

# Frequency, Treatment, And Management of Gestational Hypertension: Findings of A Retrospective Analysis from Quetta City, Pakistan

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## Abstract

**Objective:** There is a scarcity of information about the treatment and management of GHTN especially from the developing world. Therefore, keeping the importance and urgency of the issue in hand, the current study was aimed to evaluate the frequency, treatment, and management of gestational hypertension among pregnant women visiting a public healthcare institute of Quetta city, Pakistan. **Methods:** A retrospective, cross-sectional design was employed for the current study. The study was conducted at the Obstetrics and Gynecology (O&G) ward of Bolan Medical Complex Hospital, Quetta. For the retrospective analysis, we collected the data of one year. Patients' data were recorded on a verified data collection form. In addition to the demographic, anthropometric, and clinical information, the National Institute for Clinical Excellence (NICE) guidelines was used to compare the treatment and management of GHTN as a reference. **Results:** A total of 2974 medical records were collected over a period of one year out of which 79 were diagnosed with GHTN ( $f=2.65\%$ ). Forty six patients (58.2%) were prescribed methyldopa while 18 (22.8%) were prescribed labetalol for GHTN. Additionally, hydralazine, furosemide, and captopril were prescribed to 5 (6.3%), 4 (5.1%), and 2 (2.5%) of the patients, respectively. Recommendation of lifestyle modification was completely ignored and not a single patient was instructed for dietary control neither any sort of exercising activity was recommended as per records. **Conclusion:** Our study found major insufficiencies in terms of GHTN treatment and management. A clear deviation from the guidelines was evident as practitioners failed to identify women at high risk of developing GHTN and were unable to segregate the risk by missing out essential parameters. Screening parameter for evaluation, as suggested by NICE Guidelines for segregating patients at high risk of developing GHTN and associated complications were also suboptimal.

**Keywords:** Frequency, treatment, management, gestational hypertension

## INTRODUCTION

The Sustainable Development Goal (3.1) as proposed by the United Nation focuses on reducing the global maternal mortality ratio to <70 per 100,000 live births by 2030 [1]. However, the burden of maternal mortality still remains higher especially in the developing world [2]. Among the reasons for the mentioned maternal mortality, pregnancy-induced hypertension (PIH) or gestational hypertension (GHTN) is a noteworthy complication. Pregnancy and the transition to motherhood involve major psychological and physical changes among women that are linked to the development of a number of disorders [3-5]. Within this context, GHTN complicates about 6-10% of pregnancies worldwide that occur in the second half of pregnancy in a previously normotensive woman, without significant proteinuria or other features of pre-eclampsia [6]. Medically, GHTN is defined as systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg [7]. Furthermore, GHTN is classified as mild (SBP 140-149 and DBP 90-99 mmHg),

moderate (SBP 150-159 and DBP 100-109 mmHg), and severe (SBP  $\geq 160$  and DBP  $\geq 110$  mmHg) [8].

Although GHTN normalizes by six weeks postpartum [9] nearly 40,000 maternal deaths were reported because of

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GHTN worldwide [10,11]. A study in the UK reported that 1 out of 20 Intensive Care Unit admissions in pregnancy were associated with severe pre-eclampsia/ eclampsia [12,13]. Long term effects of GTH on women include higher risks of cardiovascular and renal diseases and proportionality of morbidity and mortality is associated with early diagnosis and apposite management of such conditions [14-16].

