A PROSPECTIVE STUDY TO ASSESS THE CLINICAL RISK FACTORS AND THE DRUG UTILIZATION PATTERN IN FEMALE PATIENTS WITH GESTATIONAL HYPERTENSION

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ABSTRACT

Hypertension in pregnancy is a pregnancy specific, multisystem disorder characterized by the development of edema, elevated blood pressure and proteinuria after 20 weeks of gestation. Hypertensive disease occurs in 5% to 10% of all pregnancies and is a major cause of maternal and perinatal morbidity and mortality. A prospective observational study was performed to assess the risk factors that potentiate gestational hypertension and also to evaluate the drug utilization pattern in patients diagnosed with gestational hypertension. 72 patients who were admitted with gestational hypertension in the Gynaecology department of Pushpagiri Medical College Hospital were enrolled for this study. A standardized data collection form was prepared and necessary data were collected which includes the demographic details, obstetric history, past medical history, past medication history, current medication etc. The risk factors, complications associated with gestational hypertension and drug utilization pattern were analyzed. Pre-existing hypertension and diabetes mellitus are found to be the most common risk factors of gestational hypertension in this study. Most commonly prescribed anti-hypertensive drug was Labetalol and found to be safe. The antihypertensive drug therapy was found to be significant. From the study it was found out that the overall drug utilization pattern in gestational hypertension patients was in accordance with the specific hypertensive treatment guidelines.
KEYWORDS: Gestational hypertension, Drug utilization, Antihypertensives, Pregnancy, Maternal complications, Fetal outcomes.

INTRODUCTION
Hypertension in pregnancy is a pregnancy specific, multisystem disorder characterized by the development of edema, elevated blood pressure and proteinuria after 20 weeks of gestation.[1] In normotensive women, blood pressure in early pregnancy decreases up to 20 weeks of gestation and gradually increases to normal or higher than pre-pregnancy levels before delivery.[2]

Hypertensive disease occurs in 5% to 10% of all pregnancies and is a major cause of maternal and perinatal morbidity and mortality. From 15% to 24% of maternal deaths in developed countries are attributed to hypertensive disorders in pregnancy.[3] Though the exact cause of hypertensive disorders in pregnancy is not understood, it is believed to be a disorder of the blood vessel lining. Abnormalities of placenta also described as a causative factor. It also arises due to a combination of genetic and environmental factors.[4] The early prediction and detection of hypertensive disorders of pregnancy is important for its monitoring and management to reduce maternal and fetal mortality.[5] Factors considered to place a pregnancy at high risk include previous severe preeclampsia, renal disease, autoimmune disease, diabetes, and chronic hypertension. During pregnancy, maternal risk factors which may lead to PIH including nulliparity, previous history of PIH, more than 5 years since last gestation, multiple pregnancies, maternal blood pressure of 130/90 mmHg or more in the first trimester of pregnancy, urinary tract infection and periodontal disease.[1] The antihypertensives indicated for maternal benefits, it may prolong the pregnancy and improves foetal maturity. But in severe hypertension, since the uteroplacental blood flow reduces, women are delivered soon after their blood pressure is controlled. This results in quick reduction in maternal blood flow that adversely affects the fetal health.[6] For a blood pressure ≤ 140/90 mm Hg, drug therapy is not generally recommended. Severe hypertension should be treated with antihypertensive drugs such as methyl dopa and labetalol as first line choice of drugs. Nifedipine is suggested as second line drug. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) are associated with adverse fetal outcomes and hence contraindicated in pregnancy.[7] Majority of the hypertensive individuals cannot be controlled by single drug therapy and may require two or more antihypertensive agents selected from various drug classes.[4] The effective management of hypertensive
disorders in pregnancy can be achieved by the use of a number of drugs in various combinations. But the usage of such drugs should be in accordance with the guidelines for treatment of hypertension and rationality, effectiveness and tolerance of the drug use should be evaluated. To reduce the blood pressure in order to assure safety of the mother and the foetus, is the greatest challenge in treatment of pregnancy induced hypertension. In pregnancy, drug therapy presents a special concern due to the threat of potential teratogenic effects of the drug and physiologic adjustments in the mother, in response to pregnancy.\textsuperscript{[8]}

This is a prospective observational study performed with an aim to assess the risk factors that potentiate gestational hypertension and also to evaluate the drug utilization pattern in patients diagnosed with gestational hypertension. 72 patients who were admitted with gestational hypertension in the Gynaecology department of Pushpagiri Medical College Hospital were enrolled for this study.

