



STUDY ON INCIDENCE, RISK FACTORS AND MANAGEMENT OF GESTATIONAL HYPERTENSION AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Hypertension is the one of the common medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. The objective of the study is to study the prescribing pattern of antihypertensives in relation with FDA categories and essential drug list used in Pregnancy Induced Hypertension (PIH) and to study the risk and benefits of various management strategies in the selected study population as per the inclusion criteria. A prospective observational study was conducted. The only resolution for preeclampsia and pregnancy induced hypertension is the delivery of the fetus and placenta. Often medications are used to manage maternal blood pressure and prolong gestation. Although many treatment options exist for hypertension, additional consideration must be utilized when selecting a pharmacotherapeutic agent in pregnancy. The chosen medication must not only be effective and safe for the mother, but also have minimal impact on the development of the fetus. A total of 71 patients were included in the study, their prescriptions were analysed to determine the prescribing pattern and appropriateness. The patients in our study population was categorized as mild 17(23.94%), moderate 44(61.97%) and severe 10(14%). One of the risk factor inducing PIH is the gravidity status and majority of patients were primigravida 39(54.92%) than multigravida 32(45%). Out of 71 patients centrally acting drugs were prescribed more 28(39.43%), followed by beta blockers 19(26.76%), calcium channel blockers in 6(8.45%). The results reveal that, for mild to moderate hypertension, the antihypertensive methyldopa is often recommended. Alternative choices include labetalol and calcium channel blockers. Maternal awareness regarding its complications, management, dietary modifications, life style changes should be facilitated.

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INTRODUCTION

Hypertension is the one of the common medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. Hypertension in pregnancy is defined as systolic blood pressure (sBP) 140mmHg and diastolic blood pressure (dBP) 90mmHg, or by increase in sBP 30mmHg, or in dBP 15mmHg from preconception or first trimester blood pressure confirm by two measuring 6 hours apart.

National High Blood Pressure Education Program Working Group classifies hypertensive disorder in pregnancy into 4 categories:⁽¹⁾

1. Chronic hypertension
2. Preeclampsia- eclampsia
3. Preeclampsia superimposed on chronic hypertension
4. Gestational hypertension

- Chronic hypertension is the known hypertension before pregnancy or hypertension diagnosed first time before 20 weeks of pregnancy.
- Preeclampsia is a multi system disorder of unknown etiology characterised by development of hypertension to the extent of 140/90mmHg or more with proteinuria after 20th week in a previously normotensive and non-proteinuric women.⁽²⁾
- Preeclampsia frequently occurs in primigravidae (70%). It is more often associated with obstetrical-medical complications such as multiple pregnancy, polyhydramnios, pre-existing hypertension, diabetes.
- Eclampsia may occur quite abruptly, without any warning manifestations.

Eclamptic convulsions or fit: The fit are epileptiform and consists of four stages, includes:

Premonitory stage: The patient becomes unconscious. There is

twitching of the muscles of the face, tongue and limbs. Eye balls roll or are turned to one side and become fixed. This stage lasts for about 30seconds.

Tonic stage: The whole body goes into a tonic spasm, the trunk-opisthotonus, limbs are flexed and hands clenched. Respiration ceases and the tongue protrudes between the teeth. Cyanosis appears. Eye balls become fixed. This stage lasts for about 30seconds.

Clonic stage: All the voluntary muscles undergo alternate contraction and relaxation. The twitching start in the face then involves one side of the extremities and ultimately the whole body is involved in the convulsion. Biting of the tongue occurs. Breathing is stertorous and blood stained frothy secretions fill the mouth; cyanosis gradually disappears. This stage lasts for 1-4minutes.

Stage of coma: Following the fit, the patient passes on to the stage of coma. It may last for a brief period or in others deep coma persists till another convulsion. Occasion, the patient appears to be in a confused state following the fits and fails to remember the happenings.

- Preeclampsia superimposed on chronic hypertension: The development of preeclampsia in a patient with chronic hypertensive vascular or renal disease.
- Gestational hypertension: Sustained rise of blood pressure to 140/90mmHg or more on at least two occasions 4 or more hours apart beyond the 20th week of pregnancy or during the first 24hours after delivery in previously normotensive women is called gestational hypertension.

