



ANALYSIS OF RISK FACTORS OF PREECLAMPSIA AND ECLAMPSIA AND ITS EFFECTS ON MATERNAL AND FETAL OUTCOME AS PER GESTOSIS SCORE

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ABSTRACT

Objectives: Observation and analysis of the risk factors associated with preeclampsia and eclampsia and its effect on maternal and fetal outcome. **Methods:** It is a prospective study where 500 diagnosed cases of preeclampsia and eclampsia were recruited after taking informed consent. Data collected on the basis of detailed history and clinical evaluation. **Result:** The maximum number of preeclampsia and eclampsia in the present series occurred between the age group 21 to 25 years (46%). Majority of cases (71.4%) in our study presented between 35.1 to 40 weeks of gestational age. 24.4% cases had BMI in range of 25-29.9. 51.4% women were primipara and 53.2% cases were unbooked. Majority of the cases (45.2%) belonged to the upper lower socio-economic class. Out of 500 cases, 23.2% had anaemia, followed by hypothyroidism in 14.8% cases, GDM in 3.8% cases, obesity 2.8% cases, chronic hypertension in 2.2% cases, diabetes mellitus in 2% cases, and PCOD in 0.4 % cases. Risk factors found in our study that affected maternal and perinatal outcome severely were: primiparity, unbooked status, lower middle class III and upper lower class IV, BMI > 24.9, gestational age < 34 weeks, anaemia, hypothyroidism and chronic hypertension and gestational diabetes mellitus. **Conclusion:** Our study reveals that if patients present with multiple risk factors (three and more), maternal morbidity and mortality increased significantly.

KEYWORDS : Obstetrics; Medical Problems in Pregnancy , Preeclampsia/ Eclampsia , gestosis score

INTRODUCTION

Preeclampsia and eclampsia are important causes of morbidity as well as mortality in both mother and fetus. Incidence of preeclampsia was found to be 10.3% (National Eclampsia Registry 2013). The incidence of eclampsia is 1.9% out of which more than 50% of the cases are antepartum, and approximately 13% of the cases reported post-partum. Maternal Mortality attributed to eclampsia is 4-6 % . Among all maternal deaths 19 % deaths are due to hypertension in pregnancy (WHO 2014)⁽¹⁾

Preeclampsia is defined as elevated systolic blood pressure of 140 mm Hg or diastolic blood pressure of 90 mm Hg or more, or both the systolic and the diastolic blood pressure are above $\geq 140/90$ mm Hg, measured twice with a gap of 4 h with proteinuria in 24 h-urine ≥ 300 mg or protein/creatinine ratio ≥ 0.3 or in absence of quantitative methods one can use the read proteins in urine on a test tape 1+.

Identification of its risk factors in the pre pregnancy and initial stage of pregnancy can help in lowering morbidity and mortality.

At present there is no single cost effective and reliable screening test for preeclampsia and eclampsia. Looking at the magnitude of the social and economic impact of preeclampsia and eclampsia, there is a need to anticipate this condition. The first step would be to recognize the risk factors associated with preeclampsia. There are several maternal and clinical risk factors that either alone or in combination may contribute to the high risk of pre-eclampsia; genetic factors, diet, parity, gestational weight gain, maternal age, twin pregnancy, previous history of pre-eclampsia, maternal pre-existing conditions (such as diabetes, chronic hypertension) are considered to play influential roles in the development of pre-eclampsia^(5,6) Pregnancy induced hypertension is associated with increased risk of acute renal failure, abruptio placentae, DIC, HELLP syndrome, pulmonary oedema, adult respiratory distress syndrome,

convulsions and even maternal death^(6,7).

