazoxide) and cyanide intoxication (sodium nitroprusside only), making them the agents of last resort [18] .

Pre-eclampsia

Pre-eclampsia can be defined as hypertension among pregnant women after 20 weeks of gestation or in other words new-onset end organ damage [19;14] In addition to high blood pressure, pre-eclampsia women have proteinuria (urinary spot protein: creatinine ratio>30 mg mmol [14] or 24- h urine collection with >300 mg protein) and swelling in the legs, hands, and feet, ranging from mild to severe [19;20] .

Diagnostic Criteria for Preeclampsia

Blood pressure

- after 20 weeks of pregnancy, in a woman with a preexisting normal blood pressure, greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions, at least four hours apart.
- Hypertension can be identified in a brief period of time (minutes) if the systolic or diastolic blood pressure is greater than or equal to 110 mm Hg or greater than or equal to 160 mm Hg [21].

Proteinuria

- Protein/creatinine ratio larger than or equal to 0.3* or greater than or equal to 300 mg per 24-hour urine collection (or this amount calculated from a timed collection).

Alternatively, in the absence of proteinuria, newly developed hypertension along with any of the following:

- Platelet counts less than 100,000/microliter is a sign of thrombocytopenia.
- Serum creatinine levels above 1.1 mg/dL or a doubling of serum creatinine levels in the absence of other renal disease indicate renal insufficiency. liver function impairment.
- Elevated blood concentrations of liver transaminases to twice normal concentration Pulmonary edema Cerebral or visual symptoms [22] .

Risk factors

Many factors can increase the chance of getting pre-eclampsia including nulliparity, history of pre-eclampsia, mother and sister who had preeclampsia, multiple pregnancies (2 years apart) or inter-pregnancy gab more than 10 years apart, obesity, maternal age >40 years, body mass index 35 kg m^{-2} and finally the mother undergo from another disease including renal frailer, hypertension, rheumatoid arthritis, and lupus (due to presence of anti-phospholipid antibody) [23;24;25].

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Complications of preeclampsia:

Preeclampsia can harm the developing infant since it is mostly linked to spiral artery failure, which results in placental hypoperfusion and small-for-gestational-age babies. Fetal growth restriction or even premature births are what this is known as, and the latter can lead to various issues for the baby in the future, such as epilepsy, cerebral palsy, learning difficulties, hearing, and visual issues [6,26]. Preeclampsia, on the other hand, can also result in more severe harm to the mother, such as postpartum bleeding, stroke, seizures, fluid in the chest, heart failure, reversible blindness, and liver bleeding [27].

HELLP syndrome and preeclampsia

HELLP syndrome occurs when preeclampsia or eclampsia causes damage to the liver and blood cells resulting in [9]: Hemolysis, breakdown of the red blood cells and Elevated liver enzymes are a sign of liver disease, and high levels of these compounds in the blood also indicate low platelet numbers, which prevent proper blood clotting [27].

Pathogenesis of pre-eclampsia

There are two stages to the development of preeclampsia. the first is early in the first trimester aberrant placentation, which is followed by maternal syndrome. [28;29)]. Oxidative stress, aberrant natural killer cells (NKs) at the maternal-fetal interface, genetic and environmental variables, as well as defective placentation, are all contributing factors [30]. The spiral artery only partially changes in the first stage because cytotrophoblasts are unable to switch from the proliferative epithelial subtype to the invasive endothelial subtype. Placental ischemia and restricted maternal arteries are both caused by inadequate spiral arteriolar remodeling. The placental flow is further compromised by the arthrosis of the narrow spiral arteries, which is characterized by fibrinoid necrosis of the arterial wall, the presence of lipid-laden macrophages inside the lumen, and a mononuclear perivascular infiltration [31;32] .

Along with endothelial dysfunction, preeclampsia is characterized by a shift in the Th1 phenotype of T helper cells, which increases the release of proinflammatory cytokines including interleukin (IL)-12 and IL-18 while reducing IL-10, which induces apoptosis and inhibits trophoblast invasion [33]. It's possible that more CD19+CD5+ B cells are producing antiangiogenic substances. Because uterine natural killer cell suppression may result in improper spiral artery remodeling [33], uterine natural killer cells, which vary from peripheral natural killer cells, are probably implicated.

The pathophysiology of preeclampsia has been linked to numerous hereditary factors. Preeclampsia-related mutations in complement component 3 may contribute to complement system dysregulation [34]. Additionally located in uterine tissue, the cardiac protein corin triggers atrial natriuretic peptide, and mutations in corin linked to

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preeclampsia have been discovered [34;35]. A genetic predisposition to preeclampsia has been suggested by global transcriptional profiling of chorionic villus samples from preeclamptic mothers [34,36]. Decidual tissue from preeclamptic patients showed abnormalities in gene expression, while endometrial stromal cells from non-pregnant women with a history of severe preeclampsia failed to decidualize in vitro and were transcriptionally inactive [37]. Preeclampsia has been linked to long-chain L-3 hydroxy acyl-CoA dehydrogenase insufficiency, a condition of fatty acid metabolism [35].