Hypertension is a sign of an underlying pathology which may be pre-existing or appears for the first time during pregnancy. The identification of this clinical entity and effective management play a significant role in the outcome of pregnancy, both for the mother and the baby. In the developing countries with an inadequately cared pregnancy, this entity on many occasion remains undetected till major complications supervene. Hypertension complicates approximately one out of every ten pregnancy. The only resolution for preeclampsia and pregnancy induced hypertension also known as gestational hypertension is the delivery of the fetus and placenta. When hypertensive disorders complicate a pregnancy before full term, the risks of preterm delivery must be considered in addition to the risks of the mother. Often medications are used to manage maternal blood pressure and prolong gestation. Although many treatment options exist for hypertension, additional consideration must be utilized when selecting a pharmacotherapeutic agent in pregnancy. The chosen medication must not only be effective and safe for the mother, but also have minimal impact on the development of the fetus.^(3,4,5)

The complications of uncontrolled high blood pressure during pregnancy affect multiple organ systems and can be detrimental to both mother and fetus. Maternal complications of preeclampsia include seizure activity, placental abruption, stroke, HELLP syndrome (hemolysis, elevated liver enzymes and low platelets), liver hemorrhage, pulmonary edema, acute renal failure, disseminated intravascular coagulation (DIC). There could be significant morbidity and mortality for the fetus as well. Fetal and neonatal complications include intrauterine growth restriction, preterm birth, low birth weight, neonatal respiratory distress syndrome, increased admission to

neonatal intensive care unit and fetal or neonatal death. While the exact causes of preeclampsia are not well understood, certain factors may increase a womens risk of developing pregnancy induced hypertension or preeclampsia.⁽⁶⁾ It is widely known that preeclampsia occurs most often during a womens first pregnancy. Additionally, womens with a history of preeclampsia are more likely to have recurrence in a subsequent pregnancy. Multiple gestations, such as twins or triplets, increase risk. Moreover, certain pre-existing chronic conditions increase a women risk, including diabetes mellitus, gestational diabetes, insulin resistance, chronic hypertension, obesity, chronic kidney disease, lupus, and vascular or connective tissue disorders. Women over the age of 35 years and women of African American race are considered more at risk for developing preeclampsia. Prompt recognition of pregnancy induced hypertension and preeclampsia is vital in preventing progression of the condition.⁽⁷⁾

Management of preeclampsia

Ideally all patients of preeclampsia are to be admitted in the hospital for effective supervision and treatment. There is no place of domiciliary treatment in an established case of preeclampsia. However, in some centres cases of preeclampsia is more and hospital facilities are meagre, there is no alternative but to put the uncomplicated mild preeclampsia in domiciliary treatment regime.⁽⁸⁾ Rest, high protein diets are prescribed and the patient is investigated and checked. If the treatment fails to improve the patient is to be admitted. It is essential that patient should be warned against the ominous symptoms such as headache, visual disturbances, vomiting, epigastric pain or scanty urine.^(9,10)

Treatment thresholds recommend initiation of pharmacologic therapy at elevated blood pressure values. Various antihypertensive medications exist; however the severity of blood pressure elevation dictates the choice of agents. A number of drugs in various combinations are generally used for effective long-term management of hypertension. Therefore, drug utilization studies, which evaluate, analyze the medical, social and economic outcomes of the drug therapy, are more meaningful and observe the prescribing attitude of physicians with the aim to provide drugs rationally.^(10,11,12)

Women with chronic illnesses already stabilized on treatment will at times require to take the drugs during pregnancy for a better maternal and fetal outcome⁽²²⁾. Appropriate dosing medications also play an important role during pregnancy which can be difficult, as physiological changes occur throughout pregnancy, that can cause deviation from the expected pharmacokinetic process in pregnant patients and necessitate dose adjustments.

A fine balance needs to be maintained to avoid overdosing as well as inadequate treatment. Most drugs admitted to the pregnant mother cross the placenta and may affect the physical and mental development of the fetus or may be delayed effect on the neonate.