Fetal morbidities in pregnancy induced hypertension include preterm delivery, IUGR, stillbirth, low birth weight babies⁽⁸⁾. The purpose of this study was to evaluate the risk factors in Patients of pre-eclampsia and eclampsia at tertiary centres during study period and to determine its effect on maternal and fetal outcome. The assessment of clinical risk factors helps us to be more vigilant and this can be done with HDP- Gestosis score (ICOG Good Clinical Practice Recommendations 2019). Mild, moderate and high risk factors carry score 1,2 and 3, respectively and careful history gave total score.

AIMS AND OBJECTIVES

- To study risk factors for preeclampsia and eclampsia included in gestosis score.
- To study maternal and fetal outcome according to increasing gestosis score.

METHODOLOGY

This was a prospective study conducted over a period of 18 months from 1st march 2019 to 30th august 2020. 500 patients diagnosed as preeclampsia and eclampsia admitted in Shyam Shah Medical College, Rewa were enrolled in this study. All patients were examined in labour room. An informed consent was taken from the patient and husband's consent was taken in eclampsia cases. A set of questionnaire was given to the patients and relevant medical history, family history and past history was elicited and noted. These patients were followed during labour and maternal and perinatal outcome was noted. The details of women like age, education, occupation, family income, gravida, parity, antenatal care, (medical problems) PCOD, hypothyroidism, chronic hypertension, multiple pregnancy, chronic kidney disease, gestational age and thorough examination was done. Informed consent was documented. All patients having risk factors were grouped into six groups according to number of risk factors present in them and risk factor score was given

according to HDP gestosis score. Their maternal and fetal outcome was analysed according to sum total of risk factors.

Inclusion Criteria For The Cases

- Patients with blood pressure >140/90 after 20 weeks of gestation with proteinuria.
- Patients with severe preeclampsia (blood pressure >160/110) and with end organ damage.
- Patients with history of convulsions diagnosed as eclampsia.

Exclusion Criteria For The Cases

- Patients with seizure disorder.
- Patients delivered in periphery and referred to medical college.
- Patients with congenital malformation in baby

STATISTICS

Qualitative data analysed and explained as frequency and percentage. Appropriate statistical tests were applied (Yate's Chi Square test).

RESULTS

Table 1: Distribution of cases according to age (N=500)

Age Group	No. of patients	Percentage
<=20 years	43	8.6%
21-25 years	230	46%
26-30 years	161	32.2%
31-35 years	50	10%
>=36	14	2.8%
Total	500	100%

The maximum number of women in the study was between the age group 21 to 25 years (46%). The youngest age was 19 years and oldest was 44 years.

Table 2. Distribution of cases according to gestational age

GESTATIONAL AGE	No. of Patients	Percentage
<=30	21	4.2%
30.1-35	77	15.4%

Table 5. Risk Factor analysis on the basis of Maternal Complications

RISK FACTOR	ABRUPTION	ARDS	ARF	DIC	HELLP	MORTALITY	PPH	PRESS	PULMONARY EDEMA	TEMPORARY LOSS OF VISION	TOTAL
0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0
2	0	2	0	0	0	0	4	0	0	0	6
3	3	2	2	0	0	0	7	0	4	2	20
4	6	3	6	0	6	6	19	2	2	0	50
5	11	0	5	5	8	7	15	1	0	0	52
6	2	2	0	0	6	3	2		0	0	15
Total	22	9	13	5	20	16	47	3	6	2	143

Yate's Chi-square = 52.565, p-value = 0.05433

One risk factor: 47 cases - most common risk factor among them i.e. 40 cases belonged to lower middle class III socioeconomic status.

Two risk factors: 94 cases- most common was primipara (33 cases), lower middle class III socioeconomic status (53 cases).