Management of pre-eclampsia:

1- Blood pressure management:

In order to achieve the main goal of blood pressure regulation, which is to prevent intracerebral hemorrhage, systolic and diastolic blood pressure must be adjusted to between 150 and 80 and 100 mm Hg, respectively[38]. A 1-2 mm Hg drop in blood pressure should occur every minute. Nifedipine and methyldopa, which can be taken orally, are alternatives to labetalol, which is frequently the first medicine prescribed. When treating severe hypertension, intravenous labetalol or hydralazine injection provides control that is more dependable when oral medication falls short [39]. Continuous fetal monitoring should be done until blood pressure is stable , I.V. antihypertensive therapy with fluid restriction, the option of invasive blood pressure monitoring in a high dependency area, as well as regular urine output monitoring and 6-hourly blood tests to monitor platelet count, renal function, and liver enzymes, should all be taken into consideration. [40].

Eclamptic seizures management

Patients with preeclampsia are thought to die most frequently from seizures. The medication of choice for both treating and preventing seizures is magnesium sulfate. Rapid prenatal neuroprotection and a decreased incidence of cerebral palsy are two additional advantages of magnesium sulfate [40]. Magnesium sulfate-treated preeclamptic patients should be periodically checked for signs of toxicity, which include weakened reflexes, slowed breathing or low oxygen saturations, and progressive paralysis. If renal impairment is suspected, the medication should be stopped, and serum magnesium levels should be measured. Low urine output and renal impairment can predispose the patient to magnesium poisoning [41].

2- Pulmonary oedema

Acute pulmonary edema in preeclampsia patients occurs in 3% of cases overall and has the potential to be fatal [41]. Clinical symptoms, a chest radiograph (even if the mother is still pregnant), and in serious circumstances, an immediate echocardiography to evaluate ventricular function are used to make the diagnosis. Approximately 70% of cases (after birth) are related to heart failure and excessive fluid

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administration [19]. Therefore, it is advised that women with severe pre-eclampsia limit their fluid intake to 80 ml per hour (including oral, pharmacological, and intravenous fluids), assuming that there are no continuous fluid losses. First-line therapy includes oxygen, fluid restriction, 20–60 mg furosemide boluses, and prompt fetal delivery [42,43].

Conclusion

Measuring and monitoring blood pressure periodically for pregnant women is very important in diagnosing blood pressure disorders during pregnancy, in addition to the need for accurate measurement and evaluation of blood pressure and its fluctuations.

There is also a need for a study to determine the appropriate levels of postpartum blood pressure control, especially as there are no longer reservations about the effect of treatment on the fetus, especially after studies have recorded the occurrence of health problems for mothers with postpartum pressure disorder and may require hospitalization after childbirth.

Treatment of high blood pressure, prevention of seizures, and timely delivery are the main treatment options for women with pre-eclampsia, as well as conducting more detailed assessments that include knowing the heart rate and conducting a complete blood picture, which are effective in protecting women from complications that may occur after childbirth, especially the consequences of heart diseases. Therefore, it is that women be examine during pregnancy by obstetricians and gynecologists, and later by cardiologists.

Conflict of interests;-

There are no conflicts of interest.

References

[1] C. Arnott , M. Nelson , M . Alfaro Ramirez , J. Hyett , M. Gale , A. Henry, DS. Celermajer , L. Taylor and M. Woodward. Maternal cardiovascular risk after hypertensive disorder of pregnancy. *Heart* , vol. 106 , pp. 1927–1933, 2020.

[2] MC. Brown and KE. Best , MS . Pearce , J. Waugh , SC. Robson and R. Bell. Cardiovascular disease risk in women with pre-eclampsia: systematic review and metaanalysis. *Eur J Epidemiol*., no. 28, pp.1–19, 2013 .

[3] DC. Scantlebury, GL. Schwartz , LA. Acquah , WM . White , M. Moser and VD . Garovic. The treatment of hypertension during pregnancy: when should blood pressure medications be started? *Curr Cardiol Rep*., vol .15, pp. 412, 2013.

[4] CV. Ananth , CM . Duzyj , S. Yadava , M . Schwebel , AT. Tita and KS. Joseph . Changes in the prevalence of chronic hypertension in pregnancy, United States, 1970 to 2010. *Hypertension*, vol.74, pp. 1089–1095, 2019 .

