Original Article

TARGET ORGAN DAMAGE IN MASKED HYPERTENSION AND ROLE OF ABPM

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ABSTRACT

With the widespread use of ABPM, new phenotypes of essential hypertension have been uncovered. One of such phenotypes is the so-called masked hypertension wherein a patient has a normal office bp but hypertension on ABPM or HBPM. It is important to recognize this phenotype because it may be associated with HMOD in presence of normal office bp. We carried out a study to find out the prevalence of masked hypertension in patients who had office bp in high normal range with or without diabetes, CKD, alcohol intake, smoking, obesity, and sedentary lifestyle. The prevalence of masked hypertension was 17%. Statistically significant association was found between masked hypertension and obesity, diabetes and CKD. 29.4% of patients with masked hypertension had retinopathy, 17.9% had nephropathy, and 26.9% had LVH. Our study makes a strong case for screening for masked hypertension in all patients who present with high normal office bp with or without obesity, diabetes and CKD.

Keywords: Masked hypertension, Hypertension on ABPM/HBPM, Chronic kidney disease (CKD)

INTRODUCTION AND BRIEF REVIEW

While auscultatory mercury blood pressure metres have been the standard for decades, digital oscillometer manometers have also become more popular in the last 20 years. Ambulatory blood pressure monitors became widely used because of the implementation of this new technology. The new device allowed patients to check their own blood pressure at home, as opposed to the general practitioner's office, and it also allowed for ambulatory blood pressure monitoring and a more thorough examination of blood pressure variations.

In the management of adult hypertension, the use of ambulatory blood pressure monitoring devices is particularly widespread. Because the fluctuations in blood pressure values collected in this way more clearly correlate with the target organ damage. 24-hour ambulatory blood pressure monitoring is essential for both defining and accurately evaluating cardiovascular risks. This tool which has been in use for the past ten years, also makes it possible to tell the difference between white coat hypertension and masked hypertension. White coat hypertension is when the blood pressure readings taken in the doctor's office are consistently higher than the readings taken at home, which are normal. The results are high at home but normal in the doctor's office when there is masked hypertension.

The scientific knowledge on 24-hour ambulatory blood pressure monitoring tests conducted on teenagers and adults is also helpful in episodic hypertension and drug resistance.

Thomas G. Pickering described a syndrome in 1992 where a few patient's office blood pressure levels were within the normal range, but their home or 24-hour ambulatory blood pressure readings were hypertensive (Thomas G. Pickering 1992)[1]. Status of blood pressure was not questioned. When Sokolow and his colleagues published the first report utilizing ambulatory blood pressure monitoring in the 1960s, the first seeds of doubt were planted (Thomas G. Pickering *et al* 2005) [2]. It was discovered in one of these studies that ambulatory blood pressure monitoring is a stronger predictor of target organ damage than casual blood pressure monitoring. It was also demonstrated that ambulatory blood pressure monitoring is a better predictor of cardiovascular mortality (Skolow *et al* 1966)[3]. A clinical condition known as "masked hypertension" is when a patient's office or clinic blood pressure readings are within the normal range, but their 24-hour ambulatory blood pressure or home blood pressure readings are higher than normal. The diagnosis of masked hypertension offers a significant clinical difficulty and calls for the attending physician to have a high index of clinical suspicion. It takes 24-hour ambulatory blood pressure monitoring to diagnose masked hypertension (Dimitris P *et al* 2007)[4]. The diagnosis of masked hypertension offers a significant clinical difficulty and calls for the attending physician to have a high index of clinical suspicion.

Like isolated office hypertension, masked hypertension is common in the population. People who are more likely to develop cardiovascular issues, such as those with renal disease, diabetes, obesity, alcoholics, smokers, and sedentary lifestyles, should be checked for masked hypertension. It has been demonstrated that people with masked hypertension have a higher-than-average prevalence of organ damage, especially when metabolic risk factors are elevated[1-2] , target

organ damage in terms of increased left ventricular mass (LVH), hypertensive retinal disease, ratio of spot albumin to creatinine, carotid intima media thickness, pulse wave velocity, central aortic blood pressure. Pulse Wave Velocity and central aortic blood pressure are utilized to check for target organ damage (E J Kim *et al*)5. Both parameters – pulse wave velocity and central aortic blood pressure - were introduced after 2017 and have fundamentally altered how we see target organ damage in masked hypertension. The development of target organ damage in masked hypertension is implied by a rise in central aortic pressure or pulse wave velocity in the patient.

Cardiovascular:
Heart failure, ischemic heart disease, left ventricular hypertrophy and atherosclerosis are few of the cardiovascular consequences of masked hypertension.

Hypertensive Retinopathy7:
Fundoscopy is used to demonstrate hypertensive retinopathy. Keith and Wagner have categorized the alterations in the fundus associated with hypertensive retinopathy.
Grade 1: Tortuosity (twisting) of retinal arteries with increased reflectiveness (silver wiring).
Grade 2: grade 1 plus arterio-venous nipping (thickened retinal arteries pass over retinal veins)
Grade 3: grade 2 plus flame shaped hemorrhages plus cotton wool exudates
Grade 4: grade 3 plus papilledema.

Hypertensive Nephropathy:
The oldest method of detection is by spot urine albumin creatinine ratio. Microalbuminuria, which indicates 30 mg/g to 300 mg/g of albumin, is detected by spot albumin creatinine ratio. The initial indicator of endothelial dysfunction brought on by hypertension is microalbuminuria. The only drawback to this is that it is not specific to masked hypertension; it can also happen in other illnesses, like diabetes, etc.

Carotid intima Media Thickness:
It is one of the earliest indicators to show target organ damage in masked hypertension that is not being seen. It can be measured with an MRI or an ultrasound scan in B mode. Normal carotid intima media thickness ranges from 0.4 to 0.5 mm at age 10, increasing to 0.7 to 0.8 or greater by the end of the fifth decade.

Pulse Wave Velocity:
Vascular ageing affects anyone with known hypertension or masked hypertension (vessels becoming stiff). So, pulse wave velocity serves as an indirect indicator of vessel wall stiffness, which is a sign of target organ damage.5

Hypertension or masked hypertension causes vascular ageing, stiffens the blood arteries, and increases pulse wave velocity, which is a sign of target organ damage. The initial indicators of target organ damage in masked hypertension are pulse wave velocity and central systolic blood pressure. Arterial stiffness is the square root of the pulse wave velocity. Loss of elastin is a side effect of hypertension. Pulse wave velocity should constantly be examined in central vessels because they are formed of elastin (Carmel M. Mceniery *et al* European Heart Journal 2014).