Three risk factors: 134 cases - most common was unbooked

Table 6. Risk Factor Analysis on the basis of Perinatal Outcome

Maternal Risk factor	HEALTHY	IUD	NICU	PRETERM (admitted in NICU)	STILL BIRTH	PERCENTAGE
0 Risk Factor	17	0	0	0	0	3.2%
1 Risk Factor	49	0	0	0	0	9.4%
2 Risk Factor	92(6twins)	0	2	2	0	18.5%
3 Risk Factor	83(6twins)	28	25	2	0	26.6%
4 Risk Factor	34	26	48	17(3twins)	2	24.5%
5 Risk Factor	9	28	30	6(3twins)	2	14.4%
6 Risk Factor	0	8	6	0	2	2.7%
Total(518) (18 twin pregnancy)	284	90	111	29	4	100

35.1-40	357	71.4%
>40	45	9%
TOTAL	500	100%

Majority of cases (71.4%) in our study presented between 35.1 to 40 weeks of gestational age, followed by 15.4% cases presented between 30.1 to 35 weeks of gestation, 9% cases with greater than 40 weeks of gestation and 4.2% cases presented with less than 30 weeks of gestation.

Table 3. Distribution of cases according to BMI (N=500)

BMI	No. of Patients	Percentage
< 18.5	0	0%
18.5-24.9	364	72.8%
25-29.9	122	24.4%
>30	14	2.8%
Total	500	100%

Out of 500 cases, 72.8% cases had their BMI in range of 18.5-24.9, 24.4% cases in range of 25-29.9, 2.8% cases beyond 30 and none was below 18.5 BMI.

Primipara women (51.4%) have more incidence compared to Multipara (48.6%).

Out of 500 cases, 46.8% cases were booked patients who had regular antenatal visits and 53.2% cases were unbooked with no or 1 antenatal visit

Cases were categorised into socio-economic status using modified kuppuswamy scale using family income, occupation and education of head of household. Majority of the cases (45.2%) belonged to the upper lower socio-economic class and none of them belonged to the high socio-economic status.

Primipara were 257 and unbooked cases were 266.

23.2% had anaemia, followed by hypothyroidism in 14.8% cases, GDM in 3.8% cases, obesity 2.8% cases, chronic hypertension in 2.2% cases, diabetes mellitus in 2% cases, and PCOD in 2% cases.

status (85 cases), primipara (64 cases) and lower middle class socioeconomic status (57 cases).

Four risk factors: 124 cases - most common was primipara, anaemia, hypothyroidism and BMI > 24.9. Majority of our cases belonged to this group and had severe maternal complications leading to maternal mortality.

Five risk factors: 72 cases - most common was primipara , anaemia, BMI >24.9, hypothyroidism and GDM.

Yate's Chi-square = 236.266, p < 0.00001

Late preterm babies who were healthy were kept mother side. Perinatal outcome was analysed and p value was < 0.00001 which was statistically significant.

Table.7. Risk Factor Analysis on the basis of Gestosis score

RISK FACTORS IDENTIFIED	HDP Gestosis Score	No. of Patients	Percentage
NO Risk factor		236	47.2%
ANAEMIA	1	116	23.2%
OVERWEIGHT (BMI > 25)	1	122	24.4%
OBESITY (BMI > 30)	1	14	0.2%
PRIMIGRAVIDA	1	257	51.4%
FAMILY H/O CARDIOVASCULAR DISORDER	1	5	1%
PCOD	1	2	0.4%
CHRONIC VASCULAR DISEASE	1	2	0.4%
MATERNAL HYPOTHYROIDISM	2	74	14.8%
FAMILY H/O PREECLAMPSIA	2	7	1.4%
GESTATIONAL DIABETES MELLITUS	2	19	3.8%
MULTIFETAL PREGNANCY	2	18	3.6%
CHRONIC HYPERTENSION	3	11	2.2%
PREGESTATIONAL DIABETES MELLITUS	3	10	2%
CHRONIC KIDNEY DISEASE	3	2	0.4%

Risk factors found in our study was compared with risk factors in gestosis score and it revealed that as the number of risk factors increases, score increases and there by increasing the risk of preeclampsia.

DISCUSSION

Preeclampsia is a syndrome that mainly includes the origination of new onset hypertension in the latter half of the pregnancy. The determination of its predisposing factors before pregnancy as well as during initial stages of pregnancy will aid in lowering morbidity and mortality.