[5] P. Wu , CA. Chew-Graham , AH. Maas, LC. Chappell , JE . Potts, M. Gulati, KP. Jordan and MA. Mamas .Temporal changes in hypertensive disorders of

pregnancy and impact on cardiovascular and obstetric outcomes. *Am J Cardiol*, vol. 125, pp. 1508–1516, 2020

[6] MA . Brown , LA. Magee , LC. Kenny , SA. Karumanchi , FP. McCarthy , S. Saito , DR. Hall , CE. Warren , G. Adoyi and S. Ishaku . The hypertensive disorders of pregnancy: ISSHP classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertens*, vol.13,pp. 291–310, 2018.

[7] JJ. Stuart , LJ. Tanz , SA. Missmer, EB . Rimm , D. Spiegelman , TM . James-Todd and JW. Rich-Edwards. Hypertensive disorders of pregnancy and maternal cardiovascular disease risk factor development: an observational cohort study.*Ann Intern Med*. , vol.169, pp. 224–232, 2018.

[8] R . Townsend , P. O'Brien and A. Khalil . Current best practice in the management of hypertensive disorders in pregnancy. *Integrated Blood Pressure Control* , no. 9, vol. 79, pp. 79-94, 2016.

[9] SA. Lowe , L. Bowyer , K. Lust , LP. McMahon , RA . North and M . Paech.The SOMANZ guideline for the management of hypertensive disorders of pregnancy. *Society of Obstetric Medicine of Australia and New Zealand* , no. 55, vol.1, pp. 6-11, 2015.

[10] H. Teng , Y. Wang , B. Han , J. Liu , Y. Cao , Q . Ling , C. Xiao Z and J. Yin. Gestational systolic blood pressure trajectories and risk of adverse maternal and perinatal outcomes in Chinese women.*BMC Pregnancy Childbirth* , vol . 21, pp. 155, 2021

[11] R . Bakker , EA . Steegers , A. Hofman and VW. Jaddoe . Blood pressure in different gestational trimesters, fetal growth, and the risk of adverse birth outcomes: the Generation R Study . *Am J Epidemiol* , vol. 174, pp. 797–806, 2011

[12] EB . Haug , J. Horn , AR. Markovitz , A. Fraser and LJ. Vatten , MacdonaldWallis C, Tilling K, Romundstad PR, Rich-Edwards JW, Åsvold BO. Life course trajectories of cardiovascular risk factors in women with and without hypertensive disorders in first pregnancy: the HUNT Study in Norway. *J Am Heart Assoc*., vol. 7, pp. e009250, 2018.

[13] VD. Garovic , WM. White , L. Vaughan , M. Saiki, S. Parashuram , O. Garcia-Valencia , TL. Weissgerber, N . Milic , A . Weaver and MM. Mielke . Incidence and long-term outcomes of hypertensive disorders of pregnancy. *J Am Coll Cardiol*.,vol. 75, pp. 2323–2334, 2020.

[14] ACOG practice bulletin no. 202: gestational hypertension and preeclampsia. Obstet Gynecol 133: e1-e25, 2019.

[15] DV. Garovic . Hypertension in Pregnancy: Diagnosis and Treatment . *Mayo Clin Proc*., vol. 75, pp. 1071-1076, 2000.

[16] National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol*., 183(1, suppl):S I-S22 ,2000

[17] CM. Brown and VD. Garovic . Drug Treatment of Hypertension in Pregnancy . *Drugs*., no.74 , vol. 3 , pp. 283–296.2014.

[18] WO.Cooper, S. Hernandez-Diaz , PG. Arbogast , JA. Dudley , S. Dyer and PS. Gideon . Major congenital malformations after first-trimester exposure to ACE inhibitors. *The New England journal of medicine* , no. 354, vol . 23, pp. 2443–2451, 2006.

