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Analysis of the current trend in the prescription of anti-hypertensive drugs among pregnant females in a tertiary care hospital

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ABSTRACT

Background

Hypertensive disorders are the leading cause of maternal and perinatal mortality and morbidity in India and worldwide, as it is among the most common of all medical complications in pregnancy.

Material & Methods

A single centric, observational, cross-sectional, non-randomized study conducted in the department of pharmacology in collaboration with Antenatal care (ANC) Outpatient department of Obstetrics & Gynecology.

Results

Among the 116 hypertensive patients, 108 patients participated in the study. Age distribution showed majority of the participants, 101 (93.51%) were in the reproductive age group i.e. 20-35 years. Trimester wise distribution of the participants showed more than half of the participants, 57 (52.77%) were in third trimester of their term. 62 (57.40%) participants were diagnosed as mild hypertensive and 46 (42.59%) as severe. Gestational hypertension was the most common of all the hypertensive disorder among the study participant. Majority of the patients, 73(67.59%), were preferred for monotherapy. Beta blocker was the preferred class as a monotherapy among the pregnant females followed by centrally acting anti-hypertensive drugs. Labetolol was the preferred antihypertensive followed by centrally acting Methyl dopa. Combination of two antihypertensive drugs was given to 12 participants and combination of anti hypertensive along with anticonvulsants was preferred in 23 participants. Combination of two drugs was used in 19 (17.59%) participants and combination of three drugs was used in 16 (14.81%) participants in the treatment of hypertension.

Conclusion: Hypertension is one of the most common problems encountered in pregnancy. Monotherapy was preferred as a treatment of choice and future study should include detailed outcomes of risk and benefit for both the mother and baby.

Keywords: Anti-hypertensive, Pregnancy, Prescription.

INTRODUCTION

Hypertensive disorders are the leading cause of maternal and perinatal mortality and morbidity in India and worldwide, as it is among the most common of all medical complications in pregnancy.

⁽¹⁾ It is defined as systolic blood pressure (sBP) ≥ 140 mmHg and/or diastolic blood pressure (dBp) ≥ 90 mmHg, or by increase in sBP ≥ 30 mmHg, or in dBp ≥ 15 mmHg, from preconception or first trimester blood pressure confirmed by two measuring, 6 hours apart. ⁽²⁾ Hypertension disorder tends to occur globally, complicating 5-20% of all pregnancies. Its incidence varies from 2 to 8% of pregnancies in developed countries reaching 10% or more in developing countries like India. ^(3, 4) It is estimated that 192 women die every day because of complications arising of hypertension in pregnancy. ⁽⁵⁾

National High Blood Pressure Education Program Working Group classifies hypertensive disorder in Pregnancy into 4 categories:

- 1) Chronic hypertension,
- 2) Preeclampsia-eclampsia,
- 3) Preeclampsia superimposed on chronic hypertension, and
- 4) Gestational hypertension ⁽⁶⁾.

A multicentre study conducted in Taiwan showed approximately 30% of hypertensive disorders of pregnancy were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension/preeclampsia ⁽⁷⁾ Pregnancies complicated by hypertension are associated with increased risk of adverse foetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction (IUGR), perinatal death, acute renal or hepatic failure, ante partum haemorrhage, postpartum haemorrhage and maternal death. ⁽⁶⁾

The greatest challenge in treating hypertension in pregnancy is to reduce the blood pressure to assure the safety of mother and at same time not to compromise uteroplacental perfusion or cause harmful effects on the fetus. Also, the challenge is in deciding when to use antihypertensive medications, and what level of blood pressure to target. The ideal therapy of hypertension in pregnancy should be potent, rapidly acting and without any adverse maternal or fetal effect. The necessity for antihypertensive therapy and the selection of certain

antihypertensive agents during pregnancy should be estimated upon of the relative risks and/or benefits for the individual pregnant women. Still, there is dilemma in clinical practice when to use antihypertensive medications or what level of BP to target during pregnancy.