The maximum number of pre-eclampsia and eclampsia patients occurred in the range of age group 21-25 years (46%) and 26-30 years (32.2%). The rate of preeclampsia is more common in younger age groups especially below the age of 25 years old and the rate reduces with increasing age. It may be due to initial trophoblastic invasion and how the patient reacts to it.

Primipara women (51.4%) have maximum incidence in our study, and the findings are in good agreement with observations in a study by Shaikh S et al.⁽¹⁰⁾ in 2003. Research conducted at Dr. Hospital M. Djamil in 2012-2013 shows a evidentiary relationship with parity and the occurrences of preeclampsia. Primigravidae have a greater probability to experience preeclampsia as to those with multigravida.

A study by Katz et al.⁽¹¹⁾, in 2000 reported 70% of their patients as primigravidas. Emotional stress that occurs in primigravidae because of increased release of corticotropin releasing hormone (CRH) by the hypothalamus, which then leads to an increase in cortisol. The effects of cortisol are to prepare the body to react to all stressors by increasing sympathetic response, including response aimed at increasing cardiac output and keep down blood pressure⁽¹²⁾. Other potential mechanisms include insulin resistance, immune maladaptation, angiogenic factors, and genetic predisposition. Wolf et al.⁽¹³⁾, in 2005 suggested that higher sFlt-1 levels may predispose primiparous women to an elevated risk of preeclampsia.

Booked patients were 46.8% who had regular antenatal visits and 53.2% were unbooked with no or 1 antenatal visit. Neelima B et al.,⁽¹⁴⁾ in 2019 conducted a study and reported 86.52% unbooked cases.

Majority of the cases (45.2%) belonged to the upper lower socioeconomic class. Cases were categorised into

Risk factors found in our study that affected maternal and perinatal outcome severely were: primiparity, anaemia, BMI > 24.9, hypothyroidism and chronic hypertension and gestational diabetes mellitus. In our study patients having four or more risk factors had poor outcome.

socioeconomic status using modified Kuppaswamy scale using family income, occupation and education of head of household. Our finding is consistent with study by Guerrier et al.,⁽¹⁵⁾ in 2013 that revealed low socio educational status was strongly associated with preeclampsia and eclampsia. El-Moselhy et al.,⁽¹⁶⁾ conducted a study on socio-demographic risk factors of the preeclampsia cases and controls. Collectively, 59.0% of the patients belonged to lower social levels and represented a significant risk factor. When SES is low, maternal nutrition is low and medical care is found to be deficient and this has been ascribed to adverse outcomes^(17,18). In pregnant women, low SES can substantially increase the risk of untoward pregnancy outcomes. Previous studies have showed that low SES is connected with pregnancy complications such as preterm delivery, abortion, eclampsia, preeclampsia and gestational diabetes^(19,20,21).

In our study 71.4% presented between 35.1 to 40 weeks of gestational age, followed by 15.4% presented between 30.1 to 35 weeks of gestation. The findings are in good agreement with Shaikh S et al.⁽¹⁰⁾, 64% cases had gestational age between 31 to 37 weeks and 35% of patients had term pregnancy. Early preeclampsia has been related to poor placentation and dysfunctional spiral artery remodelling. These are uncommonly found in late onset preeclampsia, which tends to be milder and may occur without placental dysfunction.^(22,23)

In present study 364 cases (72.8%) had their BMI in range of 18.5-24.9 i.e. normal range, 122 cases (24.4%) were in range of 25-29.9 i.e. overweight range and 14 cases (2.8%) were > 30 i.e. obese. As per study done by Bodnar et al., in 2005 it was found that the altered risk of developing preeclampsia was twice for overweight females with a BMI of 26 kg/m², and almost thrice for obese mothers with a BMI of 30 kg/m.⁽²⁴⁾ Obesity is considered as a risk factor for preeclampsia and there are various common mechanisms that link obesity with a higher risk of developing preeclampsia.⁽²⁵⁾ In gestosis score, BMI > 30 was given score one but according to above mentioned study BMI > 25 was also associated with preeclampsia. So, score one was given when BMI > 25