The objectives of the study include:
- To evaluate the clinical risk factors that leads to the development of gestational hypertension.
- To assess the fetal and maternal outcomes associated with gestational hypertension.
- To assess the effective utilization of various drugs on the disease.
- To evaluate the complications.

**REVIEW OF LITERATURE**

Smita L. Gaidhankar et al\textsuperscript{[9]} (2017) conducted a study to assess the clinical outcome and evaluate drug utilization according to WHO core drug prescribing indicators in hypertensive disorders of pregnancy. This prospective, observational study in a tertiary care hospital was conducted in 150 pregnant women with hypertensive disorders of pregnancy from January 2014 and December 2014 who fulfilled the inclusion criteria. Antepartum and intrapartum care and the maternal and perinatal outcome were noted. The data was analyzed to evaluate clinical outcome and drug utilization according to WHO core drug use indicators. Gestational hypertension was most common among hypertensive disorders of pregnancy seen in 62/150 (41.3\%) women. The most common symptom was headache (48\%) while sign noted was edema (69\%). A total of 66\% women had preterm delivery and 42\% babies weighed less than 2.5 kg. Average number of drugs per encounter was 9.7. Percentage of drugs prescribed by generic name and from essential drug list was 64\% and 79\% respectively. The most
commonly used drugs were vitamins and minerals prescribed in 100% patients followed by antihypertensive drugs (92%). The most common antihypertensive used were calcium channel blockers and anticonvulsant was magnesium sulphate. There was increased maternal and perinatal morbidity and operative intervention among pregnant women with hypertensive disorders of pregnancy. Most of the drugs were used appropriately and were in accordance with standard guidelines. The important problems identified were inappropriate use of antimicrobials, use of sublingual nifedipine and use of brand names in 1/4th of prescriptions.

Arihiro Shiozaki et al[1] (2017) conducted a study to assess the risks of developing gestational hypertension (GH) and preeclampsia (PE) during pregnancy. This was a retrospective cohort study based on clinical information using the Perinatal Database of the Japan Society for Obstetrics and Gynecology between 2001 and 2010. GH was diagnosed in women with a blood pressure of 140/90 mmHg or more for the first time during pregnancy (after 20 weeks of gestation) but no proteinuria, and in whom blood pressure normalized by 12 weeks postpartum. PE was diagnosed if hypertension (blood pressure of 140/90 mmHg or more) accompanied by proteinuria exceeding 300 mg/24 h was evident for the first time after 20 weeks of gestation, and was followed by normalization of these symptoms by 12 weeks postpartum. Patients were diagnosed with severe hypertension if blood pressure was 160 mmHg systolic or 110 mmHg diastolic or more on at least two occasions. Patients were diagnosed with severe proteinuria if proteinuria was 2 g/day or more or 3+(300 mg/dl) or more on at least two occasions. Maternal background factors analyzed in the present study included: age, parity, smoking during pregnancy, pre-existing renal disease, pre-existing hypertension, pre-existing diabetes mellitus, pre-pregnancy body mass index (BMI), and fetal gender. These factors have previously been reported as risk factors for GH and PE. They calculated logit scores of GH and PE by multivariate analysis to estimate their individual risk ratios. The estimated risk ratios determined in this study may identify women at high risk of GH or PE before disease onset.