Because of the potential risk of teratogenicity, FDA has categorized drugs into different categories like Category A,B,C,D and X. The prescribed drugs should be reviewed for their category and safety.⁽¹⁾

METHODOLOGY

A Prospective observational study is planned to be conducted in the Department of Obstetrics and Gynecology of a 750

bedded multi-specialty tertiary care hospital, after taking permission from the Hospital Ethics Committee. All the Pregnant women attending the antenatal clinic and registered with the department of OBG having single or multiple live intrauterine gestations, diagnosed as a case of hypertensive disorder by the treating physician and willing to give consent for the study were included. Patients with acute medical emergency condition requiring hospitalization and attending outpatient department for Medical termination of Pregnancy were excluded. Subjects who are not willing to give/ understand the informed consent were also excluded from the study. In pregnant women, gestational hypertension is defined as: SBP 140 mm Hg or DBP 90 mm Hg that occurs after 20 weeks of gestation in a woman with previously normal blood pressure. If blood pressure elevations described above occur before 20 weeks of gestation, this is a patient with chronic hypertension. If a woman with chronic HTN develops preeclampsia during pregnancy, the nomenclature to describe this is: chronic hypertension with superimposed preeclampsia. The Case record sheets of the patients diagnosed for pregnancy induced hypertension or gestational hypertension admitted to the obstetrics ward are to be reviewed. The information regarding patient demographics, Past medical and medication history, lab investigations done, diagnosis, any allergy, adverse drug reactions, total number of drugs prescribed, with dosage, frequency, duration are to be recorded in a pre-designed patient profile record form.

Information about patient demographics, education status, family and past medical history of hypertension, stage of hypertension, comorbid condition, gravidity status were gathered and screened for its influence in gestational hypertension.

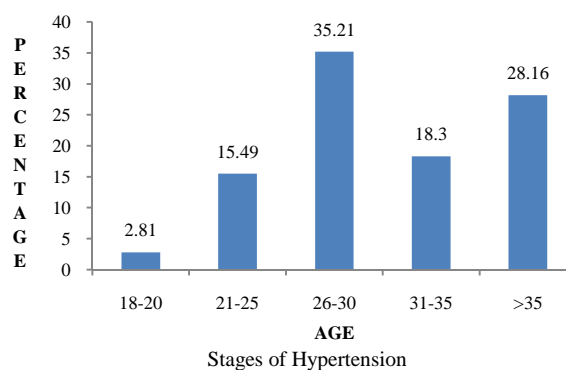
RESULTS AND DISCUSSION

We have conducted this study in order to identify the possible risk factors for hypertensive disorders in pregnancy. We found that, the risk factors for hypertensive diseases in pregnancy included early teenage status, illiteracy, housewife status, nulliparity and family and the personal histories of hypertension. The extreme ages of reproductive years are well known risk factors for hypertension during pregnancy with high incidence rates in teenagers^(23,24).

Many authors have identified young age as a risk factor for hypertension during pregnancy, as is the case in the present study^(25, 26). *deyinka et al.* found the prevalence of eclampsia and preeclampsia among adolescents to be 20% in comparison to only 3.33% among the controls⁽²⁵⁾. In another study, a 2.9% vs. 0.6% preeclampsia prevalence was reported in teenagers compared to women aged 25-34 years⁽²⁶⁾. In the present study, the number of patients with age group between 18-25 years with hypertension was 18%. We found that age group between 26-30 were associated with an increased risk (35%) for hypertensive disorders in pregnancy. Similar findings were reported by *Saftlas et al.*⁽²⁴⁾ who revealed that black teenagers aged 15-17 years had 2.6-fold risk for preeclampsia compared to women aged 24-34 years.

Studies have reported that a higher age is also an important risk factor for hypertension in pregnancy, especially in developed countries^(27, 28). *Assis et al.*⁽²⁸⁾ found that age above 30 years was associated with a risk for preeclampsia superimposed on chronic hypertension⁽²⁸⁾. A similar result was reported by *Suzuki et al.*⁽²⁷⁾ who found that, in singleton

pregnancies, the developing preeclampsia was associated with maternal age 35 years or above. Both studies reported the association of infertility treatment with an increased risk for hypertensive disorders in pregnancy as this was also recently reported by *Poon et al.*⁽¹⁹⁾, In the present study, the percentage of women aged above 35 years old (28%) was similar in the two study populations revealing that, this age group was not associated with an increased risk of hypertensive disorders in pregnancy. Some studies are necessary to understand better why there is lack of effect of the age progress on the occurrence of hypertensive disorders in pregnancy.