116 cases (22.44%) in our study had anaemia at the time of admission. Abdel A Ali et al., in 2011 revealed in their study, women with severe anaemia had a 3.6 times higher risk of preeclampsia than women with no anaemia⁽²⁶⁾. The vulnerability of women diagnosed with severe anaemia to preeclampsia is because of a deficiency of micronutrients and antioxidants. As per gestosis score anaemia score is one.

Maternal hypothyroidism was given gestosis score 2. 74 cases (14.31%) in our study had hypothyroidism in current pregnancy which is similar to study done by Basbug et al. (27) and Sardana et al., (28) which revealed a high incidence of biochemical hypothyroidism in preeclampsia. In preeclampsia, there is failure in estrogen generation due to placental dysfunction resulting in lessening of TBG, TT₃, TT₄ along with growth retardation of the fetus (29). Experimental studies have found that release of nitric oxide is changed in hypothyroidism and the subsequent endothelial cell dysfunction may be a pathogenetic mechanism for hypothyroidism in preeclampsia (30).

18 cases (3.6%) had twin pregnancy in our study and 482 cases (96.4%) were of singleton pregnancy. The increased preeclampsia risk and prevalence in twin pregnancies may be associated to larger placental mass, associated with higher levels of circulating placental markers (31). Multifetal pregnancy was given score two as per gestosis score.

In present study 5.4% of cases had family history of chronic hypertension. Family history of chronic hypertension is a representative for familial factors and frequent environmental or behavioural vulnerabilities that may underlie preeclampsia risk. Family history was given gestosis score one and chronic hypertension had score 3. Family history in case of women with chronic hypertension is very important and simple to obtain clinical risk markers of preeclampsia in opposition to the biochemical markers.

19 cases had gestational diabetes as a co morbidity in our study. It is unclear whether a common etiologic pathway support both GDM and preeclampsia. These include endothelial dysfunction, angiogenic imbalance, increased oxidative stress and dyslipidemia. Gestational Diabetes Mellitus was given score 2 in gestosis score and for pregestational diabetes mellitus 3 score was given which shows severity of risk factors.

2 cases had history of polycystic ovarian disorder. PCOD was given one gestosis score. Naver et al. found that Women with PCOS and hyperandrogenemia compared with the background population, had a more than two fold increased risk of both preterm deliveries and preeclampsia, whereas normoandrogenic women with PCOS were not at an increased risk. (32) In present study all risk factors mentioned in gestosis score was not found.

In our study of 500 cases of preeclampsia and eclampsia, 167 cases (33.4%) developed maternal complications. Risk factor association with maternal complication was studied.

p value was equal to 0.05 which was statistically significant.

Majority of our cases presented with 3 and 4 risk factors which were associated with increased mortality and morbidity of patients. Though, the number of cases in 6 risk factors group were less but maternal mortality on the basis of maternal complications was 20% (highest compared to other groups) and perinatal outcome was very poor (IUD-8). Our study reveals that if patients present with multiple risk factors (3 and more), development of preeclampsia, maternal morbidity and mortality increases significantly. Results are similar to HDP Gestosis score as the number of risk factors increases, the risk of developing preeclampsia also increased.

In our study with 482 singleton pregnancies and 18 twin pregnancies (Total 518 babies) with preeclampsia and eclampsia were studied on the basis of risk factors in cases and their perinatal outcome. p value came out to be <0.00001 which was highly significant. Clustering of cases was seen in patients with 3 and 4 risk factors. Our study reveals that if a patient presents with multiple risk factors (3 and more),

perinatal morbidity and mortality increased significantly. 90 babies (17.3%) were IUD in our study as majority of the cases were unbooked and referred from PHC or CHC, most of the patients presented late in labour with IUD.

