ORIGINAL RESEARCH PAPER

Cardiovascular

A CROSS SECTIONAL STUDY; COMPARISON OF DIAGNOSTIC PARAMETERS AND COMORBID CONDITIONS IN HYPERTENSION ALONE AND HYPERTENSION PLUS DIABETES

KEY WORDS: Diabetes-hypertension; Type 2 diabetes; Hypertension; End organ damage

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ABSTRACT

Comorbidities such as hypertension and type 2 diabetes are widespread. Hypertension is twice as common in diabetic individuals as it is in non-diabetics. The purpose of this research was to better understand the clinical profile, laboratory features, and vulnerability to end organ damage in hypertensive patients with and without diabetes. **Method:** This was a cross-sectional observational study conducted in the outpatient and inpatient departments of Medicine. Study participants were divided into two groups according to their presence of hypertension or diabetes mellitus. Patients were examined clinically and the data was further analysed using statistical methods. **Results:** We observed the mean age of 53.08 years (±11.48) and 55.96 years (±11.23) with no associations between the age group and gender of the hypertensive patient group ($p<0.344$) and the hypertensive diabetic group ($p<0.597$). The most frequent symptom of presentation in both groups was a headache. There was a significant statistical difference in mean systolic blood pressure between hypertensive and hypertensive-diabetic group t (165.8) =4.643, $p<0.001$. Our study shows a higher value of mean HbA1c, mean postprandial glucose levels, and mean fasting blood glucose levels in the hypertensive diabetic group as compared to the hypertensive group. **Conclusion:** Our study demonstrated that end organ damage was more prevalent in hypertensive diabetic individuals, indicating the effect of diabetes-hypertension co-morbidity on target organs.

INTRODUCTION

According to the World Health Organization, more than 1 billion people worldwide are suffering from high blood pressure, a significant number of whom live in countries with poor and moderate incomes. In 2015, one man out of every four and one female out of five developed hypertension. Worldwide, hypertension is a leading cause of early mortality. (WHO,2019). Additionally, between 1980 and 2008, the number of patients with uncontrolled hypertension was found to have grown globally owing to population expansion and aging. [1]

Hypertension is a disease where arterial blood pressure is unusually high. Normal blood pressure is defined by the Joint National Committee 7 (JNC7) as a systolic blood pressure less than 120 mmHg and a diastolic blood pressure less than 80 mmHg. Due to hypertension's widespread Prevalence around the world, it is a significant public health concern. [2-4] Hypertension is the leading cause of preventable deaths and illnesses in India. It is a major predisposing factor for heart disease, which caused more than 30% of adult deaths between 2010 and 2013. [5] According to the Worldwide Burden of Hypertension research, India accounted for 18% of the worldwide overload of 212 million Years of Disability-Adjusted Life (DALYs)due to high blood pressure in 2015. [6] The number of people suffering from high blood pressure in India is predicted to increase significantly in the following years due to fast environmental and 'lifestyle' changes brought about by dangerous working conditions and increased societal demands to survive. [7]

Diabetes mellitus (DM) is a group of metabolic diseases described by chronically increased blood sugar levels. Diabetes affects and impairs every body system, such as cardiovascular, neurological, kidney, etc. [8-10] Diabetes afflicted approximately more than 450 million people worldwide in 2019, with type 2 diabetes responsible for around 90% of cases. [11] Rates are comparable between males and women. [12] Based on previous patterns, values are projected to continue to rise ahead. Diabetes increases an individual's risk of death by more than twice prematurely. Diabetes claimed > 4 million lives in 2019. It is the 7th leading cause of mortality worldwide. [13,14]

Comorbidities such as type 2 diabetes and hypertension are widespread. Hypertension is much often observed in diabetic individuals than it is in non-diabetics.

Cardiac disease is the main reason for morbidity and death in diabetes, which is potentiated by hypertension. Due to shared predisposing factors, diabetes and hypertension are inextricably connected. Additionally, there is considerable convergence in the cardiovascular consequences of hypertension and diabetes, which are predominantly caused by micro-and macrovascular pathology.

Numerous research on hypertension developing in diabetic individuals is accessible in the literature; however, there are fewer investigations on diabetes as a comorbidity. Recognizing and effectively treating these two factors may be critical in lowering cardiovascular mortality in India. The goal of this study was to get a better understanding of hypertension individuals with and without diabetes' clinical profile, laboratory characteristics, and susceptibility to end organ damage.