Lokeshwari Jayaraman et al[10] (2016) conducted a study on the pattern of feto-maternal outcome and complications in pregnancy induced hypertension from a tertiary level health care teaching institution of Tamil Nadu. Most deaths in PIH occur due to its complications and not due to hypertension. The objective of the study was to undertake to study the pattern of feto-maternal outcome and complications in cases of PIH with a view to identify them at the earliest. The survey was planned using a predesigned questionnaire among 245 study
participants who were pregnant women seeking care for PIH. Out of the total 245 cases of pregnancy induced hypertension, there were 146 (59.6%) cases of mild PIH, 54 (22%) cases of moderate PIH and 45 (18.4%) cases of severe PIH. Regarding maternal complications in PIH, there were CCU admissions in 89% cases, imminent eclampsia in 31% cases and abruptio placentae, CVA, acute renal failure in 2.2% cases, maternal mortality in 4.4% cases. Regarding fetal complications in PIH, there was birth asphyxia (31.1%), IUGR (24.4%) intrauterine deaths, prematurity. Antenatal care was found to be the most important determinate of early detection of PIH. The empirical evidence of current study indicated that early detection and prompt intervention of complications is vital to ensure healthy outcome to both mother and baby.

Dr. Anujeet Kaur et al[4] (2015) conducted a study on Pregnancy induced hypertension a retrospective study of 200 cases of pregnant women. The study was planned to evaluate the patients of PIH and evaluate maternal and fetal outcomes in these according to severity of PIH. The present study was carried out on 200 pregnant women admitted in the year 2015, suffering from PIH admitted through antenatal clinic as well as in emergency and data analysed for maternal and foetal outcome Age, gravidity, mode of admission, gestation time, mode of treatment, severity etc were evaluated. They concluded that there is no way to prevent pre eclampsia and eclampsia. However outcome can be improved with routine health screenings.

Carmen D’Amore et al[7] (2015) conducted a study on anti-hypertensive drug use during pregnancy: a population based study. The study was aimed at assessing if the European guideline on the use of anti-hypertensive drugs in pregnancy are followed in clinical practice. They also evaluated association between the use of non recommended drugs and individual characteristics. The study population included all singleton pregnancies and women with first prescription of antihypertensive drugs. Methyldopa, Labetalol and Nifedipine were considered as “recommended drugs”; all other antihypertensive drugs were considered as “non-recommended”. Among the 1009 patients exposed to antihypertensive drugs during pregnancy, 675 were incident users. Among the incident users 31% received non recommended drugs; this proportion decreased to 18% among women who started treatment in the third trimester. Women with at least four concomitant diseases had an elevated risk of receiving non recommended drugs during pregnancy. They concluded that further studies are needed to provide comparison on the implementation of guidelines as well as safety of
different anti-hypertensive drugs to define the optimal approach to therapy during pregnancy.

**Tirthankar Deb et al** (2014) performed a retrospective observational study on the basis of case record sheets of patients admitted with PIH. The study was conducted in the Department of Obstetrics & Gynaecology, College of Medicine & JNM Hospital, Kalyani after taking permission from the Institutional Ethics Committee. The case record sheets of the patients diagnosed for pregnancy induced hypertension or gestational hypertension admitted to the obstetrics ward during the period July – December 2013 were reviewed. The information regarding drugs prescribed, number of drugs, dosage, frequency, duration, whether generic names used were recorded and from this the core indicators like prescribing indicators and complementary indicators were evaluated. Out of the total prescriptions studied the most commonly prescribed antihypertensive was Methyldopa, followed by Labetalol, Nifedipine, Amlodipine, and Magnesium sulphate were the other drugs prescribed. Majority drugs prescribed were from category B and C. Single drug therapy was prescribed in 79.87% patients. Methyldopa was the commonly prescribed antihypertensive. None of the prescribed drugs were from teratogenic category D and X.

**CONCLUSION**

From the study it is found that gestational hypertension is one of the most common disorders observed in pregnancy. Patients of the age group 25-30 are found to be more in number diagnosed with gestational hypertension. Pre-existing hypertension and diabetes mellitus are found to be the most common risk factors of gestational hypertension in this study. Preeclampsia and anemia are the most encountered maternal complications. Low birth weight and premature birth were found to be the most common neonatal complication. Most prescribed anti-hypertensive drug is Labetalol and was found to be safe. The antihypertensive drug therapy was found to be significant. Most of the drugs were used appropriately and was in accordance with standard guidelines. None of the contraindicated antihypertensive drugs were prescribed to a single patient. None of the drugs prescribed were in teratogenic category. The outcomes can be improved with proper diagnosis and management that can be achieved through regular health screenings. Proper antenatal checkup and follow up are crucial for the prevention and management of hypertensive complications.
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