

Incidence of pregnancy induced hypertension and prescription pattern of antihypertensive drugs in pregnancy

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ABSTRACT

Aim: To determine the frequency and distribution of different types of hypertensive disorders of pregnancy and to assess the drug utilization pattern of antihypertensive drugs in pregnancy. **Method:** A prospective study was conducted over a period of one year in inpatients of Gynaecology and Obstetrics Department at Bharati Hospital, Pune. Patients diagnosed as hypertensive disorder of pregnancy were taken for primary evaluation. The data regarding demographic details, presenting complaints, gestational age, obstetrics history, diagnosis, blood pressure monitoring, current medications, antihypertensive drugs prescribed were collected and the utilization of antihypertensive drugs in pregnancy was evaluated. **Result:** A total of 1330 pregnant women visited the OBG department, out of which 104 patients were diagnosed with hypertension. The overall prevalence of hypertensive disorders in pregnancy was 7.8%. The mean maternal age was 23.8 years during the hospital admission. The prevalence of Preeclampsia, gestational hypertension, chronic hypertension, and eclampsia were 5.6 %, 1.5%, 0.15 %, and 0.60 % respectively. Highest incidence of hypertension was occurred in age group of 18-22 years (41.3%) and primigravidae patients (53.8%). A majority of patients 67.3 % were on combination therapy whereas 32.7% were on Monotherapy. Methyldopa was the commonest prescribed antihypertensive as monotherapy (17.3 %) as well as in combination therapy (i.e. 28.8 % with methyldopa and Nifedipine). **Conclusion:** Our study concluded that the incidence of hypertensive disorders in pregnancy was high. Methyldopa was the commonest prescribed antihypertensive in monotherapy and combination, as it is safest during pregnancy.

INTRODUCTION

Hypertension is the most common medical problem encountered in pregnancy and remains an important cause of maternal and fetal morbidity and mortality¹. It complicates almost 10% of all pregnancies². Pregnancies complicated by hypertension are associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction (IUGR), perinatal death, acute renal or hepatic failure, antepartum haemorrhage, postpartum haemorrhage and maternal death³.

Hypertensive disorders during pregnancy are classified into 4 categories, as recommended by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy: 1) chronic hypertension, 2) preeclampsia-eclampsia, 3) preeclampsia superimposed on chronic hypertension, and 4) gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy)⁴. In a multicenter study, approximately 30% of hypertensive disorders of pregnancy were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension/preeclampsia⁵.

Treating the hypertension does not alter the progression of disease. However it has been shown that early treatment decreases not only the frequency of hypertensive crisis, but also the rate of neonatal complications. Antihypertensive medications are mainly used to prevent or treat severe hypertension, to prolong pregnancy for as long as safely possible thereby maximizing the gestational age of the infant, and to minimize fetal exposure to medications that may have adverse effects. During pregnancy, the challenge is in deciding when to use antihypertensive medications, and what level of blood pressure to target. The antihypertensive drugs that may be used in pregnancy are methyldopa, beta blockers, calcium channel blockers and vasodilators. Methyldopa has been available for many years and is widely used. Literature supports the safety and efficacy of Nifedipine and Atenolol used in essential hypertension in pregnancy⁶.

Antihypertensive use during pregnancy is relatively common and increasing. The wide range of agents used during pregnancy includes medications considered contraindicated during pregnancy. The choice of antihypertensive agents is less complex because only a small proportion of currently available drugs have been evaluated adequately in pregnant women and many are contraindicated⁷. The present study focused on the antihypertensive drug utilization pattern in women attending the antenatal clinic of obstetrics and gynaecology department at a tertiary care teaching hospital.

MATERIALS AND METHODS

A prospective study was conducted over a period of one year in inpatients of Gynaecology and Obstetrics Department at Bharati Hospital, Pune. All pregnant women attending the antenatal clinic were screened for hypertension and patients diagnosed as hypertensive disorder of pregnancy were taken for primary evaluation. The data regarding demographic details, presenting complaints, gestational age, obstetrics history, diagnosis, blood pressure monitoring, current medications, antihypertensive drugs prescribed were gathered from medical record files. The utilization of antihypertensive drugs in pregnancy was evaluated.