Methods

Study Population:

This was an observational cross-sectional study conducted in Medicine out-patient and in-patient departments of Dr. D Y Patil Hospital, Nerul, over twelve months, from February 2019 to February 2020.

Patients above eighteen years of age of either gender who were diagnosed essential hypertension (JNC 7) and diabetes were included in the study. Pregnant females, patients with secondary hypertension, gestational Diabetes mellitus, and Type 1 DM were excluded from the study.

Ethics approval from the institution's ethics committee was obtained prior to the study's initiation.

Sample Size Calculation:

The sample size was calculated with the help of the formula: (p=present prevalence, q=100-p, L= 15% of p),

$N= 4pq/l^2$

The minimum sample size estimated was 180. We analyzed 200 samples; out of them, 100 were hypertensive subjects, and 100 were hypertensive diabetic subjects.

Study Procedure:
The study participants were assessed and enrolled based on inclusion and exclusion criteria. Written informed consent was obtained from all participants before conducting standardized interviews.

From the sample size, 200 study subjects selected, two groups were done based on the criteria of presence of hypertension and diabetes mellitus (Table 1).

The data was collected through predesigned data collection forms and all participants were interviewed in a standardized manner. The data included demographic information, symptoms such as headaches, sweating, giddiness, and chest pain, as well as family history and personal background such as addiction. In addition, patients were examined clinically, and their body mass index (BMI) and blood pressure (BP) were measured and noted. Laboratory parameters were collected from all the study subjects, including haemoglobin, fasting blood glucose levels, postprandial blood glucose levels, HbA1c levels, total cholesterol, total cholesterol, LDL, HDL, creatinine, and BUN levels. Furthermore, end-organ damage was assessed using nonbiochemical markers such as 2D Echo, Fundoscopy, USG Abdomen, and ECG.

Statistical Analysis:
Analyses of all data were performed using appropriate statistical tests. Qualitative data were expressed in percentage, and quantitative data were expressed as mean ±standard deviation. Between two sets of parametric numerical data, the unpaired t-test was utilized; for more than two groups, Levene's test was employed. The chi-square test was used for two groups of parametric categorical data, while Levene's test was used for more than two groups. A p-value of <0.05 was considered significant, assuming a normal distribution of dependent variables and randomization of independent variables.

RESULTS
The mean age in Group A (hypertensive subjects) was 53.08± 11.48 years, while it was 55.96± 11.23 years in Group B (hypertensive with diabetes). There were no associations between the age group and gender of the hypertensive patient group (p<0.344) and the hypertensive diabetic group (p<0.597). There was no significant difference between the two groups when comparing the history of addiction with the gender of study participants. In the present study in both Group A (83%) and Group B (81%), headache was the commonest symptoms of presentation. (table 2).

Mean systolic BP was 146.6± 18.35 mmHg in group A and in group B it was 136.62± 11.44 mmHg. There was significant statistical difference in mean systolic blood pressure between hypertensive and hypertensive-diabetic group t (165.8) =4.643, p<0.001. Conversely, the mean diastolic blood pressure (83.66*12.0) was significantly higher in the group B than in the group A (76.98*6.46), and the difference was statistically significant (p = 0.0001).

In hypertensive group 39% patients had normal BMI, 38% were overweight and 21% were obese. In hypertensive diabetic group, 27% had normal BMI, 41% were overweight and 28% were obese. BMI more than 25 was found in 59% in hypertensive subjects whereas 68% subjects from hypertensive diabetic group, BMI was more than 25. Mean BMI was 26.68 (± 4.31) in group A which was lower than mean BMI 27.30 (± 4.87) of group B, with no statistical difference in both groups (p<0.347). (figure: 1, Figure: 2)

Overall, mean Hb level was 12.66 gm% in group A which was higher as compared to group B in which mean Hb level was 11.92 gm% with a significant statistical difference (t (198) = 2.68, p<0.008).

Mean postprandial blood sugar level was 118.12 mg/dl in group A as compared to 246.87 mg/dl in group B and there was significant statistical difference in mean fasting blood sugar level between both the group (p<0.001). While mean HbA1c in group B (8.3) as compared to group A (4.3) and this difference in mean was found to be significant in both the groups (p<0.00.1)

Mean creatinine level was 1.06 in group A and in group B it was 1.07 and this difference in mean was not significant statistically (p<0.888). Overall mean BUN level in Group A (16.27 mg/dl) and group B (29.64 mg/dl) were statistically significant (p<0.0001).