Central Systolic Pressure/Central Aortic-Blood Pressure:
Before hypertension-related consequences such left ventricular hypertrophy, ischemic heart disease, or endothelial dysfunction manifest, central systolic pressure foretells target organ harm6.

One out of every 7-8 people with normal blood pressure in a clinic or doctor's office may have high blood pressure during their typical everyday activities. Usually, this condition is described as masked hypertension. Depending on patient features, communities investigated, and various definitions of masked hypertension, prevalence differs among research papers. 24-hour ambulatory blood pressure monitoring and home blood pressure monitoring have both been used extensively to identify patients with masked hypertension. Various elements have been noted as potential predictors of masked hypertension. In ordinarily normotensive people, cigarette smoking, alcohol use, physical activity, a stressful work, and psychological stress can raise blood pressure outside of a professional setting, which can result in masked hypertension9.

In most investigations, target organ damage was more in patients with masked hypertension and chronic hypertension as compared to normotensive patients. The risk of significant cardiovascular illness was 1.5–3 times higher in subjects with masked hypertension than in those with normotension and it was like that of individuals with chronic hypertension (Fabio Angeli et al. American Heart Journal 2007. 7

Cross-sectional studies have revealed considerable variations in the prevalence of masked hypertension, which ranged between 8 and 38%9. These variations have been related to various patient traits, populations investigated, and masked hypertension criteria. Indeed, few studies were done on the public, various on normotensive participants who were referred, yet others untreated or treated hypertensive patients, various on older persons, and various, particularly in men.

In research, office blood pressure was measured using a mercury sphygmomanometer, however numerous studies also used automatic Oscillometer equipment while some used 24-hour ambulatory blood pressure monitoring. The individuals participating in the evaluation of office blood pressure and the position used to take the readings may have been more important in explaining the variation in the incidence of masked hypertension.

The prevalence of masked hypertension did not significantly alter when diagnosis was based on self-measured blood pressure or 24-hour ambulatory blood pressure monitoring, which is notable. It is still unclear if masked hypertension, as determined by selfmeasured blood pressure or 24-hour ambulatory blood pressure monitoring, is reproducible. There are very few data that have systematically investigated this matter worth of mention is a recent retrospective analysis on middle-aged subjects by Ben-Dov et al 10 and a prospective study by Lurbe et al 11 in youths. Ben-Dov et al10 examined a cohort of 196 subjects (mean age 58 years, 59% female, 73% treated for hypertension) who did 24-hour ambulatory blood pressure monitoring; masked hypertension (or "isolated ambulatory uncontrolled hypertension") was defined as abnormal daytime blood pressure ($\geq$135/85mmasked hypertension) with normal office blood pressure. Prognostic significance of 24-hour ambulatory blood pressure monitoring and home blood pressure monitoring over office blood pressure measurement is well documented in various cross-sectional and longitudinal. Several studies of the prognosis of masked hypertension suggest that it portends risks for cardiovascular morbidity and mortality that are comparable to the risks of sustained hypertension, both being much higher than those of normotensive patients. Verdecchia et al12 and Pickering and James, for example, assessed the long-term prognosis of masked hypertension using an international ambulatory blood pressure database, including data from the New York prognostic effects of 24 hour ambulatory blood pressure monitoring (Nypeap)13; the progettoipertensione umbria monitoraggio ambulatories (Piuma)14 from Italy and the Ohasama study15 and the Jichi medical school (JMS)–24 hour ambulatory blood pressure monitoring study were both from Japan16. A total of 1,272 people (135/85 mm Hg) had normal office blood pressure; all others were normotensive according to both criteria. The rate of cardiovascular events was higher in people with masked hypertension than in people with normal blood pressure, according to the authors. Although not all researchers have done so, several have supported similar conclusions. For instance, the International Database of Ambulatory Blood Pressure in Relation to Cardiovascular Outcome (Idaco) group evaluated 7,030 randomly selected adults from Belgium, Denmark, Japan, and Sweden for the risk of masked hypertension.

In multivariable analyses using true normotension as the reference, the adjusted hazard ratios for all cardiovascular events were also found in the SHEAF (self-measurement of blood pressure at home in the elderly: assessment and follow-up) study17 using controlled hypertension as the reference group. The relative risk of cardiovascular events was found to be higher in patients with uncontrolled hypertension and in those with masked hypertension.

Target organ damage in masked hypertension was initially discussed by Liu and colleagues in 1999. Patients with masked hypertension had carotid plaque more frequently (28%) than true normotensives. In the seminal study18 of 61 masked hypertensives, 64 sustained hypertensives, and 234 true normotensives; as a result, target organ damage in masked hypertensives was like sustained hypertensives in terms of their left ventricular mass index, which was on average 13 g/m2 higher than in normotensives. Since then, research have looked at target organ damage in patients with masked hypertension, considering antihypertensive therapy status and masked hypertension in children. Target organ damage in masked hypertension in populations without treatment have supported Liu et al19 findings.

Moreover, it was discovered that masked hypertensives had target organ damage levels that are higher than those of real normotensives, or that they have intermediate values between true normotensives and persistent hypertensives. An analysis of the Pamela study20, a longitudinal epidemiologic study involving 3,200 Italian men and women (of whom 1,637 were untreated), showed that masked hypertensives had higher left ventricular mass index and a higher prevalence of left ventricular hypertrophy than true normotensives, but had lower left ventricular mass index and left ventricular hypertrophy than sustained hypertensives. Kotsis et al21 discovered that, on average, masked hypertensives had larger left ventricular mass index and carotid intima media thickness than normotensives in a study of 1,535 untreated participants and found that masked hypertensives have more target organ damage than true normotensives, they have levels of target organ damage comparable to those of sustained hypertensives or have intermediate levels between true normotensives and sustained hypertensives. An analysis from the Pamela study20 a longitudinal epidemiologic study of 3,200 Italian men and women (of whom 1,637 were untreated) demonstrated a higher left ventricular mass index and higher prevalence of left ventricular hypertrophy among masked hypertensives than among true normotensives, but lower left ventricular mass index and left ventricular hypertrophy prevalence than among sustained hypertensives. In a study of 1,535 untreated individuals, Kotsis et al21 it was discovered that, on average, masked hypertensives had higher left ventricular mass index and carotid intima media thickness than normotensives. Matsui et al 22 found that in their study of untreated individuals, masked hypertensives had higher carotid intima media thickness than the other categories of hypertensives, and that their pulse wave velocity, a measure of arterial stiffness, was significantly higher than that of normotensives and sustained hypertensives.

