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A meta-analysis on pre-eclampsia and ocular fundus changes associated during pregnancy

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ABSTRACT

Introduction: Pre-eclampsia is a severe life threatening complications of pregnancy and it is characterized by hypertension and significant amount of protein in urine usually occurring during the second half of pregnancy which is mostly after 20 weeks of pregnancy.
Materials and Methods: A systemic meta analysis was planned to analyze and study the recorded pre-eclampsia cases and their fundus changes associated during pregnancy. This systemic self-study have reviewed the facts which were published earlier to determine the current scenario by vast study of statistics and derivation of facts. Vast meta-analysis were conducted with proper examination of data were made to evaluate with final conclusion.
Observation and Discussion: Based on our meta-analysis & systematic evaluation on pre-eclampsia and ocular fundus manifestation during pregnancy we observed, studied and derived into several facts and results. We also inferred that ocular examination in patients with pregnancy induced hypertension should be considered as an important tool of clinical evaluation to asses, predict and diagnose the safety of fetal outcomes and the complication and future risk of mother's life.
Conclusion: We conclude that well-being of both mother and fetus is very crucial during pregnancy. This well-being mostly depends upon the placental circulation. Ophthalmic examination of mother's fundus could be very important tool to assess the health and well-being of both mother and fetus which might indicate to similar microcirculatory changes in placenta and indirectly to fetal well-being.

1. Introduction

Pre-eclampsia is a severe life threatening complication of pregnancy and it is characterized by hypertension and significant amount of protein in urine usually occurring during the second half of pregnancy which is mostly after 20 weeks of pregnancy. It has been reported that preeclampsia is one of the leading and predominating factors to cause perinatal and maternal mortality and morbidity across the globe.[1] According to one official report stated by World Health Organization that pre eclampsia usually affects 2 to 8% approximately all pregnancy worldwide.[2] World Health Organization further reports that approximately one-tenth of all maternal deaths in Africa, Asia and $\frac{1}{4}$ of Latin America occurs due to Hypertension Induced Pregnancy(HIP), a category which encompasses pre eclampsia.[3]

Robbins and Cotran have stated in pathological basis of disease that preeclampsia is a very common and frequent in

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women who are pregnant for the very first time.[4] Woman who also have chronic pre-existing conditions such as obesity, hypertension, diabetes and even lupus and advanced maternal age has higher chances to affect with preeclampsia. It also has been observed that women who inhabit of higher altitude are more likely to suffer from preeclampsia. It has been reported in Lancet that preeclampsia has resulted in 46,000 deaths in the year 2015.[5]

2. Materials and Methods

A systematic meta analysis was planned to analyze and study the recorded pre-eclampsia cases and their associated fundus changes during pregnancy. With the application of electronic databases we searched PubMed, Google Scholar, Web of Science, Medline Plus, Health line & Cleveland Clinic and NIH web which were published in English Language. This systemic self study have reviewed the facts which were published earlier to determine the current scenario by vast study of statistics and derivation of facts.

3. Observation and Discussion

Based on our meta-analysis & systematic evaluation on Pre-eclampsia and Ocular fundus manifestation during pregnancy we observed, studied and derived into several facts and results. According to National Institute of health, preeclampsia or pregnancy related high blood pressure disorder which could arise due to mother's high blood pressure in turn reduces the ongoing blood supply to fetus. This brings low oxygen and fewer nutrients to fetus during pregnancy causing further complications. National Institute of health also has stated that the exact cause and mechanism of preeclampsia and eclampsia are still unknown to this day.[6] Earlier preeclampsia was believed to be caused by a toxin that's the reason why it is also termed as toxemia. The scientist investigated and discarded this theory as they witnessed several factors contributes to development and progression of pre eclampsia which includes several genetic factors, nutritional factors, cardiovascular and inflammatory changes and hormonal imbalance.

3.1. What are the various major complications of preeclampsia?

3.1.1. Eclampsia

Based on our critical analysis on several studies, we inferred that there are several complications of preeclampsia associated with hypertensive disorders during pregnancy the most serious complication which can affect both mother and fetus of preeclampsia is eclampsia. Eclampsia in simpler terms could be defined as the seizures which occurs during pregnancy. This seizures which arise due to pre eclampsia do not correlate with an existing brain condition. It is also reported by American College of obstetrics and gynecologists that patient who have gestational hypertension have higher risk of acquiring eclampsia.[7] Another article by Gardner and David G where they reported that pre eclampsia most likely to occur during 1^{st} pregnancies.[8] We also observed in several studies that women who are hypertensive before becoming pregnant also could have the possibility of acquiring eclampsia. It also has been estimated that eclampsia affects 0.56 per 1000% women in developed countries and approximately 30 times as many women in low income countries according to data reported by Arul Kumaran N in Best Practice and Research Clinical Obstetrics and Gynecology.[8] It is also documented that eclampsia occurs about one in every 200 women suffering from pre-eclampsia. According to William who stated that black patients have exhibited disproportionately higher risk of dying from eclampsia.[9] Early detection and proper management of preeclampsia is very critical as it reduces the risk of developing complications like eclampsia. The aim and objective to treat this complication should be focused on to monitoring precisely and closely for any onset of multiorgan failure, to deliver the baby as soon as possible, manage the elevated blood pressure and to prevent and stop any further complications by application of magnesium sulfate. Pritchard JA have first published the highly effectiveness of magnesium sulfate for management of eclampsia in Journal of Surgical Gynecological Obstetrics in 1955.[10]

