DISSERTATION SUBMITTED FOR THE MASTER'S DEGREE IN MEDICAL PHYSIOLOGY

INSPIRING EXCELLENCE

TITLE

"DIABETES MELLITUS TYPE II ASSOCIATEDHYPERTENSION

SUBMITTED BY

SANCHITA SINGH

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DEPARTMENT OF MEDICAL PHYSIOLOGY

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"DIABETES MELLITUS TYPE II ASSOCIATED HYPERTENSION"

Dissertation submitted to

Integral Institute of Medical Sciences and Research

In partial fulfillment of the requirements for the award of the degree of

Master of Science in Medical

Physiology

By

SANCHITA SINGH

Enrolment No.1600102936

GUIDE	CO GUIDE	CO GUIDE
PROF(DR) KHALEEL AHMED MANIK HOD DEPARTMENT OF PHYSIOLOGY	DR AYASA PARVEEN ASSISTANT PROFESSOR DEPARTMENT OF MEDICINE	DR. AUSAF AHAMAD ASSOCIATE PROFESSOR DEPARTMENT OF COMMUNITY MEDICINE

INTEGRAL INSTITUTE OF MEDICAL SCIENCES &RESEARCH INTEGRAL UNIVERSITY, LUCKNOW

DECLARATION BY CANDIDATE

I hereby declare that this dissertation entitles **"DIABETES MELLITUS TYPE II ASSOCIATED HYPERTENSION"** is a Bonafide & genuine research work carried out by me under the guidance of prof Prof. (DR) Khaleel Ahmed Manik, Professor & Head, Department of Physiology Dr. Ayasa Parveen, Assistant Professor, Department of Medicine.

Date **Signature of the candidate**

INTEGRAL INSTITUTE OF MEDICAL SCIENCES & RESEARCH,
INTEGRAL UNIVERSITY, LUCKNOW

ENDORSEMENT BY THE HOD

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Prof. (DR) Khaleel Ahmed Manik **PLACE: LUCKNOW**

Professor & HOD Physiology Vice Dean

Physiology department **DATE**

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INTEGRAL UNIVERSITY, LUCKNOW

CERTIFICATE BY THE GUIDE AND CO-GUIDE

This is to certify that SANCHITA SINGH student of M.Sc. MEDICAL PHYSIOLOGY; Integral University has completed his dissertation entitled **"DIABETES MELLITUS TYPE II ASSOCIATED HYPERTENSION"** successfully. She has completed this work at the Department of Physiology, Integral Institute of Medical Sciences and Research, Integral University under the guidance of DR (prof). KHALEEL AHMED MANIK. The dissertation was a compulsory part of his M.Sc. degree. I wish her good luck and a bright future.

Guide	CO-Guide	CO- Guide
Prof. (DR) KHALEEL AHMED MANIK	**AUSAF AHAMAD**	**DR. AYASA PARVEEN**
PROFESSOR & HOD	**ASSOCIATE PROFESSOR**	**ASSISTANT PROFESSOR**
DEPT. OF PHYSIOLOGY	**DEPT. OF COMMUNITY MEDICINE**	**DEPARTMENT OF MEDICINE**
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List of Abbreviations

NCD	Noncommunicable disease
DM	Diabetes Mellitus
HTN	Hypertension
AGT	Angiotensin
DBP	Diastolic blood pressure
SBP	Systolic blood pressure

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INTRODUCTION

DM MELLITUS ASSOCIATED HYPERTENSION

INTRODUCTION

Chronic respiratory conditions, cancer, diabetes, and cardiovascular disorders are all included in the broad category of illnesses known as non-communicable diseases (NCDs). NCDs are responsible for about 38 million (68%) deaths worldwide and 5.87 million (60%) deaths in India. Around 82% of all NCD deaths and the majority of NCD mortality and morbidity are caused by cardiovascular illnesses, chronic respiratory diseases, cancers, and diabetes (World Health Organisation - WHO, 2014).).

Most NCD fatalities occur in low- and middle-income nations, including India, which is going through an epidemiological health shift because of its growing urbanization.