In order to safely manage and treat GHTN, the National Institute of Care and Excellence (NICE) the UK has adopted the recommendation, assessment, development, and evaluation (GRADE) system for developing guidelines for antenatal, intrapartum, postnatal stages of pregnancy and neonatal monitoring [12]. The NICE guidelines also provide an outline for prognosis, prophylaxis, pharmacological management, dietary control and patient education for patients with GHTN [12]. Even though GHTN is a common issue of discussion during pregnancy, the Centre for Maternal and Child Enquiries (CMACE) in 2011 indicated a 7 fold rise in pre-eclamptic pregnancies in the developing world [17]. This is almost true to what is reported in Pakistan where Douglas & Redman reported 2.31% of pregnancies are pre-eclampsia in 1994 [18], Magee and the research group reported that 9.3% of the pregnant women had GHTN in 2019 [19]. We have to remember that these figures are reported from cosmopolitan cities of Pakistan and a higher ratio is expected from underdeveloped parts of Pakistan especially the province of Baluchistan. To the best of our knowledge and through extensive literature review, we were unable to find a study that reported the frequency and management of GHTN from Balochistan. Therefore, keeping the importance and urgency of the issue in hand, the current study was aimed to evaluate the frequency, treatment, and management of gestational hypertension among patients visiting a public healthcare institute of Quetta city, Pakistan.

## METHODS

### Study design, settings, and sampling

A retrospective, cross-sectional design was employed for the current study. The study was conducted at the Obstetrics and Gynecology (O&G) ward of Bolan Medical Complex Hospital, Quetta. Established in 2001, the hospital is a tertiary public care teaching hospital. The O&G department is equipped with 45 beds and operates with one labor room. All services are provided either free/with minimum charges and medicines are free for patients. For the retrospective analysis, we collected data of one year i.e. (1<sup>st</sup> January 2019 – 31<sup>st</sup> December 2019).

### Inclusion and Exclusion Criteria

Female patients of childbearing age with chronic or de novo hypertension during pregnancy were included in the study. Additionally, patients with hypertension-induced complications like eclampsia or preeclampsia were also our patients of interest. Women with established hypertension were excluded from the study.

## Data collection tool

Patients' data were recorded on a verified data collection form. The form contained demographic information like age, family history, and parity. Anthropometric variables like weight, height, Body Mass Index (BMI), week of pregnancy, stages of GHTN, and clinical variables like comorbidity, and blood pressure measurements were also noted. Patients' data sheets were also analyzed for prognosis, medications utilized for prevention, treatment or delaying the onset of GHTN and related complications. Frequency of diagnostic tests and educating patients regarding self-monitoring tactics to prevent or delay the onset and progression of GHTN was also recorded. In addition to the above-mentioned information, the NICE guidelines were used to compare the treatment and management of GHTN as a reference.

## Statistical analysis

The SPSS v.20.0 was used for data coding and analysis. Based on the objectives of the study, descriptive statistics were applied for data analysis.

## Ethical approval

The departmental ethics committee at the Faculty of Pharmacy and Health Sciences, University of Balochistan, Quetta approved the study. Besides, permission was also taken from the Medical Superintendent of the hospital. As the study was not aimed to identify personal data such as individual details, images, or videos, therefore, consent from the patients was not applicable.

## RESULTS

### Demographic characteristics of the study respondents

The demographic characteristics of the study patients are presented in Table 1. A total of 2974 medical records were collected over a period of one year out of which 79 were diagnosed with GHTN. Hence, the frequency of GHTN in our cohort was 2.65%. The mean age of patients with GHTN was  $27.32 \pm 7.38$  years whereby 30.4% of patients were under 20 years of age. The majority of patients had their first pregnancy (28, 35.4%) and 54 (68.3%) belonged to urban residencies. All patients were diagnosed with GHTN in the second trimester of their pregnancy period.

**Table 1: Baseline characteristics of patients**

Demographic characteristics	Frequency	Percentage
<i>Age (<math>27.36 \pm 7.36</math>)</i>		
16 -20	24	30.4
21-25	15	19.0
26-30	17	21.5
31-35	14	17.7
36-40	7	8.9
41-45	1	1.3

46-50	1	1.3
<b>Parity</b>		
First pregnancy	28	35.4
Second pregnancy	17	21.5
Third pregnancy	15	19.0
Fourth pregnancy	12	15.2
Fifth pregnancy	4	5.1
Tenth pregnancy	3	3.8
<b>Locality</b>		
Urban	54	68.3
Rural	25	31.6

### Demographic, anthropometric, and clinical investigation

Details about the documented variables of demographic, anthropometric, and clinical investigations are tabulated in Table 2. Among demographic details, age and parity were documented for every patient while a family history of HTN was written for only 34.2% of patients. Among anthropometric records, the patient's weight was mentioned for only 11.4%, height and BMI were not available for any of the patients. However, for clinical attributes, comorbidity, maximum systolic Blood Pressure, and Maximum Diastolic Blood Pressure were 100% documented.