Target organ damage and masked hypertension have not been consistently linked in the Uppsala longitudinal study and

according to a few other studies in untreated patients. The population-based cohort study of adult men23, found that real normotensives and masked hypertensives had similar mean left ventricular mass index values. Although masked hypertensives showed higher relative wall thickness than both the normotensive and sustained hypertension groups, this finding suggests that masked hypertensives may have had more concentric remodeling (a precursor to concentric left ventricular hypertrophy) than the other groups Bombelli *et al*. The Pamela Cohort's 1,653 untreated participants were analyzed, and no correlation between masked hypertension and left ventricular mass was discovered. Ormezzano *et al*24 found no significant differences in left ventricular mass index and proposed treatment algorithm for patients with masked hypertension.

Now that we have made the argument that patients with masked hypertension should be treated based on the increased cardiovascular risk and target organ damage, what should a management algorithm be is the question. All patients who have high normal office blood pressure should undergo home based blood pressure monitoring or 24 hour ambulatory blood pressure monitoring to rule out masked hypertension .If patients are found to have masked hypertension (>135/85 mm hg by either home based blood pressure monitoring or 24 hour ambulatory blood pressure monitoring), the 24 hour ambulatory blood pressure monitoring should be repeated within 2 months, to confirm the diagnosis (similar to the recommendation for diagnosis of hypertension). Patients whose home-based blood pressure monitoring reading falls within the high normal range should have a confirmatory 24-hour ambulatory blood pressure monitoring because patients whose blood pressure is in the high range of prehypertension have a greater rate of masked hypertension. Once masked hypertension is identified, patients should undergo a thorough evaluation of their cardiovascular risk (including an ECG, a fasting lipid profile, a fasting glucose profile, a basic metabolic profile, and a urinalysis), and they should receive the same antihypertensive medication as patients with sustained hypertension.

Considering the foregoing, the study to investigate the "Target Organ Damage in Masked Hypertension" was conducted and, the aim for the study was set: To evaluate patients for target organ damage in masked hypertension in highly suspected patients using 24hr Ambulatory blood pressure monitoring, Electrocardiogram, Echocardiography, fundoscopy, Ultrasound scan abdomen pelvis, routine urine examination, urine spot albumin to creatinine ratio, carotid intima media thickness.

MATERIALS AND METHODS
Type of Study:
Hospital based study of patients >18 years of age with suspected masked hypertension coming to OPD of Shri Maharaja Hari Singh and associated hospitals over one and a half year. All suspected cases will be screened using 24hr Ambulatory blood pressure monitoring and will be evaluated for target organ damage.

Brief Description of Methods and Procedures:
Study Centre: Tertiary care medicine outpatient department at Shri Maharaja Hari Singh Hospital Srinagar
Study Design: The study was a cross sectional observational study. No specific intervention was done. Patients were included in the study through random selection. No specific method of randomization was used. No controls were used in the study.
Study Period: One and half year
Sample Size: 400 patients out of which 276 were males and 124 were females who satisfied the inclusion and exclusion criteria were enrolled in the study.
History: History of risk factors including kidney disease, diabetes, alcoholics, smoking, sedentary lifestyle, high normal blood pressure.
Examination: Pulse, Blood Pressure, Oxygen Saturation (SPO2), Respiratory rate, Temperature, Relevant physical examination, Detailed cardiovascular examination.
Lab Investigations: Complete blood count, Kidney function test, Liver function test, Lipid profile, Blood glucose, Blood Sugar Fasting, Blood sugar post prandial, HBA1c, Routine urine examination, Urine albumin to creatinine ratio (ACR), Thyroid function test.

24hr Ambulatory blood pressure monitoring:
Measuring blood pressure outside the office setting with 24-hour ambulatory Blood pressure monitoring. Captures the effects of normal daily activities on blood pressure, provides information on the behavior of blood pressure during sleep and provides a greater number of readings than can be obtained during a typical office encounter.

The categories used for grading were:

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120-129	and/or	80-84
High Normal	130-139	and/or	85-89
Grade 1 hypertension	140-159	and/or	90-99

Grade 2 hypertension	160-179	and/or	100-109
Grade 3 hypertension	≥ 180	and/or	≥ 110
Isolated Systolic hypertension b	≥ 140	and/or	<90

BP Category was defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension was graded 1, 2, or 3 according to SBP values in the ranges indicated. The same classification was used for all ages from 16 years.

Electrocardiogram: Left ventricular hypertrophy, ischemic heart disease. Left ventricular hypertrophy was diagnosed by Cornell Voltage Criteria.
Chest X-ray: Target organ damage on chest X-Ray can be seen in the form of cardiomegaly. On chest x ray cardiomegaly is said when cardio thoracic ratio is greater than 0.5.
Echocardiography: Target organ damage on Echocardiography can be demonstrated in terms of Left ventricular hypertrophy, Diastolic dysfunction, ischemic heart disease.
Fundoscopy: Target organ damage on fundoscopy is demonstrated by fundus changes as described by Keith and Wagner grading.
Ultrasound scan abdomen & pelvis: Target organ damage in terms of chronic kidney disease (hypertensive nephropathy.
Carotid intima media thickness Increased Carotid intima media thickness represents atherosclerosis. B mode Ultrasound scan was used to measure Carotid intima media thickness.

Subject Selection:
Inclusion Criteria: Adult males and females >18 years of age, Diabetics, Chronic Kidney disease, Alcoholics, Smokers, Obese, Sedentary lifestyle.
**Exclusion Criteria:** Age< 18, Known hypertensives, Patients reluctant to participate.

RESULTS
The results of the study conducted on 400 patients are presented here.

The age of the study patients ranged from 21 to 89 years, with mean age being 47.66 and standard deviation of 15.35. Greater proportion of the study patients belonged to the age group 30-39, followed by 50-59. The overall results related to the age distribution of patients is presented in the Table 1.