India has a population of roughly 1.3 billion people. In India, non-communicable diseases (NCDs) account for around 5.87 million (60%) of all fatalities.[1]

DEMOGRAPHIC DATA

A study on 1.3 million persons conducted in India found that hypertension was common even in younger age groups (12.1%; 95% CI, 11.8%-12.5%; 18-25 years)..[2]

Key Risk Factors of NCDs

Risk factors are divided into two categories: those that can be changed and those that cannot, depending on the condition. High blood pressure, smoking, diabetes, inactivity, obesity, and high cholesterol are among the risk factors that can be changed. Age, gender, genetic characteristics, race, and ethnicity are risk factors that cannot be changed.[3]

DIABETES MELLITUS

The metabolic illness known as diabetes mellitus (DM) is brought on by a problem with insulin secretion, action, or both. Chronic hyperglycemia brought on by an insulin shortage also causes problems with protein, lipid, and carbohydrate metabolism. One of the chronic non-communicable diseases that has become a major worldwide health issue. Additionally, it is a known risk factor **for kidney failure, limb amputations, vascular brain disorders, and blindness**. A high risk of acquiring diabetes exists among 352 million persons who presently have impaired glucose tolerance, according to the International Diabetes Federation's (IDF) Atlas guideline study. 425 million people (20-79 years of age) were anticipated to have DM in 2017, and that number is expected to increase [4]

CLASSIFICATION OF DIABETES MELLITUS

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood)

2. Type 2 diabetes (due to a progressive loss of adequate β-cell insulin secretion frequently on the background of insulin resistance)

3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)

4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation[5]

COMPLICATIONS OF DIABETES MELLITUS TRADITIONAL COMPLICATIONS

1. Diabetic Kidney Disease
2. Retinopathy
3. Peripheral Neuropathy
4. Coronary heart disease and heart failure
5. Stroke
6. Peripheral vascular disease[6]

EMERGING COMPLICATIONS

1. Cancer
2. Infections
3. Liver disease
4. Functional disability
5. Cognitive disability

HYPERTENSION

One of the main factors contributing to the worldwide burden of disease is hypertension. More than one billion people worldwide suffer from high blood pressure, which is also thought to be responsible for 9.4 million annual fatalities. Cardiovascular illnesses include coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease (PAD) are all made more likely by hypertension. It frequently accompanies other cardiovascular disease risk factors, and the burden of risk factors overall raises the likelihood of developing cardiovascular disease. Large portions of the hypertensive population are either untreated or receiving insufficient antihypertensive medication, despite the fact that it lowers the risks of cardiovascular and renal disease.

NORMAL BLOOD PRESSURE

Understanding the variables involved in the regulation of both normal and increased arterial pressure is helpful in providing a framework for understanding the pathophysiology and available treatments for hypertensive diseases. Peripheral resistance and cardiac output are the two factors that determine arterial pressure.

Cardiac output is determined by stroke volume and heart rate; stroke volume is related to myocardial contractility and to the size of the vascular compartment. Peripheral resistance is determined by functional and anatomic changes in small arteries (lumen diameter 100–400 μm) and arterioles [7]

CLASSIFICATION OF HYPERTENSION [8]

Categories	Systolic blood pressure, mm Hg	And/or	Diastolic blood pressure, mm Hg
American College of Cardiology/American Heart Association			
Normal	<120	and	<80
Elevated	120–129	and	<80
Hypertension, stage 1	130–139	or	80–89
Hypertension, stage 2	≥140	or	≥90