**Table 2: Demographic, anthropometric, and clinical investigation**

Variables	Documented N (%)	Not documented N (%)
Age	79 (100)	0 (0)
Family history	27 (34.2)	52 (65.8)
Parity	100%	0 (0)
Weight	9 (11.4)	70 (88.6)
Height	0%	79 (100)
Body Mass Index (BMI)	0%	79 (100)
Week of pregnancy	100%	0 (0)
Stage of GHTN	100%	0 (0)
Comorbidity		
Max Systolic Blood Pressure	79 (100)	0 (0)
Max Diastolic Blood Pressure	79 (100)	0 (0)

### Management of GHTN (medications, prophylaxis, and lifestyle modification)

The management of GHTN in terms of prescribed medications, medication for prophylaxis and counseling is presented in Table 3. Aspirin was prescribed to 10.1% of patients and only 5.1% of them were administered with platelets with platelet count less than 150,000 microliters.

Forty-six patients (58.2%) were prescribed methyldopa while 18 (22.8%) were prescribed labetalol for GHTN. Additionally, hydralazine, furosemide, and captopril were prescribed to 5 (6.3%), 4 (5.1%), and 2 (2.5%) of the patients, respectively. Two patients (2.5%) were prescribed with a combination of labetalol, methyldopa, methyldopa, and furosemide, respectively. Two patients were also prescribed enalapril for GHTN. Among drugs used to control the seizures related to eclampsia, Magnesium sulfate was administered to 50 (63.3%), diazepam to (1, 1.3%), and a combination of Magnesium sulfate and diazepam to 11.4% of the patients. Moreover, the recommendation of lifestyle modification was completely ignored and not a single patient was instructed for dietary control neither any sort of exercising activity was recommended as per records.

**Table 3: Management of GHTN (medications, prophylaxis, and lifestyle modification)**

Medications used for GHTN	Yes (Frequency)	Yes (Percentage)
<b>Prophylactic</b>		
Aspirin	8	10.1
Aspirin (In case of HELLP)*	4	5.1
<b>Treatment</b>		
Methyldopa	46	58.2
Labetalol	18	22.8
Hydralazine	5	6.3
Furosemide	4	5.1
Captopril	2	2.5
Labetalol + methyldopa	4	5.1
Methyldopa and furosemide	2	2.5
Enalapril	2	2.5
<b>Eclampsia-related seizures</b>		
Magnesium sulfate	50	63.3
Diazepam	1	1.3
Magnesium sulfate + diazepam	9	11.4
Life style modification	0	0
Dietary control	0	0
Exercise	0	0

\*Hemolysis, elevated liver enzymes, low platelets

### Comparison of documentation with NICE standards of treatment

Globally, NICE recommends guideline parameters for diagnosis and management of GHTN and its induced complications in pregnant women [12]. According to what is recommended by NICE, maximum systolic and diastolic blood pressures, electro encephalopathy, and gestation induced hypertensive disorders were recorded in 100% of our patients. However, creatinine records of only 26.6% of the patients were available. Albuminuria was reported in 16.5%, fetal monitoring in 3.8%, hemoglobin percentage in 35.4%, uric acid in 16.5%, and blood glucose level were reported in 27.8% of patients. Importantly, creatinine to albumin ratio was neither calculated nor recorded (Table 4).