Total cholesterol levels of group A (192.1 mg/dl) and group B (192.6 mg/dl), were not found significant. t (198) = 0.091, p<0.927. Similarly, there was no significant difference in the mean level of triglyceride level between the groups (p<0.927). But, when we compared the mean level of LDL from group A (118.1 mg/dl) and group B (91.5 mg/dl), the difference was found to be significant. p<0.001, similarly mean HDL level from group A (43.36 mg/dl) was significantly higher as compared to HDL level from group B (40.02 mg/dl). (p<0.019)

End organ damage was more common in subjects having hypertension with diabetes ad comorbidity in our study. 44% (20% males and 24% females) from the hypertensive group and 57% (25% males and 32% females) from the hypertensive diabetic group had one or other complication related to end organ damage. In the hypertensive group, the most common end organ damage was retinopathy both in male (29.2%) and in female (27.1%) followed by CAD. CKD was more common in the hypertensive diabetic group as compared to the hypertensive group both in male and female.

DISCUSSION
The combination of hypertension and diabetes increases the risk of vascular problems and may hasten their progression. It is also critical to understand hypertension and diabetes occurrence and significant risk factors related to them (gender, hyperlipidemia, and central obesity) in hypertensive patients, particularly in the urban environment. We observed the mean age of 53.08 years (±11.48) and 55.96 years (±11.23) in hypertensive subjects and hypertensives with diabetes as comorbidity, respectively. Our findings are comparable to those of another Indian study by Salagre SB et al., who found that the mean age of individuals in the research who also had diabetes was 57.88±10.72 years.[15]

Eguchi et al. found a mean age of 67±8.8 years in an analysis of hypertensive people with diabetes conducted in Japan.[16] Taiwanese researchers Chi-Neng Hsu and colleagues showed that the mean age of hypertension patients with metabolic syndrome was 65.3±12.1 years.[17] Our cohort's mean age of hypertensive diabetic patients is over ten years younger than those reported in Japan and Taiwan, indicating a younger population afflicted and emphasizing the need to study the effect of hypertension and diabetes on essential organs.

Similarly, more than 35% of patients in both groups in the current research had a history of addiction. A study conducted by Salagre SB et al which shows smoking (8%), tobacco (26%), alcohol (9%) and mixed addictions were in 15.2% patients.[15]

Although most individual social and behavioral risk factor assessments are highly associated with disease development,

health monitoring may be more frequent in individuals with a more significant overall social and behavioral burden such as addiction than patients with similar clinical profiles but lower general social and behavioral risks.[18]

In the present study in both hypertensive and hypertensive diabetic groups, the headache was the most typical symptom of presentation. In another comparable scientific work, giddiness was the most often reported symptom.[15]

In hypertensive individuals, the presence of nonspecific headache has paradoxical importance in that it is linked with a high-risk profile. Both patients and clinicians recognized headache as a warning sign, transforming the "silent killer" into an asymptomatic condition. Probably, such symptomatic individuals were more carefully watched and treated aggressively for hypertension or other risk factors; however, this is hard to confirm in the absence of data on BP changes and medication usage. Compliance with treatment is also expected to be greater in symptomatic hypertension patients since antihypertensive medication directly affects headache alleviation.

In the current analysis, we noted a BMI of more than 25 in 59 percent of hypertension patients and 69 percent of hypertensive-diabetic patients, respectively. The results corroborate previous research implicating body mass as a significant risk factor for hypertension. Increased body mass index (BMI) has been shown as a significant predictor of hypertension in several research conducted in India and overseas.[19-21]

Ghulam Choudhary et al. found a statistically significant correlation between hypertension and obesity indices. In this investigation, hypertension was identified in 83.1% of individuals with a high BMI .[22]

A meta-analysis by Giridhara Babu and colleagues found that obesity is strongly linked to hypertension, even when confounders are considered. [23] In the current study, mean systolic blood pressure was observed in hypertensive diabetic group than hypertensive alone patients. However, no significant difference in diastolic blood pressure indicates systolic hypertension. The study conducted by Salagre SB et al. reported higher mean systolic and diastolic blood pressure in hypertensive subjects with diabetes. Likewise, Thakur S et al. found that individuals with metabolic syndrome had considerably higher mean systolic and diastolic blood pressures than those who did not have metabolic syndrome.[24]