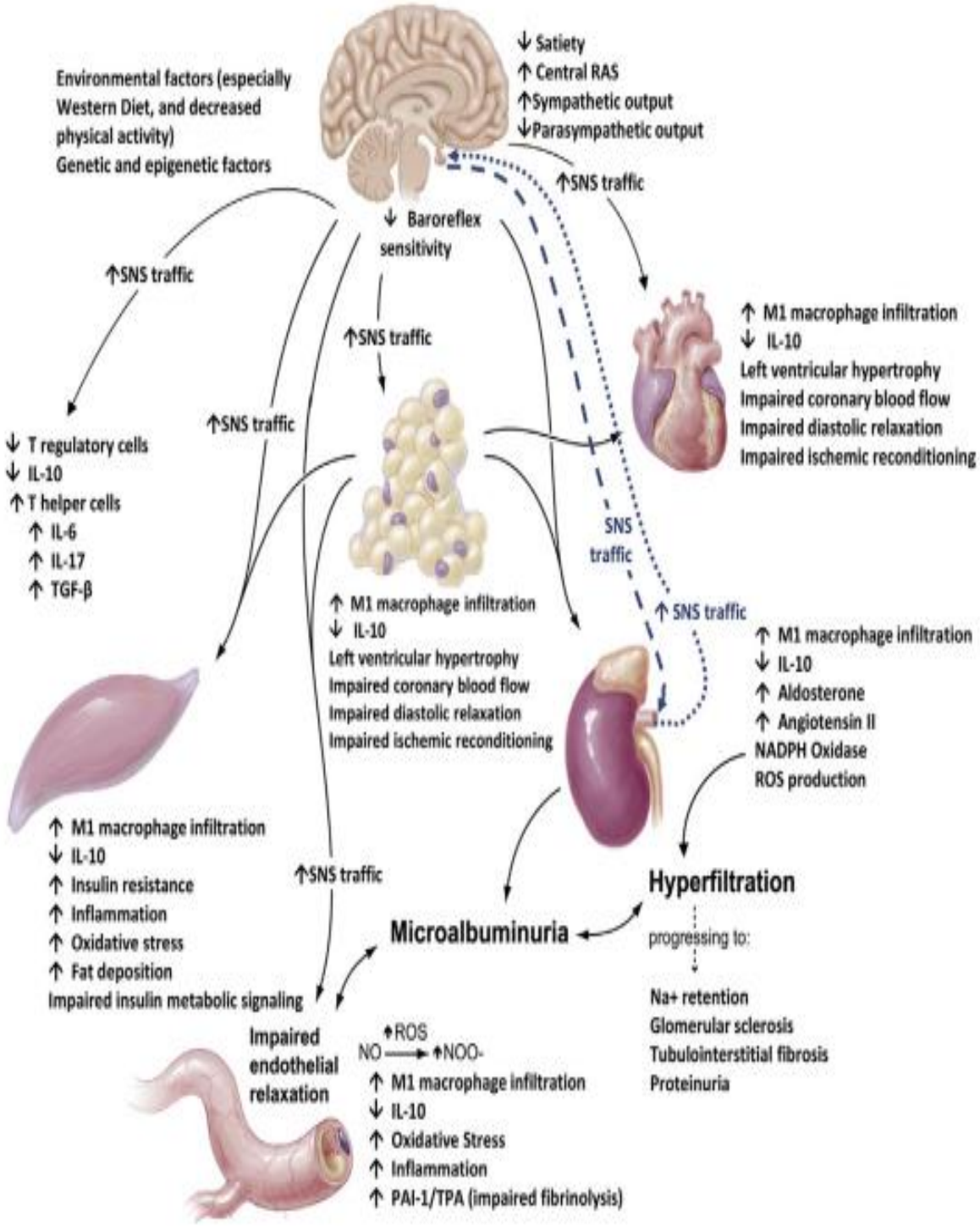
PATHOPHYSIOLOGY: CONVERGING PATHWAYS IN COEXISTING DM AND HTN

Both diabetes mellitus (DM) and high blood pressure (HTN) share a number of pathophysiologic processes, including inappropriate renin-angiotensin-aldosterone system (RAAS) activation, oxidative stress brought on by excessive reactive oxygen species (ROS) production, inflammation, impaired insulin-mediated vasodilation, increased sympathetic nervous system (SNS) activation, dysfunctional innate and adaptive immune responses, and abnormal renal processing of solutes. Obesity and increased visceral adiposity are the main contributing factors to DM and HTN cohabitation. Due to prolonged low-grade inflammation and oxidative stress, adipose tissue produces more angiotensinogen (AGT) and angiotensin II (Ang II), which activates the tissue's RAAS. Additionally, the overexpression of AGT in white adipose tissue contributes to high blood pressure. As a result, diabetes mellitus and hypertension are affected both locally and systemically by AGT and Ang II.

Increased aldosterone production and improved mineralocorticoid receptor (MR) signalling are other factors in the etiology of HTN. Corticosteroids may also be a factor in CVD in DM patients through actions that are partially mediated by MR activation. It is well known that the production of the hormone aldosterone by the adrenal zona glomerulus is increased by a lipid-soluble component produced by adipose tissue.