BMI was found to be a factor of preeclampsia; however, *BMI* was found to be higher in hypertensive women (43.6%) in our study, and it is a definite risk factor for developing pregnancy-induced hypertensive disorders, including preeclampsia. Risk increases with increased *BMI*.

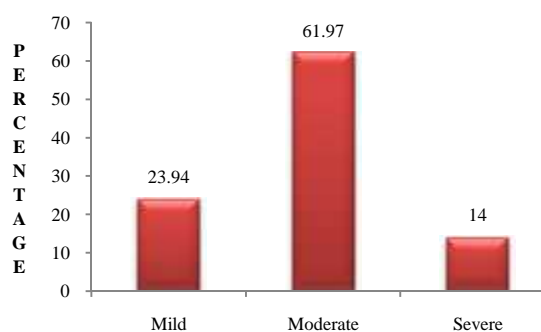
Education status has a significant role in influencing preeclampsia. In our study 18% were uneducated and 25% were below matriculation. So patient education is necessary.

A history of hypertension in pregnancy is associated with an increased risk. In our study patients with past medical history of hypertension were 15% & Patients without past medical history of hypertension were 78.87%.

Family history of hypertension increased the risk of developing *PIH*. In our study 9.85% had a family history of hypertension.

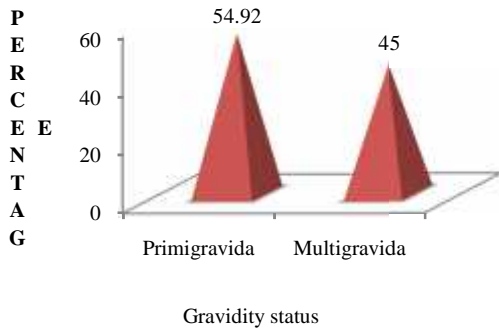
In the study diabetes, hypothyroidism and chronic hypertension were significantly more frequent in patients. That is 53.52% was found with comorbid condition.

In the study the patients were categorized as mild, moderate and severe hypertensives. Majority of the patients come under the category of moderate stage (61.97%) of hypertension.



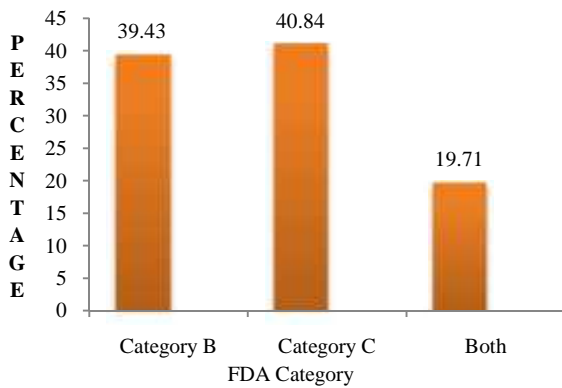
Young primigravidae under 20 years and all patients over 30 years have an increased chance of hypertension. Preeclampsia is primarily regarded as a disease of first pregnancy. In our

study, 54.9% were primigravidas and 45% were multigravidas. In our study both primigravidae and multigravida are equally affected with hypertensive disorders.

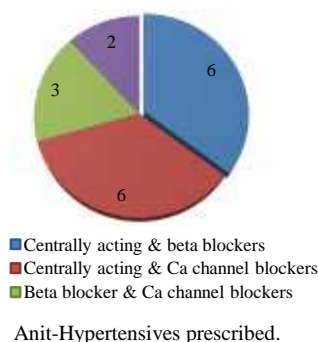
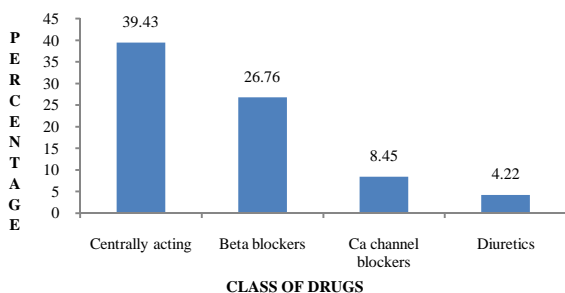


Maternal and neonatal complications are also found in preeclampsia. In our study we observed that caesarean section rate for preeclampsia cases were 47.88%. The proportion of prematurity or preterm birth was about 8.45%, neonatal death occurred about 4.22% and less number of deliveries were found to be normal from a total of 71 patients.