People with diabetes were found to have a 37.4% prevalence of isolated systolic hypertension. This might be linked to artery structural changes, notably large artery stiffness and loss of vascular compliance, significantly beyond 40. In type 2 diabetes, macrovascular and microvascular problems are highly related to systolic blood pressure. As a result, effective and conveniently attainable strategies for lowering systolic blood pressure in type 2 diabetes patients should be used.[25]

Joshi et al. reported that one-quarter of participants had a family history of diabetes in significant SITE research.[26] In the current research, hypertensive diabetic participants had a higher prevalence of family history of diabetes, whereas hypertensive subjects had a higher majority of family history of hypertension. Positive family history patients need a more understandable approach.

The mean Hb level in the hypertension group was 12.66 gm%, which was significantly higher than the mean Hb level in the hypertensive-diabetic group, which was 11.92 gm%. The mean BUN level in the renal parameters was likewise considerably higher in the hypertensive-diabetic group. Our findings may be compared to those of Salagre SB et al. [15] Additionally, this research demonstrates that hypertensive diabetics have higher S. Creatinine levels and BUN. Diabetes-related kidney damage is progressive, and anemia may contribute to this development. One such explanation is renal ischemia induced by decreased oxygen supply caused by low hemoglobin. Hypertensive people have reduced eGFR, which contributes to diabetic kidney damage. Anemia in this population is widespread and is associated with decreased quality of life and an increased risk of harmful consequences, including death. Anemia treatment can potentially improve one's quality of life.[27]

Our study shows the higher value of mean HbA1c, mean postprandial glucose levels, and mean fasting blood glucose levels in the hypertensive diabetic group as compared to the hypertensive group. Although the results are comparable to previous studies, they underscore the need to maintain good diabetes management to avoid subsequent end-organ damage.[15]

Both groups had similar mean total cholesterol and mean triglyceride levels. However, we discovered a statistically significant difference when we compared the mean LDL level in hypertension (118.1 mg/dl) and hypertensive-diabetic subjects (91.5 mg/dl). $p<0.001$, similarly, the mean HDL level in the hypertension group was substantially higher (43.36 mg/dl) than in the hypertensive-diabetic group (40.02 mg/dl). ($p<0.019$)

Our findings may be compared to those of Thakur S et al., who found that lower HDL was the most often seen lipid abnormality in hypertension individuals (56.8 percent).[24]

In people with diabetes, low HDL cholesterol is prevalent; one in two diabetic women and one in four diabetic men have extremely low HDL cholesterol.[28]

Diabetes dyslipidaemia is thought to be one of several causes of accelerated macrovascular disease in diabetic individuals. If cholesterol and atherosclerotic burdens are reduced, therapy of lipid abnormalities might cut cardiovascular events by more than half. As a result, it's reasonable to predict that treating high cholesterol levels will enable diabetic patients to live longer and better lives.

In our research, end-organ damage was more prevalent in hypertension and diabetes as comorbidities. In the hypertensive group, retinopathy was the most often seen end-organ damage, followed by CAD. CKD was more prevalent in the hypertension diabetic group than in both males and females in the hypertensive group. Systemic hypertension that is not well-managed damages the retinal microcirculation, making a diagnosis of hypertensive retinopathy critical in stratifying hypertensive patients' cardiovascular risk. Hypertension that is not well regulated (HTN) has a detrimental effect on multiple cardiovascular, renal, cerebrovascular, and retina systems. [29] The current study's findings may be compared to those of Salagre SB et al., who reported that end-organ damage was evident in 45 percent of individuals with hypertension and diabetes.

Limitations of the present study

The research was carried out at a single tertiary city hospital. As a result, the study's findings and conclusions may not also be applied to the entire community, mainly from remote locations. It might be prudent to expand the sample size. The research should be extended over many years by examining follow-up visits that may provide additional relevant details on the subjects being studied.

CONCLUSION

Diabetic and hypertensive disorders are both curable. Analyzing diabetes, hypertension, and the elements that contribute to it across a more expansive and diversified

population is critical to comprehending disease epidemiology. With the twin epidemic's impact rising in India, public awareness and disease preventive campaigns must be launched. Additionally, our research underscores the necessity of metabolic screening and assessment for the involvement of end-organs in all hypertension patients at the time of diagnosis and regular intervals subsequently.