Table 1: Age distribution of study patients		
Age (Years)	**Number**	**Percentage**
20-29	49	12.3
30-39	103	25.8
40-49	67	16.8
50-59	81	20.3
60-69	57	14.2
70-79	41	10.3
80-89	2	0.5
Total	400	100
Mean±SD (Range) = 47.66 ±15.35 (21-89 Years)		
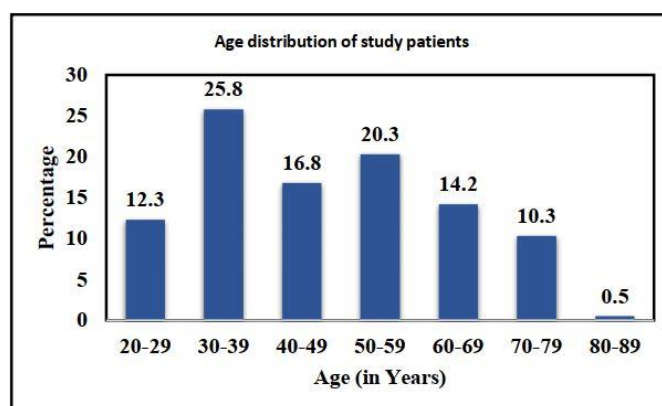
As for the gender of the patients is concerned, it is revealed from the above table that the maximum number of patients 276 (69%) belonged to male group and 124 (31%) belonged to female group. The Male: Female ratio came out to be

2.23:1. The results of the gender distribution of the study patients is presented in Table 2.

Table 2: Gender distribution of study patients		
Gender	**Number**	**Percentage**
Male	276	69
Female	124	31
Total	400	100
Male: Female=2.23:1		
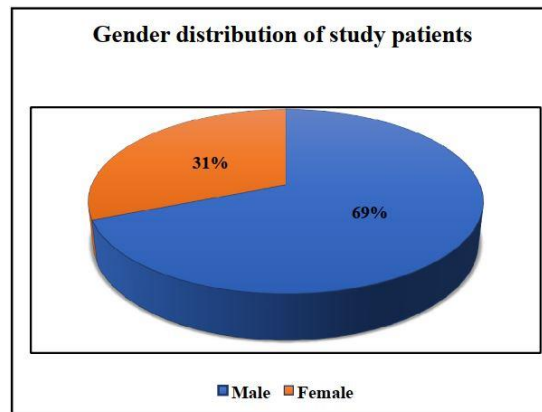
The patients were assessed for the comorbidities and Obesity was one of the chief comorbidities and out of 400 patients, 123 (30.8%) were Obese, followed by chronic kidney disease, with 87 patients out of 400 (21.8%), 94 (23.5%) patients were diabetic, 68 (17%) patients were smokers, 15 (3.8%) had Sedentary lifestyle, and 9 (2.3%) were alcoholic. Rest of the patients had a combination of comorbidities. The results are presented in Table 3.

Table 3: Distribution of patients based on comorbidities		
Type	**Number**	**Percentage**
Obesity	123	30.8
Chronic kidney disease	87	21.8
Diabetes	94	23.5
Smoking	68	17
Sedentary Lifestyle	15	3.8
Alcoholic	9	2.3
Chronic kidney disease + Diabetes	1	0.3
Obesity + Diabetes	1	0.3
Obesity + Dyslipidemia	1	0.3
Smoker + Diabetes	1	0.3
Total	400	100
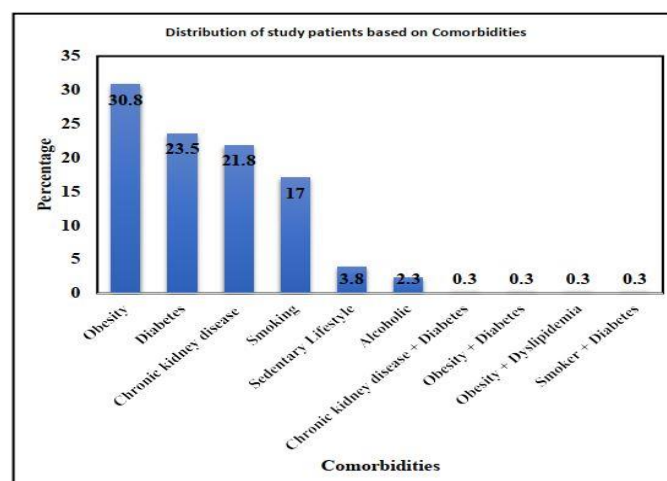
The prevalence of masked hypertension was 68 out of 400 study patients, constituting 17% of the study population. The results are presented in Table 4.

Table 4: Distribution of patients based on presence and absence of masked hypertension		
Masked Hypertension	Number	Percentage
Yes	68	17
No	332	83
Total	400	100
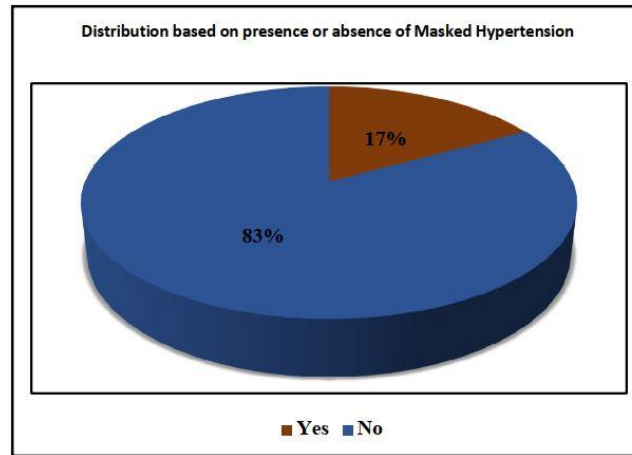
Among 68 masked hypertension patients, 27 were males and 41 were females. The variable gender is not significantly associated with masked hypertension as the respective p-value is greater than 0.05. The results are presented in Table 5.

Table 5: Association of gender with masked hypertension		
Variable	Number of patients with masked hypertension	P-value
Gender	Male	27	0.08
	Female	41	

Among 68 masked hypertension patients 40 were Obese and 28 were not obese. 45 were diabetic and 23 were not diabetic, 12 were smokers and 56 were non-smokers, 32 had chronic kidney disease and 36 did not have. Moreover among 9 alcoholic patients 6 had masked hypertension and 3 were non-alcoholic.