RESULTS

During one year study, 1330 pregnant women visited the OGD, out of which 104 patients were diagnosed with hypertension. The prevalence of Hypertensive Disorders of Pregnancy was 7.8%. The mean maternal age at delivery was 23.8 years. Total distributions of patients with respect to age group shows that highest number of patients was found in the age group of 18-22 years (41.3 %) and least was above 32 years age group (3.8%). Table 1 provides various hypertensive disorders in the age groups of patients.

TABLE 1: AGE DISTRIBUTION ACCORDING TO HYPERTENSIVE DISORDERS OF PREGNANCY

Age (in years)	Gestational hypertension (n=20)	Eclampsia (n=8)	Chronic hypertension (n=2)	Preeclampsia (n=74)	Percentage (%)
No. of patients					
18-22	7	6	0	30	41.3
23-27	11	2	0	28	39.4
28-32	0	0	2	14	15.4
>32	2	0	0	2	3.8

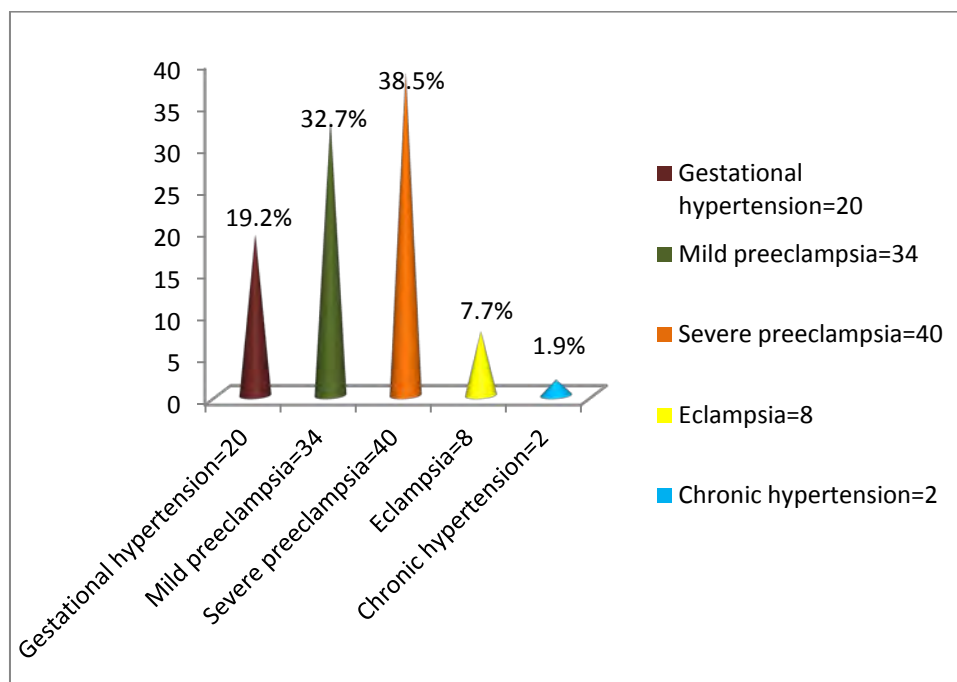
The Subject characteristic of woman who were diagnosed as a hypertensive having an average weight of 61.8 kg and a mean gestational age 32.7 weeks at the time of admission. The mean Systolic Blood Pressure was 156.6 mmHg, while the mean Diastolic Blood Pressure was 101.4 mmHg (**Table 2**).

TABLE 2: SUBJECT CHARACTERISTICS OF STUDY POPULATION

	Mean (n=104)	S.D
Age (years)	23.8	4.0
Weight at time of admission(kg)	61.8	10.6
Systolic Blood Pressure (mmHg)	156.6	22.2
Diastolic Blood Pressure (mmHg)	101.4	11.5
Mean Arterial Pressure	105.7	7.8
Gestational age at enrolment (weeks)	32.7	4.6

Preeclampsia was the most common cause of hypertension during pregnancy (71.2%). This was followed by Gestational Hypertension (19.2 %) population. Results are summarized in Figure 1.

FIGURE 1: SUBJECT CLASS ACCORDING TO DIAGNOSIS (N=104)



Gestational age at the time of admission varied from 21 weeks till term (Table 3).

TABLE 3: GESTATIONAL AGE OF SUBJECTS ACCORDING TO DIAGNOSIS (N=104)

Gestational Age (weeks)	Gestational Hypertension	Mild Preeclampsia	Severe Preeclampsia	Eclampsia	Chronic Hypertension
21-24	2	0	4	2	2
25-30	2	2	10	2	0
31-35	6	14	22	2	0
>36	10	18	4	2	0

In this study, the incidence of hypertension in pregnancy was highest among primigravidae. Out of 104 patients, 56 were primigravida (53.8 %) and 48 were multigravida (46.1%) (Table 4).