**Table 4: Comparison of documentation with NICE standards of treatment**

NICE Standards of Treatment	Documented (%)
<i>Diagnostic Guidelines Recommendations</i>	
Maximum Systolic Blood Pressure	79 (100.0)
Maximum Diastolic Blood Pressure	79 (100.0)
Creatinine	21 (26.6)
Albuminuria	13 (16.5)
Creatinine: Albuminuria (predicting Pre-Eclamptic stage)	0 (0)
Stage of Complication	79 (100.0)
Thrombocytopenia	2 (2.5)
Fetal Monitoring	3 (3.8)
Hb Levels	28 (35.4)
Electroencephalography	79 (100.0)
Uric Acid	13 (16.5)
Blood Glucose Levels	22 (27.8)

## DISCUSSION

Gestational hypertension is a distinct type of hypertension that requires characteristic management strategies due to the potential teratogenic properties of major antihypertensive agents and even diuretics [20-22]. Therefore, medication for GHTN-induced disorders involves risk vs. benefit ratio for every patient, with a comprehensive objective of upgrading fetal and maternal outcomes. Hence, the therapy choices become limited to drugs proved to be safe, have been in use for long times with a high obstetrician acceptance due to a safer side effect profiles. Summarizing, this limitation renders the treatment methods and choices that are available for treating other forms of hypertension in general. Within this context, various guidelines are available for medical practitioners subjecting the management of hypertensive disorders of pregnancy, NICE guidelines being one of them [23]. The NICE guidelines are developed by adopting Recommendation, Assessment, Development, and Evaluation (GRADE) system; a system adopted by over 60 major organizations including Nation Institute for Health and Care Excellence. These guidelines provide evidence-based recommendations for women suffering from chronic hypertension with a wish to conceive for women with a history of hypertension complicating pregnancy and chronic hypertension history in expecting mothers. These guidelines are linked to other guidelines by NICE to incorporate them effectively into health provision [24]. Therefore, around the globe, the NICE guidelines are applied with a focus on eliminating teratogenic effects of antihypertensive drugs along with significant control of blood pressure to lower fetal and maternal mortality and morbidity.

In line with what is suggested by NICE guidelines, labetalol (licensed for usage in pregnancy) should be the first-line treatment followed by nifedipine [25]. Methyldopa is the third

option in cases that both labetalol and nifedipine fail to control risen blood pressure [12]. While a meta-analysis indicated the efficacy of hydralazine equivalent to labetalol in managing hypertensive emergencies in pregnancy, labetalol was found safer for mothers and was preferred over hydralazine due to maternal side effects of more frequent headaches, maternal palpitation, and maternal tachycardia. That is the reason labetalol is preferred for managing hypertension among first-line medication therapies for GHTN [26,27].

Despite being the safest among all other antihypertensive agents, labetalol was prescribed to only 22.8% of women as a solo remedy and to 5.1% of patients in combination with methyldopa in the current study. Nifedipine was not administered to any patient for managing GHTN and hydralazine was prescribed to 6.1% of patients only. A majority (58%) of patients were prescribed the third option of methyldopa despite its least efficacy than labetalol, hydralazine, and nifedipine. Our study revealed irregular prescribing patterns towards the management of GHTN that poses a number of threats for the pregnant mothers and to the fetus. This limitation of prescribing practice needs immediate attention and should be highlighted by the policymakers as a priority matter in order to resolve pregnancy-related hypertension and its complications. Additionally, the pharmacological intervention for managing GHTN complications in pregnancy is not very clear throughout the world. But evidence-based studies settled priority drugs based on the side effects of these drugs on maternal and fetal health. On the contrary, developing countries report no clear evidence about the priority of antihypertensive drugs to be used during pregnancy. Despite the least efficacy of methyldopa, it is the majorly prescribed drug in the developing world [28]. This is also the same in our case where clinical practitioners prescribed methyldopa for the majority of cases of pregnancies complicated by hypertension and hypertension-related emergencies. Thus, the findings of our study are considerably opposite to what has been advised by NICE Guidelines and practiced in developed countries.