Further, the variables obesity, diabetes and chronic kidney disease were associated with masked hypertension as for these variables the p-value was less than 0.05. However, for the variables smoking and alcoholic the respective p-values were 0.07 and 0.09 which were both greater than 0.05, thus making smoking and alcoholic not significantly associated with masked hypertension. The results of which are presented in Table 6.

Table 6: Association of comorbidities with masked hypertension			
Variable		Number	P value
Obesity	Yes	40	<0.001
	No	28	
Diabetes	Yes	45	<0.001
	No	23	
Smoking	Yes	12	0.07
	No	56	
Chronic Kidney Disease	Yes	32	<0.001
	No	36	
Alcoholic	Yes	6	0.09
	No	3	

Mean age of patients with masked hypertension was significantly higher (53 years) than patients who did not have masked hypertension. (41 years) with a p-value < 0.05. The results are presented in Table 7.

| Table 7: Mean Age group (Years) with and without masked hypertension		
Masked Hypertension	Mean Age group (years)	P value
Present	53	<0.001
Absent	41	
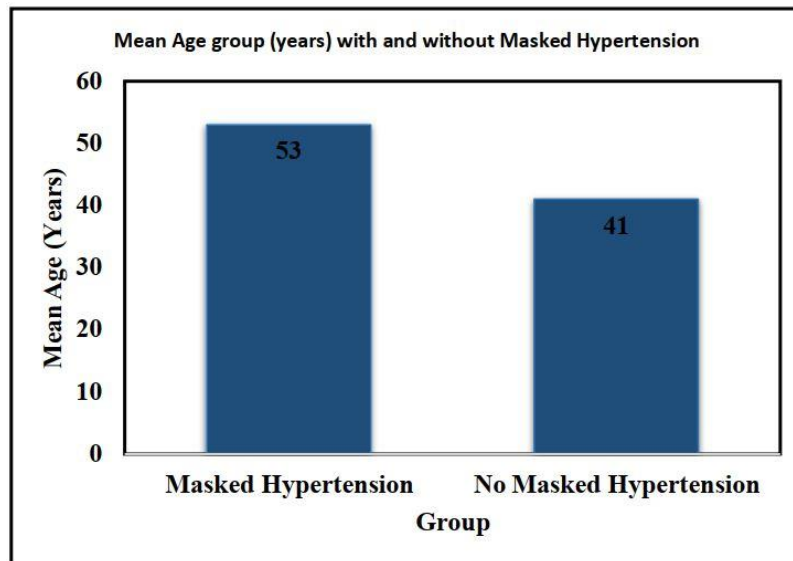
Mean Body Mass Index is significantly higher among patients with masked hypertension (29.5) than among patients without masked hypertension (23.2). This difference was statistically significant (p-value <0.05). The results are presented in Table 8

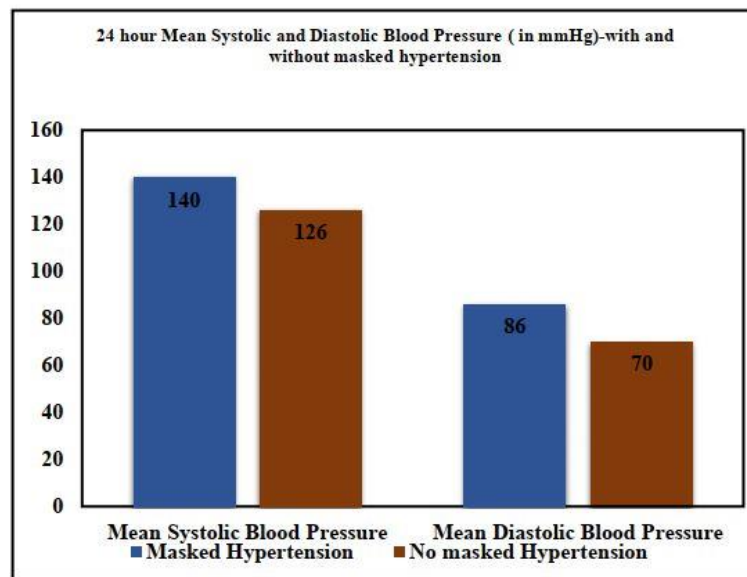| Table 8: Mean Body Mass Index- with and without masked hypertension		
Masked Hypertension	**Mean Body Mass Index**	**P value**
Present	29.5	<0.001
Absent	23.2	
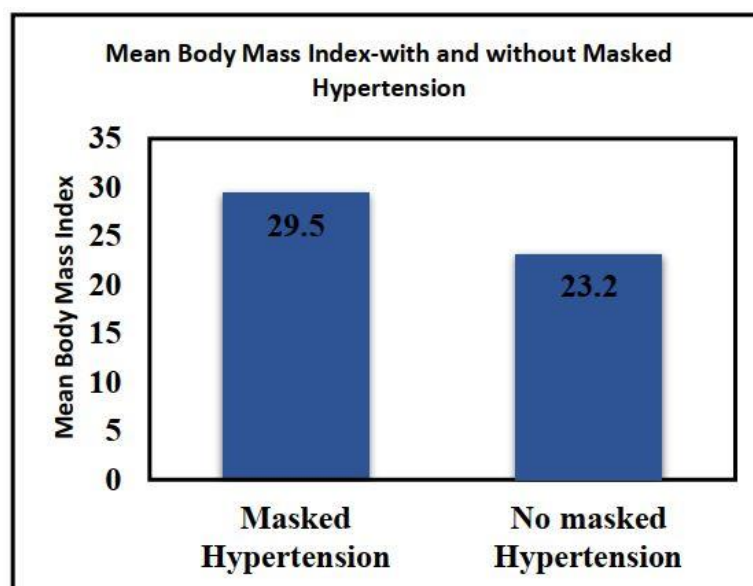
24hour Mean systolic and diastolic Blood Pressure measured in mm Hg were significantly higher i.e., 140 (systolic) and 86 (diastolic) among patients with masked hypertension than among patients who do not have masked hypertension i.e., 126 (systolic) and 70 (diastolic) respectively. (p-value <0.05). The results are presented in Table 9.