3.2. HELLP syndrome

Another very serious complications of this syndrome which causes damage to liver and blood cells. The abbreviation HEELP stands for H stands for Hemolysis, EL stands for elevated Liver Enzyme and LP means Low Platelet Count. HEELP syndromes could be potentially life threatening complications of pre-eclampsia which most often occur at 20^{th} week of pregnancy.[11] This syndrome also could occur after birth of child. Based on our observational analysis, we inferred that HELLP syndrome could occur in approximately 0.7% of pregnancies.[12] It also has been indicated that HELLP syndrome usually affects the population of 10 to 20% pre-eclampsia patients.[13] According to Barton Jr, where he documented that in 70% of pregnancies before childbirth this condition arises in usually third trimester. In more than 30% cases postpartum occurrences also has been witnessed.[14] HELLP syndrome is also associated with increase in scale of maternal and fetal morbidity and mortality. Age had been reported to predominating factor to increase the risk of this syndrome. Another interesting study we came across by Conde Agudelo A in Ann J obstetrics gynecology in 2022 January where they stated that patients with SARS-COV-2 infection during pregnancy have relatively higher risk of suffering from pre eclampsia and HELLP syndrome.[15] The etiology of this syndrome is still unknown but is considered to be a systemic inflammatory disorder.[16] According to

one article by Wallace K where he reports that medical management of preeclampsia is mainly supportive based which includes Vasopressor support, Ventilator support, Pain control management and proper evaluation and monitoring of vitals and nutritional support.[17]

3.3. What are the common risk of pregnancy in patients or preeclampsia?

We analyzed several studies and found that common risk of pre-eclampsia during pregnancy is mild, but however this mild form of preeclampsia could progress to severe pre-eclampsia or sometimes even full preeclampsia within a very short duration. It also has been indicated that women suffering from pre-eclampsia during pregnancy have higher risk for damage to liver, brain, kidneys, circulatory system and even has the potential to cause multi organ faliure in very progressive stages. Furthermore this complication could lead to preterm birth, still birth or even placental abruption.[18] According to one major report documented by World Health Organization where they stated that preeclampsia and eclampsia causes approximately 14% of total maternal death each year. It also has been estimated that about 50,000 to 70,000 deaths of pregnant women worldwide reported by Leeman L in American family physician journal.[19]

3.4. What are the risks associated with preeclampsia after Pregnancy?

Various studies upon our critical analysis has shown that women who had pre eclampsia has the potential to develop hypertension which is also followed by stroke and ischemic heart diseases.[20] However once the child is delivered, women with preeclampsia are at higher risk for developing seizures which is eclampsia a severe complication of preeclampsia.[21] Sometimes when after the delivery preeclampsia develops between 48 hours and six weeks duration and this type is referred as postpartum preeclampsia.[22] According to one study by Skurnik G where he reported that more than one $\frac{1}{2}$ of women who were suffering from postpartum preeclampsia after they delivery did not even have preeclampsia during pregnancy.[23] If any woman is having seizures just after 72 hours of delivery, that condition is referred as postpartum eclampsia. Postpartum preeclampsia and eclampsia must be treated at earliest otherwise this could lead to stroke and sometimes even death.[24]

3.5. Analysis on prevalence of preeclampsia and eclampsia across the world

Pre-eclampsia is such a serious pregnancy related disorder which affects 2 to 8% of all pregnancies, a leading cause of maternal and perinatal morbidity and mortality across the globe. It also has been estimated that hypertensive disorders of pregnancy is one of the most common causes of death in pregnancy worldwide which have resulted in 46,900 death reported in 2015. According to one study conducted by Tessema in BMC pregnancy and childbirth, where stated that pregnancy complication causes and affects around 2,89,000 deaths of women worldwide and majority of them were reported from developing countries.[25] As estimated by World Health organization that prevalence of preeclampsia is higher in developing countries seven times more as compared to developed countries with the range between 1.8 and 16.7% in developing nations across the globe.[26] Another report documented by World Health Organization which have stated that nearly one tenth of all maternal death due to pre eclampsia across the globe have been indicated in Africa and Asia and $\frac{1}{4}$ in Latin America.[3]