International societies have differed in their attitudes and recommendations for the BP which should initiate antihypertensive therapy. The U.S. professional bodies recommend starting with the therapy at BP $\geq 160/105$ mmHg, not defining the target values. ⁽⁸⁾ The Canadian Hypertension Society recommends normalization of BP for most hypertensive pregnancy disorders with BP of 140-150/90-95 mmHg, targeting dBp of 80-89 mmHg ⁽⁹⁾. The Australasian professional bodies recommend initiation of antihypertensive therapy at BP $\geq 160/90$ mmHg and conducting the therapy to the BP value of 110-140/80-90 mmHg ⁽¹⁰⁾. It should be underlined that there are still no definitive and complete data about safe BP treatment targets for women with hypertension in pregnancy, however, guidelines and reviews generally recommend the introduction of antihypertensive treatment with the BP values of 140 - 155/90 - 105 mmHg ⁽¹¹⁾.

There is no suspicion about usage of antihypertensive drugs in cases of severe hypertension. BP $\geq 170/110$ mmHg corresponds to the level standing for a high risk of cerebrovascular incident, because of which the majority of obstetricians regard antihypertensive treatment as crucial for the mother ⁽¹²⁾. In mild-to-moderate hypertension in pregnancy (BP from 140/90 to 169/109 mmHg), usage of antihypertensive drugs is still controversial. In those cases, when the situation is less certain, selection of patients, choice of drug and duration of pregnancy at the beginning of treatment may be of great importance. Benefits and risks of antihypertensive treatment for mild-to-moderate hypertension are not completely defined in recent reviews, including a Cochrane meta-analysis. ^(13, 14)

A number of drugs in various combinations are generally used for effective long-term management of hypertension. Hence, there is need to survey the pattern of usage of anti-hypertensive drugs, to see if the current usage is rational, effective and tolerated and in concordance with current guidelines for treatment of hypertension. Therefore the present study was planned with the objective to observe the

prescribing trend of anti-hypertensive drugs in pregnancy with the aim to provide drug rationality.

MATERIAL & METHODS

This was an observational, cross-sectional, non-randomized study conducted in the department of pharmacology in collaboration with Antenatal care (ANC) Outpatient department of Obstetrics & Gynecology, in multispecialty, tertiary care, teaching hospital. The study was conducted for a period of six months from 1st October 2013 to 31st March 2014. Prescriptions of patients attending the ANC Clinic and diagnosed as a case of hypertensive disorder by the treating physician were analysed. The Study was conducted after obtaining permission from the Institutional Ethics Committee (IEC) and the Obstetrics & Gynecology Department. All the data collected as a part of this study was kept strictly confidential and used for the purpose of this study only. The following steps were taken to maintain the confidentiality of the study population: Identification of patients by initials of their name only and not by name, Case records to be accessed by the principal investigator only, Patient details not to be divulged to any party. All the Pregnant females attending the Antenatal clinic are examined either by professors, lecturers or resident which are part of the unit and any one of these can prescribe the required drugs to these pregnant females. Pregnant females attending the Antenatal Care (ANC) clinic and registered with department of Obstetrics & Gynaecology, having single or multiple live viable intrauterine gestations, diagnosed as a case of hypertensive disorder by the treating physician and willing to give consent were included in the study. Those with acute medical emergency conditions requiring hospitalization and attending the Outpatient Department for Medical Termination of Pregnancy were excluded. Data were collected in a pre-designed proforma which included patient's demographic details, pregnancy duration, medical, surgical, gynecological and obstetrical illness, documented in OPD case paper were recorded on the Case Record Form. The detailed information on the prescription records given in the past and at the time of enrolment were recorded from case papers. Data obtained from prescription were sorted and analyzed. Data was compiled into Microsoft Office Excel 2010 Version and a

descriptive statistical analysis was carried out. Observations were presented as simple percentages of different variables.