Rational drug use in pregnancy is vital. The majority of drugs used in our study were from Category C followed by Category B.



In the study most commonly prescribed antihypertensives are methyldopa, labetalol, nifedipine. Methyldopa is the safest antihypertensive in pregnancy.



Monotherapy is preferred more than combination therapy in our study. The use of combination therapy will provide greater efficacy, fewer side effects and greater convenience than that can be achieved with monotherapy.

DISCUSSION

The absence of previous deliveries is widely reported as a risk factor for hypertensive disorders in pregnancy^(19, 29, 30). Assis *et al.*⁽²⁸⁾ identified primiparity as a risk factor for gestational hypertension. In the present study, we found that nulliparity was associated with a increased risk for hypertensive disorders in pregnancy. Our findings are in conformity with the aforementioned literature reports^(31, 32).

We found that the absence of school education, identified as an independent risk factor for hypertensive disorder in pregnancies, is well-documented in the literature^(33, 34). Among the risk factors for preeclampsia Mittendorf *et al.*⁽³⁵⁾ identified less than a high school education. The illiteracy rate in our population could influence the occurrence of hypertension in pregnancy by the simple reason that the low school level is associated indirectly to the precocious marriage and to limited access to health care, including family planning. Even though some authors have not found any difference in pregnancy outcomes between housewives and employed women⁽³⁶⁾, most publications state that workers have adverse outcomes (30 - 32). In the present study, housewives had an increased risk for hypertensive disorder in pregnancy. However, housewives, respectively, represent 93.4% and 87% in hypertensive and non-hypertensive study populations and could randomly influence the pregnancy risks.

A higher risk of hypertensive disorder in pregnancy was reported among women with previous hypertension in pregnancy. Personal history of chronic hypertension is one of the reported risk factors for hypertensive diseases in pregnancy^(19,40). Family history of hypertension was identified as a risk factor for hypertension in 21% of the study patients. However, little is known separately about histories of paternal, sibling or maternal hypertension, although we were able to illustrate that the last one is not a risk factor for hypertensive disease in pregnancy. Some studies have reported body mass index as risk factors for hypertension in pregnancy. In the present study, 44% of the patients were over-weight and 28% were obese.

Age has an important influence on the incidence of hypertensive disorders of pregnancy. The patients were classified as it is given in the study conducted by T Naveen Kumar⁽¹⁾. Patients been classified into five groups. Among this, 46.46% were found to be of above age above 30 and 2.81% belong to the age group of 18-20. So the distribution of patients in our study is found to be higher in age above 30. In our study patients of age above 30 had an increased risk of preeclampsia. Increased risk of preeclampsia in younger women who are less than or equal to 21 years and others have reported an association of increased risk of preeclampsia with women who are 35 years or older were found in the study conducted by Owiredun⁽¹⁴⁾.

The aim of antihypertensive therapy in the management of pregnancy induced hypertension is to prevent complications due to hypertension while prolonging the course of pregnancy. Monotherapy and combination therapy are used in our hospital for treating hypertension during pregnancies. The most commonly prescribed antihypertensive agent was adrenergic

receptor alpha-2 agonist. Majority of patients in our study were treated with a single drug (monotherapy) followed by two drugs and three drugs, similar results were found in the study conducted by Sagar B Bhagat⁽⁴⁾. Drugs preferred as monotherapy in our study were Methyldopa, Labetalol and Nifedipine. Methyldopa is the commonest antihypertensive prescribed as monotherapy as well as in combination therapy, similar results were found in the study conducted by Manjusha Sajith⁽⁵⁾. Methyldopa was the preferred drug as monotherapy in our study followed by Labetalol. Contrast results were seen in studies conducted previously, where, Labetalol was preferred in the study conducted by Sagar B Bhagat⁽⁴⁾. This shows that utilization pattern differs from hospitals, prescribers.