The NICE guidelines also advise on decisions about selecting effective and applicable treatment of seizures in hypertensive complicated pregnancies. Magnesium sulfate is advised and prescribed for treating seizures. In the current study, Magnesium sulfate was prescribed to 63.3% of patients as a single therapy and to 11.5% of patients in combination with diazepam to treat eclamptic seizures but only after ruling out the possibility of epilepsy with the help of electroencephalopathy. Drugs other than Magnesium sulfate for epilepsy are among the prohibited medications due to their effects on the nervous system and hence are prohibited in pregnancy. Significantly, electroencephalopathy is not indicated by NICE Guidelines or any other guidelines [12]. This is another limitation of the healthcare system where pregnant women are being advised irrationally and should be addressed at the earliest.



In the case of pregnancy, preventing GHTN is obtainable by identifying the possibility of developing hypertensive disorders if parameters of high-risk women can be identified [29]. Pregnancy itself does not cause a rise in blood pressure but rather is a stress test to numerous underlying metabolic vulnerabilities for cardiovascular diseases, atherosclerosis and other metabolic disorder risks like diabetes mellitus [30-32]. Thus, hypertension in pregnancy is a special condition with many underlying metabolic variations predating the possibility of developing similar conditions and complications in later pregnancies and the development of metabolic disorders. That is why NICE guidelines suggest family history and personal history as indicators for GHTN for the segregation of women at a high risk of developing hypertension-related complications. However, both parameters were least reported in the cohort of the study patients and need consideration of the prescribers as well as policymakers. Furthermore, the use of prophylactic drugs like aspirin is also advised by the NICE guidelines in order to prevent the complications of GHTN. A low dosage of Aspirin inhibits the synthesis of placental thromboxane  $A_2$  with a negligible effect on the vascular cyclooxygenase that is responsible for prostacyclin production. This altered ratio of prostacyclin to thromboxane  $A_2$  in the placenta is the basis of using aspirin in pregnancy in order to delay or prevent the onset of pre-eclampsia [29]. A meta-analysis of 31 randomized clinical trials including 32,217 patients reported that patients on antiplatelet agents primarily aspirin betokened a 10% reduction of pre-eclampsia, premature delivery, reduced ratios of SGA (Small of gestational age) babies, and maternal and Intra Uterine Fetal deaths [33,34]. Aspirin (75-150 mg) is advisable from 12 week until baby birth but its administration after 16 weeks of pregnancy does not reduce the risk of developing Preeclampsia [35]. Practitioners of the current study prescribed aspirin to only 10.1% of patients, thus indicating a complete noncompliance with NICE guidelines. Another complication of severe preeclampsia is HELLP (haemolysis, elevated liver enzymes and low platelet count) syndrome. The NICE guidelines categorize the platelet count below 15,000 under HELLP Syndrome. Despite, the chances of maternal death due to bleeding, only 5.1% of patients were administered platelet that was another limitation of our findings.

Lastly, NICE guideline not only provides directions for pharmacological prevention and management of pregnancy-induced hypertension but also signifies the lifestyle changes like mild exercise and supplementations during pregnancy in order to prevent the onset of gestational hypertension and future development of chronic hypertension. Not a single patient was advised for lifestyle changes by practitioners of Bolan Medical Complex Hospital, Quetta and such practice is disquieting as lifestyle modification can prove beneficial not only for the management of GHTN but also in controlling other complications that can occur during the pregnancy period.

## CONCLUSION

Our study found major insufficiencies in terms of GHTN treatment and management. A clear deviation from the guidelines was evident that can result in the development of complications among pregnant women and fetuses. Practitioners failed to identify women at high risk of developing GHTN and were unable to segregate the risk by missing essential parameters. Prevention and lifestyle modification were also not considered for the management of GHTN. In addition, most of the patient records were partially filled and were deficient in terms of standard documentation. Screening parameter for evaluation, as suggested by NICE Guidelines for segregating patients at high risk of developing GHTN and associated complications were also suboptimal. Inadequate record maintenance, as discovered in our study, highlights the significance of periodic upgrading of patient data sheets, as well as, regular auditing of medical forms and records at hospitals in order to improve and evaluate the quality of care.

## Disclosure

The authors have no conflict of interest to disclose. No funding was received for this study.

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