RESULTS

The present study was conducted for a period of six months, during which 116 females with hypertensive disorder attended the ANC OPD. Among the 116 hypertensive patients, 108 patients participated in the study and were included in the analysis. Age distribution among the 108 participants showed majority of the participants, 101 (93.51%) were in the middle age group i.e. 20-35 years. Among them majority were in the age group of 27-29 years. Table 1 Trimester wise distribution of the participants showed more than half of the participants, 57 (52.77%) were in third trimester of their term. Figure 1 Among the 108 participants who were enrolled in the study, 62 (57.40%) participants were diagnosed as mild hypertensive and 46 (42.59%) as severe. Gestational hypertension was the most common of all the hypertensive disorder among the study participant followed by pre-eclampsia. Figure 2 among the study participants, atleast one co-morbid condition was seen in 61 (56.48%) participants whereas 47(43.51%) participants presented without any co-morbidity. For the purpose of analysis, treatment was classified as monotherapy and combination therapy, the present study showed majority of the patients, 73(67.59%), were preferred for monotherapy in comparison to those who were prescribed combination therapy, 35(32.40%). Figure 3 Analysis of the prescription pattern of antihypertensive agents, revealed Beta blockers to be the preferred class as a monotherapy among the pregnant females followed by centrally acting anti-hypertensive drugs. Table 2 Labetolol was the preferred antihypertensive followed by centrally acting Methyl dopa. Figure 4 Among the 35 participants who were preferred for combination therapy, Combination of two antihypertensive drugs were given to 12 participants and combination of anti-hypertensive along with anticonvulsants were preferred in 23 participants. Among those 12 participants, Combination of centrally acting drug, Methyl Dopa and beta blocker, Labetolol was preferred in 8 participants, while centrally acting drug, Methyl Dopa and calcium channel blocker, Nifedipine was preferred in 4 participants. Among

the 23 participants combination of two anti-hypertensive drugs along with anticonvulsant was preferred in 9 participants. Table 3 Combination of two drugs was used in 19 (17.59%) participants and combination of three drugs was used in 16 (14.81%) participants in the treatment of hypertension. Figure 5

DISCUSSION

Hypertensive disorders of pregnancy are considered to be a major worldwide health problem running an increased risk of Perinatal and maternal mortality. The prevalence varies according to geographic regions of world and ranges from 1.5% in Sweden's to 7.5% in Brazil.⁽¹⁵⁾ This variations can be attributed to racial differences, socioeconomic status and some other parameters like parity and age. In the present study, hypertensive disorders were more common in age group of 25 years and above, which was in contrast to the study conducted by Sajith M⁽¹⁶⁾ and Nadkarni⁽¹⁷⁾ where young patients in the age group of 18-22 years were affected more commonly and pregnant females between the age group of 21-25 years were affected mostly in study conducted by Tirthankar⁽¹⁸⁾ and Kumar TN⁽¹⁹⁾. The distribution of various hypertensive disorder in the present study showed, gestational hypertension to be more common among the hypertensive disorders followed by pre-eclampsia. The above results were similar to the

study conducted by Sajith M⁽¹⁶⁾, whereas Eclampsia was more common in study conducted by Kumar TN⁽¹⁹⁾. Majority of the 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 Folic and co⁽²⁾ whereas monotherapy was not preferred in study conducted by Pandya⁽²⁰⁾, Kumar TN⁽¹⁹⁾ and Sajith M⁽¹⁶⁾. The use of combination antihypertensive pharmacotherapy suggests increased Severity of illness where optimal BP control cannot be achieved on monotherapy. Drugs preferred as monotherapy in our study were Labetolol, Methyldopa and Nifedipine. Of these, Labetalol was the preferred drug as monotherapy in our study followed by methyl dopa. Contrast results were seen in studies conducted previously, where, Methyldopa was preferred in the study conducted by Pandya⁽²⁰⁾, Kumar TN⁽¹⁹⁾ Sajith M⁽¹⁶⁾, Tirthankar⁽¹⁸⁾ and Cvijic M⁽²¹⁾ and Nifedipine in the study conducted by Begum⁽²²⁾ and Ray JG⁽²³⁾. This shows that utilization pattern differs from hospitals, prescribers and among countries also. But limitation seen with our study was that it could not evaluate the effectiveness of drugs in contrast to fetal outcome associated with harm. Future studies must include detailed outcomes of risk and benefit for both the mother and baby.