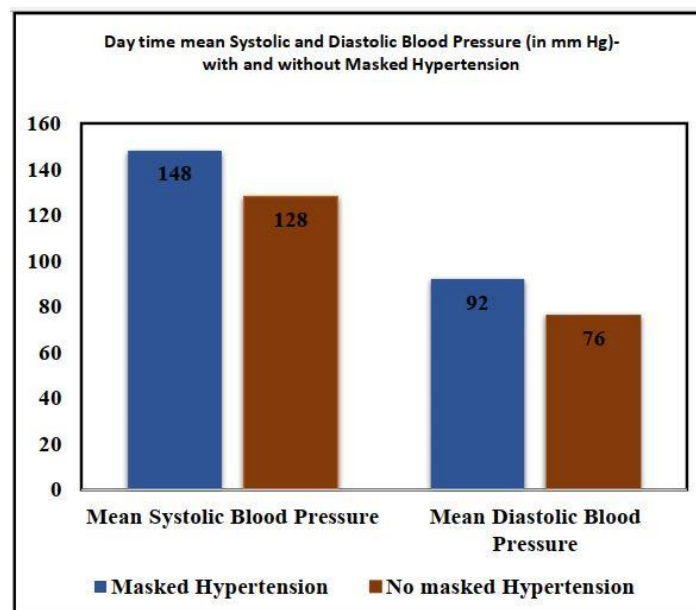| Table 9: 24 hours Mean Systolic and Diastolic Blood Pressure (in mm Hg)- with and without masked hypertension				
Masked Hypertension	**Mean Systolic Blood Pressure**	**P value**	**Mean Diastolic Blood Pressure**	**P value**
Present	140	<0.001	86	<0.001
Absent	126		70	

Daytime mean systolic and diastolic Blood Pressure measured in mm Hg were significantly higher i.e., 148 (systolic) and 92 (diastolic) among patients with masked hypertension than among patients who do not have masked hypertension i.e., 128 (systolic) and 76 (diastolic) respectively. (p-value =0.000). The results are presented in Table 10.

| Table 10: Day time mean Systolic and Diastolic Blood Pressure (in mm Hg)- with and without masked hypertension				
Masked Hypertension	Mean Systolic Blood Pressure	P value	Mean Diastolic Blood Pressure	P value
Present	148	<0.001	92	0.000
Absent	128		76	

Night-time mean systolic and diastolic Blood Pressure measured in mm Hg were not significantly higher i.e., 132 (systolic) and 80 (diastolic) among patients with masked hypertension than among patients who do not have masked hypertension i.e., 110 (systolic) and 58 (diastolic) respectively. (p-value =0.038). The results are presented in Table 11.

| Table 11: Night-time mean Systolic and Diastolic Blood Pressure (in mm Hg)- with and without masked hypertension				
Masked Hypertension	Mean Systolic Blood Pressure	P value	Mean Diastolic Blood Pressure	P value
Present	132	0.040	80	|0.038
Absent	110		58	

Night time mean Systolic and Diastolic Blood Pressure (in mmHg)-with and without masked hypertension
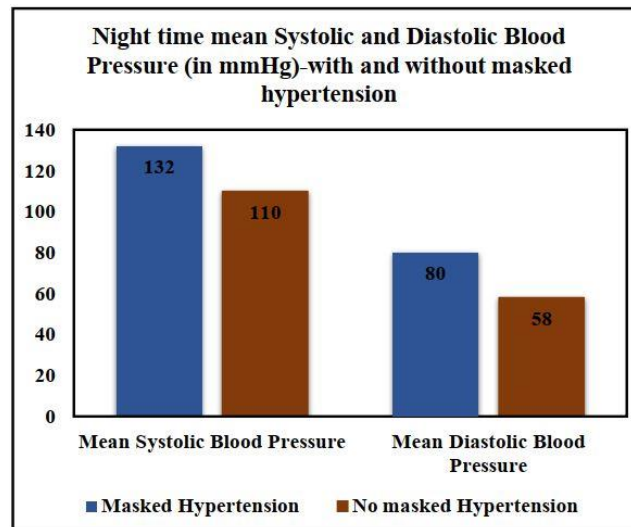
No significant difference in fasting blood sugar levels between the two groups was found (p-value <0.05).

Table 12: Fasting Blood Glucose- with and without masked hypertension		
Masked Hypertension	**Fasting Blood Glucose**	**P value**
Present	105	<0.001
Absent	97	

Fasting Blood Glucose-with and without masked Hypertension
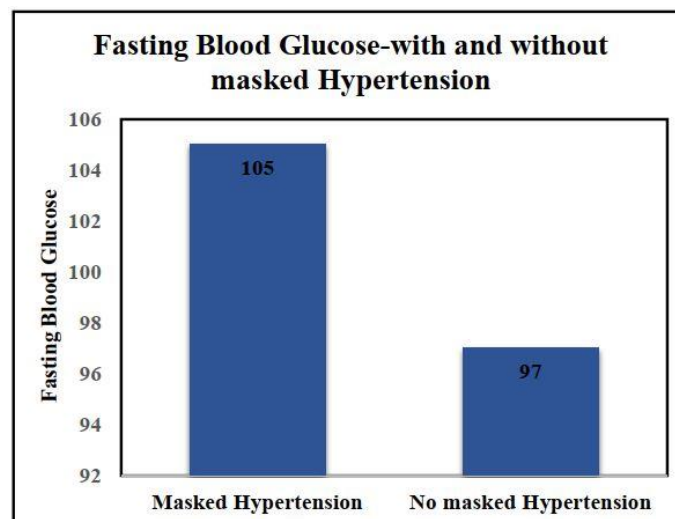
Among 68 masked hypertensive patients, 20 (29.41%) patients were positive for Hypertensive Retinopathy, 12 (17.94%) for Hypertensive nephropathy, 18 (26.47%) for Left Ventricular hypertrophy and 20 (29.41%) for Increased carotid intima media thickness.

Table 13: Evaluation of end organ involvement of the cases		
End organ	**Number**	**Percentage**
Hypertensive Retinopathy	20	29.41
Hypertensive nephropathy	12	17.94
Left Ventricular hypertrophy	18	26.47
Increased carotid intima media thickness	20	29.41

DISCUSSION AND CONCLUSION

Target organ damage and masked hypertension are on rise. Rise in one entity can be attributed to the other. India being a Diabetic Capital of the world and majority of the population is under the working group, hence the burden of non-communicable diseases is increasing. Attributes like sedentary lifestyle and shift of population from rural to urban has made the diagnosis complex.

Subjects with masked hypertension exhibited more extensive target organ damage than normotensives did, as expected

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given that 24-hour Ambulatory blood pressure is better able to predict target organ damage. It is interesting that the values of the Left Ventricular mass indices were similar in subjects with masked hypertension and those with confirmed hypertension, thereby implying that masked hypertension represents an equivalent risk for cardiovascular disease. These findings represent refinements of data from earlier studies in both adults and children. Longitudinal studies showed that subjects with masked hypertension have increased cardiovascular morbidity.