Age has an important influence on the incidence of hypertensive disorders of pregnancy. Young primigravidae under 20 years and all patients over 30 years have an increased chance of hypertension. Preeclampsia is primarily regarded as a disease of first pregnancy. In our study, 54.9% were primigravidas and 45% were multigravidas. In our study both primigravidae and multigravida are equally affected with hypertensive disorders, similar results were found in the study conducted by Manjusha Sajith and T Naveen Kumar^(5,1).

Rational drug use in pregnancy requires balancing of benefits and the potential risks associated with the use of drugs. The benefits of rational drug use during pregnancy are not only restricted to the recovery of maternal health, but also helpful in the development of the fetus. The most commonly prescribed antihypertensives are methyldopa, labetalol, nifedipine. Methyldopa is the safest antihypertensive in pregnancy. Calcium channel blockers should not be given as first line drugs because they can inhibit the contractions of uterus. The majority of drugs used in the study were from Category B and C, where similar findings from the study conducted by T Naveen Kumar and Tanuja V Hooli^(1,11).

Maternal and neonatal complications are also found in preeclampsia. In our study we observed that caesarean section rate for preeclampsia cases were 47.88%. The proportion of prematurity or preterm birth was about 8.45%, neonatal death occurred about 4.22% and less number of deliveries were found to be normal from a total of 71 patients. The proportion of prematurity or preterm birth were 35.14%, neonatal death 11.71% and only 10% deliveries were found to be normal from a total of 350 patients in the study conducted by Jangra Sarita and Bhyan Bhupinder⁽¹³⁾.

Several risk factors have been identified and modification of some of these risk factors might result in decreasing of preeclampsia frequency. In our study diabetes, hypothyroidism and chronic hypertension were significantly more frequent in patients. That is 53.52% was found with comorbid condition and 46.47% found to be without comorbid condition. Previous history of preeclampsia, high BMI, diabetes and chronic hypertension are some of the important risk factors in the study conducted by Caroline Abrao Dalmaz and Katia Goncalves dos Santos⁽¹⁵⁾.

BMI was found to be a factor of preeclampsia; however, the BMI was found to be higher in hypertensive women (43.6%) in our study, and it is a definite risk factor for developing pregnancy-induced hypertensive disorders, including preeclampsia. Risk increases with BMI and the possible explanation is the increased shear stress due to hyperdynamic

circulation associated with obesity. The worldwide increase in obesity is likely to raise the frequency of preeclampsia. Our result is similar with the study result of Caroline Abrao Dalmaz and Katia Goncalves dos Santos⁽¹⁵⁾.

Family history of hypertension increased the risk of developing PIH. In study conducted by Owiredu⁽¹⁴⁾ pregnant women with a family history of hypertension were about 10 times at risk of developing preeclampsia compared to those without a family history of hypertension. In our study 9.85% had a family history of hypertension.

Education status has a significant role in influencing preeclampsia. In our study 18% were uneducated and 25% were below matriculation. Educational status did not significantly influence the risk of developing preeclampsia in the study conducted by Owiredu⁽¹⁴⁾ So patient education is necessary.

A history of hypertension in pregnancy is associated with an increased risk. In our study patients with past medical history of hypertension were 15%. Similar results were seen in the study conducted by Vesna D Garovic and Suzanne R Hayman⁽²²⁾.

CONCLUSION

The results demonstrated the impact of clinical pharmacist in achieving a primary therapeutic goal in the PIH patients for overall positive maternal and neonatal outcomes. The ideal therapy of hypertension in pregnancy should be potent, rapidly acting and without any adverse maternal or fetal effect. Methyldopa is the commonly prescribed drug. Various betablockers are also found in medication chart. Labetalol was the commonly seen Beta-Blocker followed by Metoprolol, Carvedilol, & Propranolol. Calcium Channel Blockers (Verapamil, Diltiazem) & Diuretics (Frusemide) were also found to be prescribed in some patients.

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