CONCLUSION

Preeclampsia is a multifactorial disorder and a significant cause for maternal and perinatal morbidity and mortality in developing countries. Identification of risk factors in antenatal period has the potential to improve maternal and perinatal outcome.

Greater awareness of the correlated risk factors leads to earlier diagnosis and refined management, thereby reducing proportion of the morbidity and mortality from preeclampsia and eclampsia. In our study at the individual level, a number of sociodemographic and medical variants are significant risk factors for preeclampsia and eclampsia.

Unbooked status, primiparity, low socioeconomic status (class III and IV), overweight, anaemia, hypothyroidism, gestational diabetes mellitus and chronic hypertension posing the highest risks for the maternal and perinatal outcome. All the findings of this study show the importance of identification of risk factors from comprehensive medical history of the women in early pregnancy. Based on identification of multiple risk factors risk factors, the screening should begin early to detect and treat the condition before it imperils the survival of the mother and fetus.

In our study, as the number of risk factors increased maternal and perinatal outcome were severely affected. Early identification of risk factors like primiparity, overweight, low socioeconomic status, anaemia, hypothyroidism, chronic hypertension diabetes and gestational diabetes mellitus is essential. Identification of these multiple risk factors and their treatment in antenatal period will deliver considerable improvement in maternal and perinatal health in developing countries.

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REFERENCES

- Abalos E, Cuesta C, Carroli G, Qureshi Z, Widmer M, Vogel JP et al. Preeclampsia, eclampsia and adverse maternal and perinatal outcomes: A secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. *BJOG*. 2014; 121(Suppl 1):14-24.
- A.L. Tranquilli, G. Dekker, L. Magee et al., "classification, diagnosis and management of the hypertensive disorders of pregnancy: are revised statement from the ISSHP," *Pregnancy Hypertension: An International Journal of Women's Cardio-vascular Health*, vol.4, no.2, pp.97-104, 2014.
- American College of Obstetricians and Gynecologists. Task Force on Hypertension in Pregnancy. Hypertension in Pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol* 2013; 122(5): 1122-31.
- Magnus P, Trogstad L. Pre-eclampsia research in the Norwegian mother and child cohort study. *Norsk Epidemiologi*. 2014; 24, 97-102. [CrossRef]
- Shiozaki, A.; Saito, S. Risk Factors for Preeclampsia. In *Preeclampsia: Basic, Genomic, and Clinical*. Saito; Springer: Singapore, 2018; pp. 3-25.
- Kenni L, Baker P, Cunningham FG: Platelets coagulation and the liver. In Lindheimer MD, Roberts JM, Cunningham FG (eds): *Chesley's Hypertensive disorders of pregnancy*, 3rd Ed. New York, Elsevier, in Press 2009. & associates.
- Singhal S, Deepika, Anshu, Nanda S. Maternal and perinatal outcome in severe pre-eclampsia and eclampsia. *South Asian Fed Obstet Gynecol*. 2009; 1(3):25-8
- Singhal S, Deepika, Anshu, Nanda S. 2009. Maternal and Perinatal outcome in severe pre-eclampsia and eclampsia. *South Asian Federation of Obstetrics and Gynecology*, 1(3):25-8.
- Shaikh S, Ruby AJ, Piotrowski M. 2003. Preeclampsia related chorioretinopathy with Purtscher slike findings and macular ischaemia. *Retina*. 23:247-50.
- Katz VL, Farmer R, Kuller JA. 2000. Pre-eclampsia into eclampsia: toward a new paradigm. *Am J Obstet Gynecol*. 182:1389-96
- Elizabeth J C. *Buku Saku Patofisiologi*. Jakarta: Buku Kedokteran EGC. 2000.
- GUPTA P and GHAI O.P.: *Textbook of preventive and social medicine*, 2nded. New Delhi, CBS Publishers and Distributors, 626, 2007.
- Ali AA, Rayis DA, Abdallah TM, Elbashir MI, Adam I. Severe anaemia is associated with a higher risk for preeclampsia and poor perinatal outcomes in Kassala hospital, eastern Sudan. *BMC Res Notes*. 2011 Dec; 4(1):311.
- Basbug M, Aygen E, Tayyar M, Tutus A, Kaya E, Oktom O. Correlation between maternal thyroid function tests and endothelin in preeclampsia-eclampsia. *Obstet Gynecol* 1999; 94:551-5.