TABLE 4: GRAVIDITY STATUS OF SUBJECT (N=104)

Para	Gestational hypertension	Preeclampsia	Eclampsia	Chronic hypertension	Percentage (%)
	No. of patients				
Multigravida	8	36	2	2	46.1
Primigravida	12	38	6	--	53.8

Headache in 20 (19.2%), Epigastric pain in 18 (17.3 %), peripheral edema in 14 (13.5 %), Blurring vision in 2 (1.9 %) patients were observed and Seizures were seen in 4 patients (Table 5).

TABLE 5: SYMPTOMS OF PATIENTS WITH HYPERTENSIVE DISORDERS OF PREGNANCY

Symptoms	No. of Patients	Percentage
Peripheral Edema	14	13.5
Severe Headache	20	19.2
Epigastric Pain	18	17.3
Blurring Vision	2	1.9
Seizures	4	3.8

Overall 34 (32.69%) patients were treated with a single antihypertensive drug, and 70 (67.31%) patients were treated with antihypertensive drug combinations as represented in Figure 2.

FIGURE 2: UTILIZATION PATTERN OF ANTIHYPERTENSIVE DRUGS IN PREGNANCY

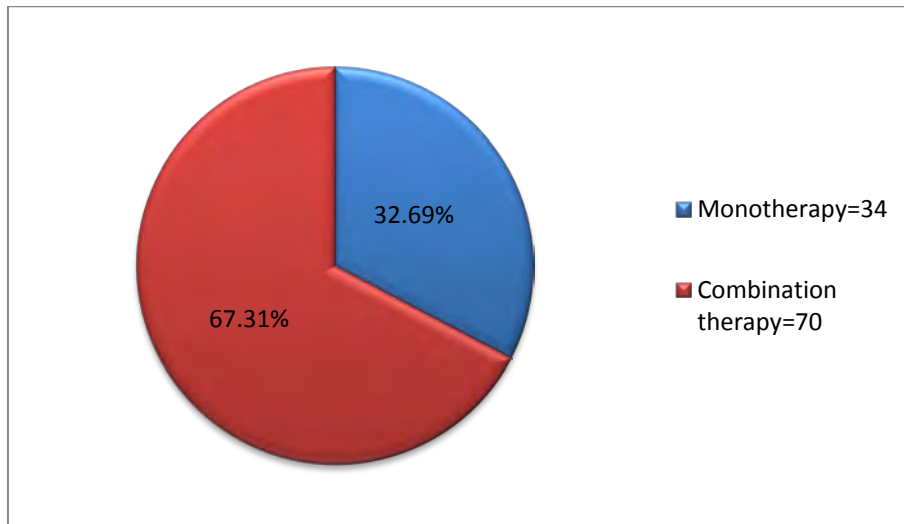


Figure 3 shows the details of patients, who were treated with a single antihypertensive drug. 18 (17.3 %) patients were treated with centrally acting antiadrenergic drugs and 16 (15.4 %) patients were treated with Calcium Channel blockers (Figure 3).

FIGURE 3: THE PATTERN OF USE OF ANTIHYPERTENSIVE DRUGS IN PATIENT TREATED WITH MONOTHERAPY

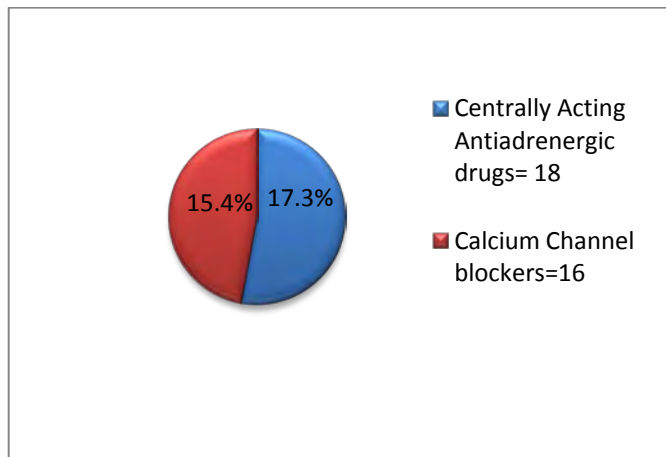


Table 6 shows details of patients treated with combination therapy, out of 70 patients, 52 (50.0 %) were prescribed with two drugs, 16 (15.4%) were prescribed with three drugs and 2 (1.9 %) with four drugs. The calcium channel blockers and centrally acting antiadrenergic drugs (28.8%) was the most frequently prescribed two-drug combinations. β -blocker agent, Calcium channel blocker and centrally acting agent (15.4 %) was the most frequently prescribed three drug combinations (**Table 6**).