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Table 1 Cohorts' Data On Clinical Characteristics

Group	Selection criteria	Male	Female	Total
Group A	HTN	41	59	100
Group B	HTN+ DM	49	51	100

HTN= Hypertension; DM=Diabetes mellitu

Table 2 Sociodemographic Details, Chief Complaints Of Patients In Hypertensive Group (Group-A) And Hypertensive-diabetes Group (Group B)

Hypertensive group (Group-A)					Hypertensive-diabetes group (Group B)			
Age group in years	**Male N=41 n(%)**	**Female N=59**	**Total N=100**	**P value**	**Male N=49**	**Female N=51**	**Total N=100**	**P value**
20 to 30	2 (4.8)	1 (1.6)	3 (3)	Chi square = 5.633, p<0.344	2 (4)	7 (13.7)	9 (9)	Chi square-3.674, p<0.597
31 to 40	4 (9.7)	7 (11.8)	11 (11)		13 (26.5)	13 (25.4)	26 (26)	
41 to 50	13 (31.7)	14 (23.7)	27 (27)		15 (30.6)	17 (33.3)	32 (32)	
51 to 60	8 (19.5)	23 (38.9)	31 (31)		14 (28.5)	10 (19.6)	24 (24)	
61 to 70	11 (26.8)	12 (20.3)	23 (23)		4 (8.1)	3 (5.8)	7 (7)	
71 to 80	3 (7.3)	2 (3.3)	5 (5)		1 (2)	1 (1.9%)	2 (2%)	
Personal Addiction history								
Yes	16 (39)	21 (35.5)	37 (37)	Chi square=0.122, p<0.727	19 (38.7)	21 (41.1)	40 (40)	Chi square=0.122, p<0.727
No	25 (60.9)	38 (64.4)	63 (63)		30 (73.1)	30 (58.8)	60 (60)	
Family H/O HTN and DM								
Hypertension	15 (36.5)	7 (11.8)	22 (22)		15 (36.5)	7 (11.8)	22 (22)	
Diabetes mellitus	8 (19.51)	9 (15.2)	17 (17)		8 (19.5)	9 (15.2)	17 (17)	
HTN and DM	3 (7.3)	11 (18.6)	14 (14)		3 (7.3)	11 (18.6)	14 (14)	
No	15 (36.5)	32 (54.2)	47 (47)		15 (36.5)	32 (54.2)	47 (47)	

Table 3- Laboratory Parameters In Hypertensive Group (Group A) And Hypertensive-Diabetes Group (Group B)

	Hypertensive group (Group A)		**Hypertensive-diabetes group (Group B)**	
Blood Parameters	**Mean (95% Confidence Interval for Mean)**			
	Male	Female	Male	Female
Hb (gm/dl)	13.4 (12.8-14.1)	12.1 (11.7-12.4)	12 (11.3-12.6)	11.71 (11.2-12.1)
HBA1C	6.2 (5.8-6.5)	6.2 (5.9-6.6)	8.55 (8.1-8.9)	8.27 (7.7-8.7)
FBS (mg/dl)	106.8 (96.6-117)	103.6 (96.9-10.3)	152.37 (140.7-163.9)	173.27 (159.3-187.1)
PLBS (mg/dl)	138.1 (120.9-155.3)	131.7 (118.5-44.9)	248.06 (226.8-269.2)	245.73 (225.2-266.2)
Total cholesterol (mg/dl)	180 (167.9-192.1)	201.1 (191.1-11.1)	190.7 (177.5-203.9)	194.5 (183.2-205.7)
Triglyceride (mg/dl)	149.8 (119.3-180.4)	139.2 (125.4-153)	145.6 (132.5-158.7)	177.6 (160.6-194.5)
LDL (mg/dl)	107.2 (94.4-120.1)	126.2 (117.4- 5.1)	90.2 (82.4-98)	92.7 (84.3-101.1)
HDL (mg/dl)	41.8 (38.6-45)	44.6 (41.8-47.5)	41.2 (38.8-43.6)	38.7(36-41.5)
Creatinine (mg/dl)	1.3 (0.9-1.8)	1 (0.9-1.1)	1.22 (0.78-1.66)	1.06(0.7-1.4)
BUN (mg/dl)	17.3 (15.3-19.4)	15.5(13.9-17.1)	30.29 (25.6-34.9)	29.1 (24.1-34.1)