Table 1: Age wise distribution of participants

Age (years)	No of participants	Percentage (%)
< 18	0	0
18-20	5	4.62
21-23	18	16.66
24-26	24	22.22
27-29	32	29.62
30-32	19	17.59
33-35	8	7.40
>35	2	1.85
Total	108	100

Table 2: Different classes of anti hypertensive prescribed as a monotherapy

Monotherapy	No of participants	Percentage
Calcium channel blocker	16	21.91
Centrally acting drug	25	34.24
Beta blocker	32	43.82
Total	73	100

Table 3: Prescription of antihypertensive drugs as combination therapy

Combination therapy	No of participants	Percentage (%)
Magnesium sulphate + Nifedipine	5	21.73
Magnesium sulphate + Labetolol	2	8.69
Magnesium sulphate + Methyl dopa + Nifedipine	9	39.13
Magnesium sulphate + Methyldopa + Labetolol	7	30.43
Total	23	100

Figure 1: Trimester wise distribution of participants

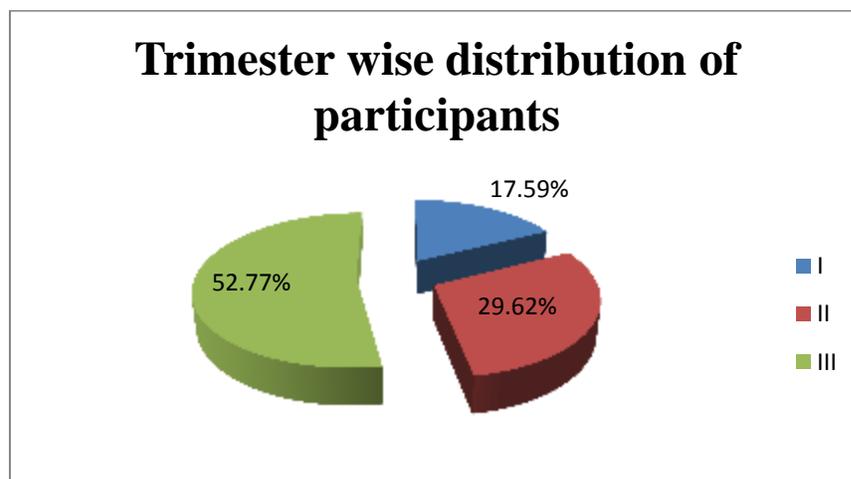