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[19] National Institute for Health and Clinical Excellence. Hypertension in pregnancy: the management of hypertensive disorders during pregnancy CG107.. Available from http:// guidance.nice.org.uk/cg107 (accessed 19 December 2014), 2010
[20] C. Macdonald-Wallis, R. J. Silverwood , A. Fraser, S M. Nelson , K. Tilling , DA. Lawlor and BL. DeStavola . Gestational-age-specific reference ranges for blood pressure in pregnancy: findings from a prospective cohort. *Journal of hypertension*, no. 33, vol.1, pp. 96, 2015.
[21) LA. Magee , A. Pels , M. Helewa , E. Rey and P. Von Dadelszen Canadian Hypertensive Disorders of Pregnancy Working Group. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *Pregnancy Hypertens* , vol. 4, pp. 105–145, 2014.
[22] CM. Brown . Garovic 2011 Mechanisms and management of hypertension in pregnant women. *Curr Hypertens Rep*. October , no. 13, vol .5 , pp. 338–346, 2011
[23] Noris M, Perico N, Remuzzi G. Mechanisms of disease: preeclampsia. Nat Clin Pract Nephr . 1: 98–114.2005
[24] H. Duckitt and D. Harrington . Risk factors for pre-eclampsia atantenatal booking: systematic review of controlled studies. *Br Med J* , vol . 330 , pp. 565, 2005.
[25] L S. Mehta , G . Sharma , A A . Creanga , AB. Hameed , LM Hollier and JC. Johnson . American Heart Association Advocacy Coordinating Committee. Call to action: maternal health and saving mothers: a policy statement from the American Heart Association. *Circulation*, no. 144, vol . 15, pp . e251-e269, 2021.
[26] Jim B and Karumanchi SA. "Preeclampsia: pathogenesis, prevention, and long-term complications". *Semin Nephrol* ; 37:386-397, 2017.
[27] K . Fitzpatrick , K . Hinshaw and J . Kurinczuk . Risk factors, management, and outcomes of hemolysis, elevated liver enzymes, and low platelets syndrome and elevated liverenzymes, low platelets syndrome. *Obstet Gynecol* , vol .123, pp . 618–27 , 2014.
[28] CW . Redman and IL . Sargent . Latest advances in understanding preeclampsia .*Science* , vol. 308 , pp . 1592–1594 , 2005.
[29] R . Romero and T. Chaiworapongsa . Preeclampsia: a link between trophoblast dysregulation and an antiangiogenic state. *J Clin Invest.* , vol. 123 , pp . 2775–2777, 2013.
[30] JM . Roberts, RN . Taylor , TJ. Musci , GM . Rodgers , CA . Hubel and McLaughlin MK. Preeclampsia: an endothelial cell disorder.*Am J Obstet Gynecol*., vol. 161 , pp. 1200–1204, 1989
[31] I . Brosens and M. Renaer . On the pathogenesis of placental infarcts in pre-eclampsia . *J Obstet Gynaecol Br Commonw*., vol . 79 , pp .794–799, 1972
[32] F. De Wolf , WB . Robertson and I. Brosens . The ultrastructure of acute atherosis in hypertensive pregnancy.*Am J Obstet Gynecol*. Vol . 123, pp. 164–174, 1975.
[34] A . Malik , B. Jee , SK. Gupta "Preeclampsia: disease biology and burden, its management strategies with reference to India". *Pregnancy Hypertens* , vol.15 , pp . 23-31, 2019.
[35] S . Rana , E . Lemoine , J. Granger and SA . Karumanchi . Preeclampsia: Pathophysiology, Challenges, and Perspectives. *Preeclampsia. Circ Res* , vol. 124 , pp. 1094-1112, 2019.

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[36] Y . Cui , W. Wang and N . Dong . "Role of corin in trophoblast invasion and uterine spiral artery remodelling in pregnancy". *Nature* , vol .484 , pp. 246-250, 2012.

[37] MB . Rabaglino , ED . Post Uiterweer , A . Jeyabalan , WA . Hogge and KP . Conrad ."Bioinformatics approach reveals evidence for impaired endometrial maturation before and during early pregnancy in women who developed preeclampsia". *Hypertension* , vol. 65 , pp. 421-429, 2015.

[38] T . Garrido-Gomez , F. Dominguez and A. Quinonero . "Defective decidualization during and after severe preeclampsia reveals a possible maternal contribution to the etiology". *Proc Natl Acad Sci U S A* , vol.114 , pp. E8468-E8477 , 2017.

(39) A . Dennis and J. Castro . Transthoracic echocardiography in women with treated severe pre-eclampsia. *Anaesthesia* ,vol. 69 , pp. 436–44 , 2014.

[40] K . Bramham , B. Parnell , C . Nelson-Piercy , PT . Seed , L. Poston and LC. Chappell . Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. *Br Med J* , vol . 2014 , pp. 348: g2301, 2014 .

[41] D. Leslie and RE. Collis .Hypertension in pregnancy. *Bja Education*, no.16 , vol. 1, pp. 33-37,2016.

[42] M . Constantine and S. Weiner .Effects of antenatal exposure tomagnesium sulfate on neuroprotection and mortality in preterm infants: a meta-analysis. *Obstet Gynecol* , vol. 114 , pp. 354–64 , 2009.

[43] S. Suvakov , H. Cubro, WM. White , YS. Butler Tobah , TL, Jordan KL. Weissgerber , XY. Zhu , JR. Woollard , FT. Chebib , NM. Targeting senescence improves angiogenic potential of adipose-derived mesenchymal stem cells in patients with preeclampsia.*Biol Sex Differ*. Vol. 10, pp. 49 , 2019.

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