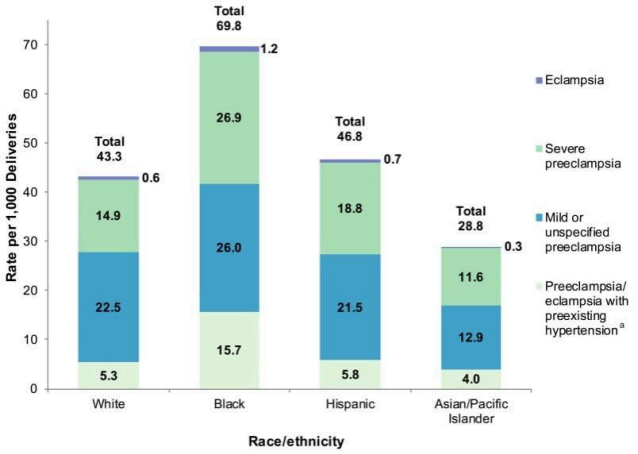

Fig. 1: Rate of preeclampsia/eclampsia per 1,000 deliveries, by race/ethnicity and type of diagnosis in 2014 Sources: https://www.ncbi.nlm.nih.gov/books/NBK442039/figure/sb222.f3/

We observed in another study by Reeta L in BMC pregnancy and childbirth where they documented that women of advanced maternal age has exhibited more pre eclampsia as compared to younger women during pregnancy. Any woman who is in 35 years or older at the time of delivery is referred as Advanced Maternal Age (AMA).[27] Several studies have also indicated that women of advanced maternal age always have the highest probability to acquire gestational diabetes, placental Previa, Pregnancy Induced Hypertension and the need for cesarean deliveries.[28] One study by Sonia H in British Medical Journal have also showcased that risk of preeclampsia in first time pregnancy was reported to four point one where is 1.7 in later pregnancies. However they also stated that risk in second pregnancy was reported to be 14.7% for those women who had pre eclampsia in first pregnancy and approximately 31.9% who had pre eclampsia in previous two pregnancies.[29] We followed and observed in another study by Krishna B Sole in pregnancy hypertension who

have documented that prevalence of preeclampsia has been decreased to 37% over last two de in Norway.

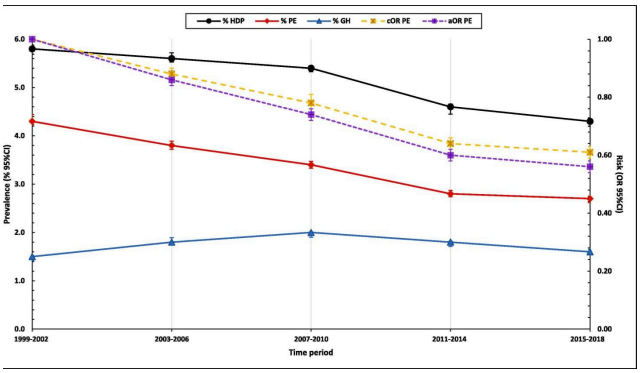

Fig. 2:

3.6. What are the various ocular fundus changes in preeclampsia during pregnancy?

During pregnancy patients of pre eclampsia and eclampsia has been diagnosed with several changes in fundus. This commonly includes focal narrowing of retinal arterials, serious retinal detachment, isolated cases of acute ischemic optic neuropathy, hemorrhages, exudates, focal retinal edema, cortical blindness, retinal detachment, temporary decrease in vision secondary to severe anterolateral spasm, retinal edema and even sometimes it could lead to permanent blindness.[30]

After brief systematic analysis on various studies, we selected few studies which showcase the prevalence of ocular fundus changes in preeclampsia and eclampsia cases. According to one study by Tadin I who have reported that 45% of retinal involvement in their 40 patients study with pregnancy induced hypertension. He further found a correlation between proteinuria, hypertensive retinopathy and blood pressure.[31] They have also inferred that hypertensive retinopathy could be relevant prognostic factor in estimation of severity level of preeclampsia which further implies that proper examination of modifications of fundus is very crucial in pregnant women with preeclampsia. Another study by Reddy SC, where he studied on 275 cases of pre eclampsia and 175 cases of eclampsia observed and reported retinal modifications in 53.4% pre-eclampsia 71.2% in eclampsia patients. The most significant changes and modification reported was narrowing of arteries.[32] In another hospital based prospective observational study conducted by Akshay Jawaharlal bhandari, where they reported that out of 100 cases who were enrolled in the study, ocular fundus changes of 50%, eclampsia of over 60% followed by mild pre eclampsia of 25%. They have further documented that highest percentage of ocular fundus changes were indicated in each group of 18 to 22 years.

4. Conclusion

We came to an end of our meta analysis by accomplishing our objective which was conducting a vast analysis on preeclampsia and ocular fundus changes associated during pregnancy. We conclude that well-being of both mother and fetus is very crucial during pregnancy. This well-being mostly depends upon the placental circulation. Ophthalmic examination of mother's fundus could be very important tool to assess the health and well-being of both mother and fetus which might indicate to similar microcirculatory changes in placenta and indirectly to fetal well-being. So thereby inferring that ocular examination in patients with pregnancy induced hypertension should be considered as an important tool of clinical evaluation to assess, predict and diagnose the safety of fetal outcomes and the complications and future risk of mother's life.

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6. Conflict of Interest

None.

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