15. Sardana D, Nanda S, Kharb S. Thyroid hormones in pregnancy and preeclampsia. *J Turk Ger Gynecol Assoc* 2009;10:168-71
16. Lee SH, Lee SM, Lim NG, Kim HJ, Bae S-H, et al. Differences in pregnancy outcomes, prenatal care utilization, and maternal complications between teenagers and adult women in Korea: a nationwide epidemiological study. *Medicine*. 2016;95:e4630.
17. Leppälähti S, Gissler M, Mentula M, Heikinheimo O. Is teenage pregnancy an obstetric risk in a welfare society? A population-based study in Finland, from 2006 to 2011. *BMJ Open*. 2013;3:e003225.
18. Bo S, Menato G, Bardelli C, Lezo A, Signorile A, et al. Low socioeconomic status as a risk factor for gestational diabetes. *Diabetes Metab*. 2002;28:139.
19. Peacock JL, Bland JM, Anderson HR. Preterm delivery: effects of socioeconomic factors, psychological stress, smoking, alcohol, and caffeine. *BMJ*. 1995;311:531-5.
20. Stephansson O, Dickman PW, Johansson AL, Cnattingius S. The influence of socioeconomic status on stillbirth risk in Sweden. *Int J Epidemiol*. 2001;30:1296-301.
21. Vatten LJ, Skjærven R. Is pre-eclampsia more than one disease? *BJOG An Int J Obstet Gynaecol*. 2004;111(4):298-302.
22. Pijnenborg R, Vercruyse L, Hanssens M. The Uterine Spiral Arteries In Human Pregnancy: Facts and Controversies. *Placenta*. 2006;27(9-10):939-58. doi:10.1016/j.placenta.2005.12.006. pmid:16490251
23. Bodnar L. M., Ness R. B., Markovic N., Roberts J. M. (2005). The risk of preeclampsia rises with increasing prepregnancy body mass index. *Ann. Epidemiol*. 15:475-482. 10.1016/j.annepidem.2004.12.008
24. Spradley F. T., Palei A. C., Granger J. P (2015). Increased risk for the development of preeclampsia in obese pregnancies: weighing in on the mechanism. *Am. J. Physiol. Regul. Integr. Comp. Physiol*. 309 R1326-R1343. 10.1152/ajpregu.00178.2015
25. B N. The study of maternal and perinatal outcome in preeclampsia in tertiary care hospital. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2018 Dec 26;8(1):285-9.
26. GUERRIER G., OLUYIDE B., KERAMROU M. and GRAIS R.: Factors associated with severe preeclampsia and eclampsia in Jahun, Nigeria: *International Journal of Women's Health*, 5: 509-13, 2013.
27. Essam A. El-Moselhy, Hamed O. Khalifa, Soliman M. Amer, Khadra I. Mohammad And Hami M. Abd El-Aal: Risk Factors and Impacts of Preeclampsia: An Epidemiological Study among Pregnant Mothers in Cairo, Egypt. *Journal of American Science*, 7 (5): 311-23. (ISSN: 1545-1003), 2011.
28. Kaye E, Sahin Y, Ozkececi Z, Pasaoglu H. Relation between birth weight and thyroid function in preeclampsia-eclampsia. *Gynecol Obstet invest*. 1994;37:30-3