Table 4 Mean Systolic BP In The Two Study Groups

Parameter	Group's	Mean	Std. Deviation	Std. Error Mean	P value
Systolic BP(mmHg)	Group A	146.66	18.35	1.83	p<0.001
	Group B	136.62	11.44	1.14	
Mean Diastolic BP (mmHg)	Group A	90.82	10.09	1	p<0.001
	Group B	91.14	7.61	0.76	
Mean Fasting blood sugar (mg/dL)	Group A	88.82	8.60	0.86	p<0.001
	Group B	164.41	44.06	4.40	
Mean Post prandial blood sugar level (mg/dL)	Group A	118.12	12.79	1.27	p<0.001
	Group B	246.87	72.98	7.29	
Mean HbA1c level (%)	Group A	4.83	0.57	0.05	p<0.001
	Group B	8.38	1.65	0.16	
Mean BMI (kg/m^2)	Group A	26.68	4.31	0.43	0.347
	Group B	27.30	4.87	0.48	
Mean Hb level (gm%)	Group A	12.66	1.83	0.18	p<0.008
	Group B	11.92	2.05	0.20	
Mean creatinine level (mg/dL)	Group A	1.063	0.70	0.07	p<0.888
	Group B	1.079	0.88	0.08	
Blood urea nitrogen level (mg/dL)	Group A	16.27	6.29	0.62	p<0.001
	Group B	29.64	17.009	1.7009	
Total cholesterol level (mg/dL)	Group A	192.14	39.20	3.92	p<0.927
	Group B	192.67	42.85	4.28	
Triglyceride level (mg/dL)	Group A	143.85	73.60	7.36	p<0.927
	Group B	161.96	55.69	5.56	
LDL (mg/dL)	Group A	118.19	37.63	3.76	p<0.001
	Group B	91.521	28.41	2.84	
HDL (mg/dL)	Group A	43.36	10.65	1.06	p<0.019
	Group B	40.02	9.18	0.91	

Table 5 Complication In Hypertensive And Hypertensive-Diabetic Group

Complication	HTN		HTN-DM	
	Male	Female	Male	Female
No	21(51.2%)	35(59.3%)	24(48.9%)	19(37.2%)

CAD	4(9.7%)	2(3.3%)	5(10.2%)	3(5.8%)
CKD	2(4.8%)	3(5%)	6(12.2%)	9(17.6%)
Retinopathy	12(29.2%)	16(27.1%)	8(16.3%)	12(23.5%)
CVA	2(4.8%)	3(5%)	6(12.2%)	8(15.6%)
Total	41(100%)	59(100%)	49(100%)	51(100%)

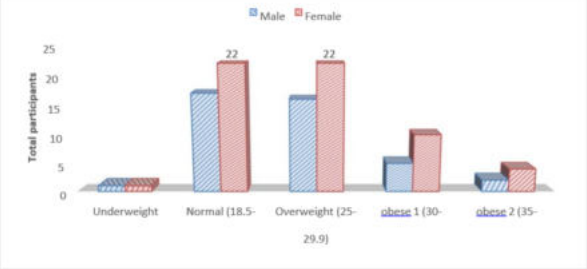

Figure 1: BMI Distribution In Patients Of Hypertensive Group A

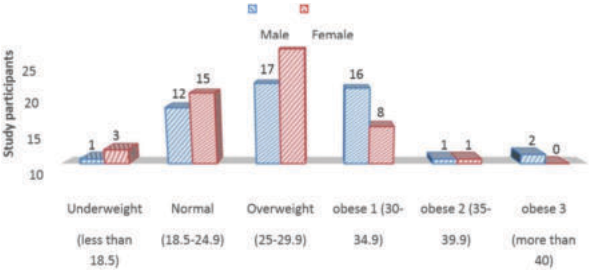

Figure 2: BMI Distribution In Patients Of Hypertensive-diabetic Group B

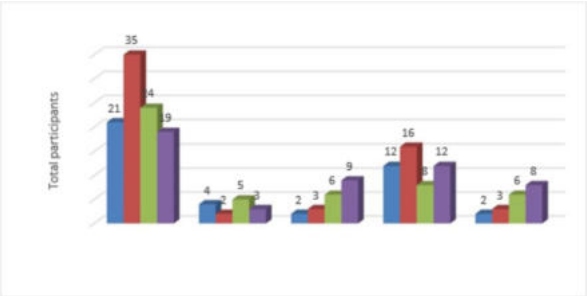

Figure 3: Complication In Hypertensive And Hypertensive-diabetic Group

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