Cardiovascular and Cerebrovascular morbidity and mortality is largely due to Type 2 Diabetes mellitus and Systemic Hypertension. Prevention is better than cure. Hence, these two attributes Masked hypertension and target organ damage help us aggressively intervene at earlier stages and hence decrease the worst outcomes.

The correlation between masked hypertension and cardiac target organ damage was presented in a study carried out on adults, particularly with type 2 DM (diabetes mellitus). It has been suggested that subjects with masked hypertension have advanced target organ damage and poor cardiovascular prognosis compared to normotensive subjects. Liu et al measured target organ damage by echocardiography and arterial ultrasonography in untreated subjects with sustained normotension, masked hypertension, and ambulatory hypertension. They showed that left ventricular mass and carotid wall thickness are greater in subjects with masked hypertension compared to those with normotension, and they are like those with ambulatory hypertension. Lurbe et al also indicated that young patients with masked hypertension have a higher left ventricular mass index than normotensive subjects. It is possible that most masked hypertensives are missed because of normal office Blood Pressure, which leads the progression of target organ damage. This study provides data on the extent of target organ damage in what is, to our knowledge, the largest untreated population with the conditions to be studied to date.

Moreover, past studies have attributed prevalence of masked hypertension around 8 to 30 percent depending on the population studied. Here we approach patients with criteria fulfilling target organ damage and assess their 24hour, daytime and Night-time Blood pressure measurement through Ambulatory blood pressure monitor and unmask their hypertension which may show normal Clinic blood pressure reading.

In our study population, masked hypertensives demonstrated statistically significant differences in target organ damage when compared with subjects with normotension. We found that masked hypertension subjects had significantly higher 24-hour Ambulatory blood pressure values than confirmed normotensive subjects, thereby implying that masked hypertensive subjects may have an increased risk of becoming confirmed hypertensive patients and may require close follow-up especially in the presence of comorbidities.

Moreover, in our study, we used 24-hour ambulatory blood pressure monitoring criteria of European Society of Cardiology for labelling patients as hypertensive, which includes hypertensive patients having 24 hours mean ambulatory blood pressure monitoring greater or equal to 130/80, daytime mean ambulatory blood pressure greater or equal to 135/85 and night-time mean ambulatory blood pressure greater or equal to 120/70.

Our study was conducted on a total of 400 patients out of which 68 came out to be masked hypertensive patients. The age of the study participants ranged from 21 to 89 years. Mean was 47.66 years with SD 15.35 years. Greater proportion was males 276 (69%) and females ranging 124 (31%).

The prevalence of masked hypertension was 68 out of 400 study patients, constituting 17% of the study population. The patients were assessed for the comorbidities and Obesity was one of the chief comorbidities and out of 400 patients, 123 (30.8%) were Obese, followed by chronic kidney disease with 87 patients out of 400 (21.8%), 94 (23.5%) patients were diabetic, 68 (17%) patients were smokers, 15 (3.8%) had Sedentary lifestyle, and 9 (2.3%) were alcoholic. Rest of the patients had a combination of comorbidities. Compared with The Jackson Heart study done by Colantino et al. Impaired glucose component was around 19.2% in their study. Hence, this shows the high incidence of metabolic and masked hypertension among our population.

The variables obesity, diabetes and chronic kidney disease were associated with masked hypertension as for these variables the p-value was less than 0.05. However, for the variables smoking and alcoholic the respective p-values were 0.07 and 0.09 which were both greater than 0.05, thus making smoking and alcoholic not significantly associated with masked hypertension.

Body Mass Index also plays a major role. In the study, mean Body Mass Index was significantly higher among patients with masked hypertension (29.5) than among patients without masked hypertension (23.2).

Hypertension is one of the major reasons for clinic visit and metabolic syndrome includes major inclusion criteria as a pre hypertensive range of Systolic and diastolic Blood Pressure readings. This helps to pick up significant number of patients to intervene at the earliest and to impart lifestyle medication and drug treatment accordingly. 24 hour and daytime mean systolic and diastolic Blood Pressure measured in mm Hg were significantly higher among patients with

masked hypertension than among patients who do not have masked hypertension. However, night-time mean systolic and diastolic Blood Pressure measured in mm Hg were not significantly higher among patients with masked hypertension than among patients who do not have masked hypertension.

Cardiovascular morbidity and mortality are linked largely to lipid profile and High-density lipoproteins and Triglycerides levels are measured. No significant difference in fasting blood sugar levels between the two groups i.e., masked and sustained hypertensive patients was found.

The frequency of Hypertensive Retinopathy 20 (29.41%), Hypertensive nephropathy 12 (17.94%), Left Ventricular hypertrophy 18 (26.47%) and increased carotid intima media thickness 20 (29.41%) were comparatively higher for masked hypertensives.

In our study important parameters like Type 2 Diabetes mellitus, Chronic Kidney Disease, Obesity is statistically significant in terms of development of masked hypertension. Early diagnosing of masked hypertension helps us to address the causative modifiable risk factors in terms of metabolic syndrome and provide a concrete solution on a long-term basis and reduce disease burden on the society.

Masked hypertension is present significant numbers in our population. 24-hour Ambulatory Blood pressure monitoring can bridge this diagnostic gap and help us in early intervention. Traditional risk factors which may be modifiable or non-modifiable still play a role in development of target organ damage.

Impaired fasting glucose is a major component in the early interpretation of metabolic syndrome, and it is an important component in the diagnostic criteria for metabolic syndrome. Hence, in view of high prevalence 24-hour Ambulatory blood pressure measurement is warranted in high-risk groups with normal clinic blood pressure.

In a nutshell, masked hypertension manifests adults and causes severe target organ damage. Office blood pressure measurement techniques are insufficient to diagnose the cases with masked hypertension. As such masked hypertension is overlooked, and late diagnosed. Patients with suspected high blood pressure should be investigated thoroughly, also to establish a final diagnosis; 24-hour Ambulatory blood pressure should be performed on patients. We shouldn't settle for the office blood pressure measurements and must certainly perform 24-hour Ambulatory blood pressure for masked hypertension.