TABLE 6: THE PATTERN OF ANTIHYPERTENSIVE DRUGS IN PATIENT TREATED WITH COMBINATION THERAPY (N= 70)

Drug Classes	No. of patients	Percentage
Centrally acting agent + Calcium channel blocker	30	28.8
Calcium channel blocker + β -blocker agent	12	11.5
Centrally acting agent+ β -blocker agent	6	5.7
Centrally acting agent + Diuretic	2	1.9
Calcium channel blocker + Diuretic	2	1.9
Centrally acting agent + Calcium channel blocker + β -blocker agent	16	15.4
Calcium channel blocker + β -blocker agent + Centrally acting agent + Diuretic	2	1.9

The most commonly prescribed antihypertensive drugs were Methyl dopa & Nifedipine (28.8 %); Methyl dopa (17.3 %), Nifedipine (15.4%), Labetalol, Nifedipine & Methyldopa (11.5 %) as represented in Table 7.

TABLE 7: INDICATIONS FOR VARIOUS ANTIHYPERTENSIVE DRUGS

Drugs prescribed	Gestational Hypertension	Preeclampsia		Eclampsia	Chronic hypertension	Percentage
		Mild	Severe			
Nifedipine	2	8	4	2	---	15.4
Methyldopa	8	8	2	---	---	17.3
Methyldopa & Nifedipine	2	12	12	2	2	28.8
Methyldopa & Labetalol	2	2	2	---	---	5.8
Nifedipine & Labetalol	---	4	2	2	--	7.7
Atenolol & Nifedipine	2	---	2	---	--	3.8
Nifedipine & Furosemide	2	---	---	---	---	1.9
Methyldopa & Furosemide	---	--	---	2	---	1.9
Labetalol, Nifedipine & Methyldopa	2	---	10	--	---	11.5
Methyldopa, Nifedipine, labetalol & Atenolol	---	--	4	----	---	3.8
Methyldopa, Nifedipine Labetalol & Furosemide	----	--	2	---	---	1.9

The most commonly prescribed medication classes were calcium supplement (92.3%), iron preparations (44.2%), nutrient supplements (40.4%), multi vitamins (38.5%), and folic acid (32.7 %) as represented in Table 8.

TABLE 8: DRUG UTILIZATION PATTERN IN OB&GY INPATIENTS OTHER THAN ANTIHYPERTENSIVE DRUGS

Drugs	No. of Patients	Percentage
Calcium supplement	96	92.3
Iron supplement	46	44.2
Nutritional supplements (protein powder)	42	40.4
Multivitamin supplement	40	38.5
Folic acid supplement	34	32.7
H ₂ Blocker	18	17.3
Analgesics & anti inflammatory	16	15.4
Anti allergic	14	13.5
Laxative	6	5.8
Anti-helminthes	6	5.8
Antispasmodic	4	3.8
Antiemetic	6	5.8
Nitric oxide donors		
Arginine	40	38.4
Progesterone	8	7.7
Antioxidants		
Vitamin E	7	13.5
Vitamin C	15	28.8
Antithrombotic agents		
Aspirin	3	5.7
Omega-3 fatty acid	12	23.1

DISCUSSION

Hypertensive disorders of pregnancy are considered to be a major worldwide health problem running an increased risk of Perinatal and maternal mortality¹. The prevalence of Hypertensive Disorder in Pregnancy varies according to geographic regions of world and ranges from 1.5% in Sweden's to 7.5% in Brazil⁸. According to our study, the frequency of hypertensive disorders of pregnancy was 7.8%. The variations can be attributed to racial differences, socioeconomic status and some other parameters like parity and age.