Figure 2: Hypertensive disorder among study participants

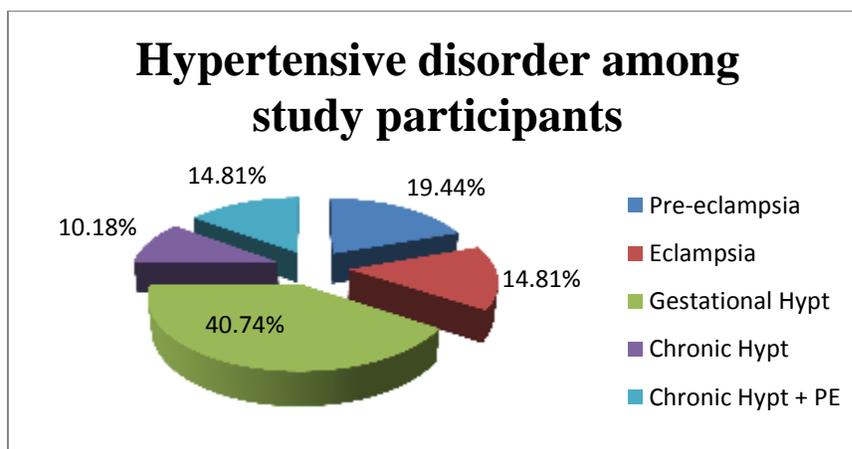


Figure 3: Approach of treatment for participants

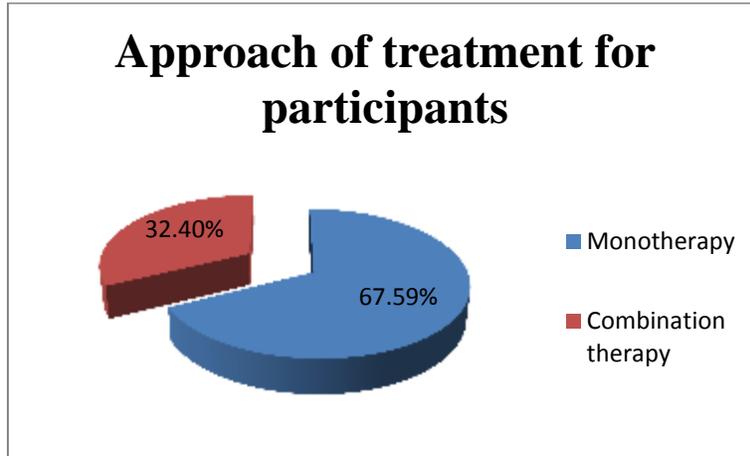


Figure 4: Prescription of different antihypertensive drugs as monotherapy

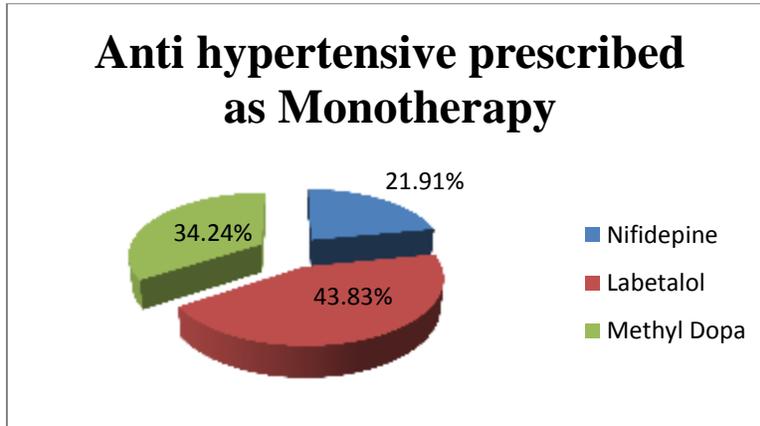
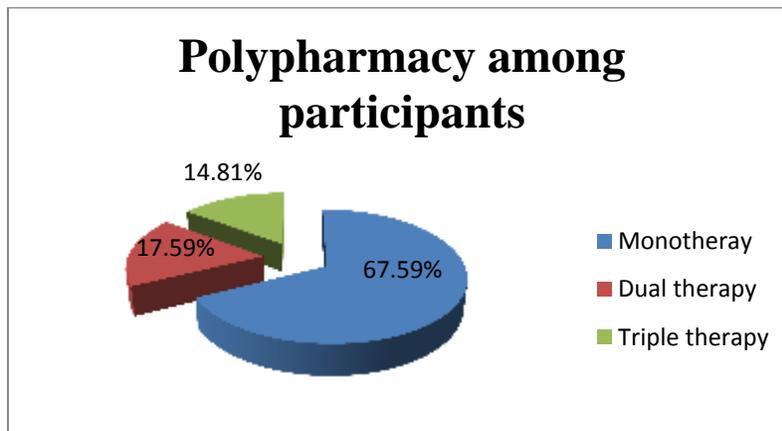


Figure 5: Polypharmacy among participants



CONCLUSION

Our study concludes that Hypertension is one of the most common problems encountered in pregnancy. Monotherapy was preferred as a treatment and Labetolol was the drug most commonly prescribed

but it varies from hospitals, prescribers and among countries. Future study should include detailed outcomes of risk and benefit for both the mother and baby so that it will improve rational drug prescription and awareness regarding safe use of drugs.

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