REFERENCES

1. T G Pickering the ninth Sir George Pickering memorial lecture. Ambulatory monitoring and the definition of hypertension. J Hypertens, 1992May;10(5):401-9. doi:10.1097/00004872-199205000 00001.
2. Pickering TG, Kuazuo Eguch and kazuomi Kario- Masked hypertension a review 2005;45:142-161.
3. Sokolow M, werdegar D, Karin HK, Hinman AT; Relationship between level of blood pressure measured casually and by portable recorders and severity of complications in essential hypertension. Circulation 1966;34;279 – 298.
4. Dimitris P, Papadopoulos MD, Thomas K. Makris MD: Masked hypertension definition, impact, outcome: Critical Review. http://doi.org/10.1111/ j.1524-6175.2007.07418.
5. E J Kim, C G Park, J S Park, S Y Suh, C U Choi, J W Kim, S H Kim, H E Lim, S W Rha, H S Seo, D J Oh; Relationship between blood pressure parameters and pulse wave velocity in normotensive and hypertensive subjects: invasive study. doi: 10.1038/ sj. jhh.1002120.
6. Carmel M. McEniery, John R. Cockcroft, Mary J. Roman, Stanley S. Franklin, and Ian B. Wilkinson: Central blood pressure: current evidence and clinical importance: European Heart Journal. (2014) 35, 1719–1725 doi:10.1093/eurheartj/eht565.
7. Aissopou, Evaggelia K, Papathanassiou, Miltiadis, Nasothimiou, Efthimia G. The Keith–Wagener–Barker and Mitchell–Wong grading systems for hypertensive retinopathy association with target organ damage in individuals below 55 years: Journal of Hypertension: November 2015 - Volume 33 - Issue 11 - p 2303-2309 doi: 10.1097/HJH.0000000000000702.
8. Ghodratollah Naseh, Mahyar Mohammadi Fard, Toba Kazemi, AliReza Mirgholami, Narges Hashemi, and Amin Saburi: Comparison of Carotid Intima-media Thickness in Hypertensive Patients and Control Group; J Cardiovasc Echogr. 2016 Apr-Jun; 26(2): 48–51. doi: 10.4103/2211-4122.183749.
9. D Edmund Anstey, Paul Muntner, Natalie A Bello, Daniel N Pugliese, Yuichiro Yano, Ian M Kronish, Kristi Reynolds, Joseph E Schwartz, Daichi Shimbo; Diagnosing Masked Hypertension Using Ambulatory Blood Pressure Monitoring, Home Blood Pressure Monitoring, Or Both: Hypertension. 2018 November; 72(5): 1200– 1207. Doi:10.1161/HYPERTENSIONAHA.118.11319.
10. Lurbe E. Sorof JM, daniels SR. clinical research aspects of ambulatory blood pressure monitoring in children. J pediatr.2004; 144:7-16.
11. Vasilios Kotsis, Stella Stabouli, Savvas Toumanidis, Christos Papamichael, John Lekakis et al; Target organ damage in "white coat hypertension" and "masked hypertension" Am J Hypertens.2008 Apr;21(4):393-9. doi: 10.1038/ajh.2008.15. Epub 2008 Feb 21.

12. Michele Bombelli, Elena Toso, Maria Peronio, Danilo Fodri, Marco Volpe, Gianmaria Brambilla, Rita Facchetti, Roberto Sega, Guido Grassi, Giuseppe Mancia et al: The Pamela study: main findings and perspective. Curr Hypertens Rep, 2013 Jun; 15(3):238-43. doi: 10.1007/s11906-013-0348-1.

13. Takayoshi Ohkubo, Yutaka Imai, Ichiro Tsuji, Kenichi Nagai, Sadayoshi Ito, Hiroshi Satoh, Shigeru Hisamichi; Reference Values for 24-Hour Ambulatory Blood Pressure Monitoring Based on a Prognostic Criterion the Ohasama Study; Originally published1 Aug 1998 https://doi.org/10.1161/01.HYP.32.2.255.Hypertension. 1998; 32:255–259.

14. Kristina Björklund 1, Lars Lind, Björn Zethelius, Lars Berglund, Hans Lithell; Prognostic significance of 24-h ambulatory blood pressure characteristics for cardiovascular morbidity in a population of elderly men: J Hypertens 2004 Sep;22(9):1691-7. doi: 10.1097/00004872- 200409000-00012.

15. Liu JE. Roman MJ, Pininfarina R, schwartz JE, pickering TG, Devereux RB. Cardiac and arterial target organ damage in adults with elevated ambulatory and normal office blood pressure. Ann intern Med. 1999; 131:564-572.

16. Lurbe E. Redon J, Liao Y, Tacons J, Cooper RS, Alvarez V, Ambulatory blood pressure monitoring in normotensive children. JHypertens, 1994;12;1417-1423.

17. Seiji Matsuoka · Midori Awazu: Masked hypertension in children and young adults; Pediatr Nephrol (2004) 19:651–654. DOI 10.1007/s00467-004-1459-3

18. Ozkahya M, Ok E, Cirit M, Aydin S, Akcicek F, Basci A, et al. Regression of left ventricular hypertrophy in haemodialysis patients by ultrafiltration and reduced salt intake without antihypertensive drugs. Nephrol Dial Transplant 1998; 13:1489-1493.

19. Nadar S, Lip GY. The prothrombotic state in hypertension and the effects of antihypertensive treatment. Curr Pharm Des 2003; 9:1715-1732.

20. Chou TC, Li CY, Yen MH, Ding YA. Antiplatelet effect of amlodipine: a possible mechanism through a nitric oxide-mediated process. Biochem Pharmacol 1999; 58:1657-1663.

21. Cuspidi C, Facchetti R, Bombelli M, et al. Is night-time hypertension worse than daytime hypertension? A study on cardiac damage in a general population: the PAMELA study. J Hypertens. 2017;35:506–512.

22. Folts JD. Inhibition of platelet activity in vivo by amlodipine alone and combined with aspirin. Int J Cardiol 1997; 62 Suppl 2:S111- S117.

23. Magee LA, Duley L. Oral beta-blockers for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev 2003;(3):CD002863.

24. Hernandez-Hernandez R, Armas-Padilla MC, Velasco M, Carvajal AR, Armas de Hernandez MJ, Guerrero-Pajuelo J, et al. Effects of amlodipine and enalapril on platelet function in patients with mild to moderate hypertension. Int J Clin Pharmacol Ther 1999; 37:323- 331.