The distribution of different hypertensive disorders of pregnancy was that, Gestational hypertension of pregnancy was diagnosed in 20 (19.2%) cases. 74 patients (71.1%) and 8 (7.7%) patients appeared to be pre-eclamptic and eclamptic respectively. In India, the incidence of preeclampsia is reported to be 8-10% of the pregnancies⁹. We also observed preeclampsia in 5.4% of the study population. The overall prevalence of Eclampsia in our study was found to be 0.6 % of pregnancies. The reported incidence of eclampsia from India is 0.71 %. These figures are comparable with our study. Chronic hypertension was found 2 (1.9 %) patients in our study. The frequency of chronic hypertension in Iran was 0.17% which is similar to our study (0.15 %) ¹⁰.

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 ¹¹. In our study highest incidence of the hypertensive disorders occurred among those aged 18 to 22 years. This could be because the majority of conceptions take place in this age group in our country. The age distribution of eclampsia patients in our study is similar to other reports and suggests that eclampsia is, probably, a disease of young women¹². Preeclampsia is more frequent in patients younger than 21 years of age and in older than 35 ¹³. In our study majority of preeclampsia patients were between the ages of 18 to 22 years. Preeclampsia and eclampsia were apparently higher in younger pregnant women (less than 30 years) as Yucesoy et al, showed in their recent investigation. The frequency of chronic hypertension appears to be higher in woman aged 30 years & same is indicating in our study also. ¹⁰

The incidence of PIH is distributed unevenly throughout late gestation, increasing with advancing gestation. Approximately half of PIH cases occur at term (weeks' gestation), including most cases of gestational hypertension. Early-onset PIH is often associated with severe preeclampsia ¹⁴. The mean gestational age at presentation was 32.7 weeks which is comparable with other study (i.e. 37 weeks) ¹⁵. The reported gestational age of onset of preeclampsia is more than 20th week of pregnancy in vast majority of patients, but recently a case was reported from Japan with typical features of preeclampsia occurring at less than 20th weeks of gestation¹⁵.

Preeclampsia is primarily regarded as a disease of first pregnancy. In our study, 53.8% were primigravidas and 46.1 % were multigravidas. Several other authors have reported primiparity in 52-73%

patients of preeclampsia. In our study, both primigravida and multigravida were equally affected with eclampsia. But literature indicates that eclampsia is a disease of primigravida. According to Hellman incidence of eclampsia in primigravida and multigravida was in the proportion of 3:1¹⁶.

Oedema was seen in 13.5 % of our patients. Oedema is a very common manifestation seen in upto 80% of normal pregnancies¹⁷. Prevalence of peripheral edema was significantly less than what would be expected. We believe that this might have been due to all information was not necessarily documented.

Antihypertensives are agents that lower blood pressure. 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 were used in our hospital for treating hypertension during pregnancies. The most commonly prescribed antihypertensive agent was adrenergic receptor alpha-2 agonists: Methyldopa, Nifedipine, Labetol. The use of combination antihypertensive pharmacotherapy suggests increased Severity of illness where optimal BP control cannot be achieved on monotherapy. The present study reveals that adrenergic receptor alpha-2 agonists (Methyldopa) were mostly prescribed single drug therapy. In the present study, two drug combinations were mostly prescribed (49.8 %) followed by three drug combinations (15.4 %). In the present study also most of the cases of PIH were treated using Methyldopa or Nifedipine. Methyldopa was the commonest prescribed antihypertensive as monotherapy as well as in combination therapy. Similarly in a study by Cvijic M et.al¹⁸, Methyldopa was most commonly prescribed antihypertensive drugs in 27.8% of patients. In contrast to this, studies from Ray JG et.al¹⁹ showed that Nifedipine (47.7%) was prescribed more frequently than Methyldopa (27.7%). This shows that utilization pattern differs from hospitals, prescribers and among countries also.

In our study, calcium supplements, iron preparations, nutritional supplement, folic-acid and Vitamins, the most frequently used drugs in pregnancy. Periconceptional folic-acid supplementation can prevent most neural-tube defects and other congenital abnormalities of the cardiovascular system, urinary tract and limb deficiencies. Moreover, folic-acid supplementation in pregnancy is associated with the decreased incidence of habitual spontaneous abortion and pregnancy complications (e.g., placental abruption and preeclampsia)²⁰.

CONCLUSION

Our study concluded that the incidence of hypertensive disorders in pregnancy was high. Early diagnosis and treatment through regular antenatal checkup is a key factor to prevent PIH and its complications. The incidence of combination therapy was high. Methyldopa was the commonest prescribed antihypertensive in monotherapy and combination, as it is safest during pregnancy.

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