Complement-C1q tumour necrosis factor (TNF)-related protein1 (CTRP1) is a novel adipokine that promotes aldosterone synthesis in a mouse model of obesity and insulin resistance. Aldosterone activation of the MR in the renal distal tubule and collecting duct, which increases sodium retention, causes an increase in plasma volume and a rise in blood pressure. Through MR activation, aldosterone may also have non-genomic effects that alter how HTN is made. [9]

Systemic and metabolic factors that promote coexistent diabetes mellitus, hypertension, cardiovascular, and chronic kidney disease[10]



Hypertension, microalbuminuria, and insulin resistance in diabetes mellitus

Patients with diabetes mellitus develop hypertension more often than non-diabetic volunteers of the same age. They run a far increased risk of developing coronary vascular disease, progressive nephropathy, and end-stage renal diseases. The most common kind of hypertension in persons with type I and type II diabetes is essential hypertension, which is most likely caused by insulin resistance and hyperinsulinemia. Both hyperglycemia and hypertension have a significant impact on the onset of diabetic nephropathy.[11]

Hypertension brought on by diabetic mellitus

Diabetes-related hypertension increases a diabetic's risk for both macrovascular and microvascular issues, complicating treatment options and driving up medical costs. Despite the fact that lowering blood pressure is accompanied by a considerable decrease in cardiovascular and microvascular morbidity and death, a high percentage of diabetics have poorly controlled hypertension. The slow clinical diagnosis of hypertension, clinical inertia, poor adherence to the prescribed regimen, and uncertainty regarding the causal relationship and treatment objectives could all have contributed to this outcome..[12]

The relationship between insulin and blood pressure elevation

Insulin is a critical hormone in the emergence of diabetes mellitus and reduces plasma glucose levels. Insulin has a variety of purposes, including facilitating the uptake of glucose by the body's organs, promoting the storage of glycogen in the liver and muscle tissue, regulating the breakdown of stored glycogen, promoting the growth of adipose tissue, and regulating the fat-burning process. The insulin receptor belongs to the same family of receptor tyrosine kinases as heparin-binding epidermal growth factor-like receptors and platelet-derived growth factor receptors. As a result, insulin also promotes the proliferation and migration of vascular smooth muscle cells.

In order to activate the Na+/H+ channel, which passively transfers sodium ions into the cell and hydrogen ions out of the cell, insulin translocates Na+/K+-ATPase from the cytoplasm to the cell membrane. Additionally, this mechanism lowers pH and raises calcium ion concentrations within cells. When intracellular sodium levels drop, the Na+/H+ exchange transporter opens as a result of an insulin-induced rise in Na+/K+-ATPase. Through renal tubule cells, sodium ions are transported into blood vessels as a result of Na+/K+-ATPase's action. The Na+/K+-ATPase activity reduces when an insulin deficit results in diabetic ketoacidosis, which increases the transfer of sodium, hydrogen, and potassium into and out of the cell. These modifications result in symptoms of elevated serum potassium and increase the density of sodium ions in the cell.

In relation to hyperglycemia-induced hyperosmolarity, the volume of the circulatory fluid might also rise. The extracellular osmotic pressure changes in diabetes instances, and it rises relative to the intracellular osmotic pressure on the side with greater glucose concentrations. To decrease the difference between intracellular and extracellular osmotic pressure, water leaves the tissue (into the vasculature), and this flow raises the extracellular volume of bodily fluid and blood (i.e., circulatory blood volume). As a result, hyperglycemia also causes an increase in systemic blood pressure by increasing the volume of the circulatory system

Renin excretion increases and sympathetic nervous system activity is stimulated by hyperinsulinemia. Renin production rises, stimulating the sympathetic nervous system and raising peripheral vascular resistance as well as cardiac output. These modifications ultimately result in an increase in blood pressure by raising both the peripheral vascular resistance and the volume of circulatory fluid. Additionally, insulin promotes obesity by causing fat to accumulate, which in turn causes obesity-related hypertension in conjunction with type 2 diabetes mellitus.. [13]

REVIEW OF LITERATURE

- A cross-sectional study titled "DM type II-induced Hypertension" by Omer Abdelbagi et al. discovered that DMII is more frequently linked to hypertension. 854 (47.5%) of the 1973 patients who participated in the study had DMII and hypertension. This study's findings indicated a relationship between diabetes mellitus and hypertension that is favorable. [13]

- Ziyad S. Almalki et. Al conducted a hospital-based cross-sectional study on DMII induced Hypertension" in 1178 DMII patients, of which 846 (71.8%) had hypertension. The extent of uncontrolled hypertension among patients with diabetes was found to be high.[14]

- Pascal Geldsetzer et .al conducted a cross-sectional nationally represented population-based study on 1320555 adults. The study concluded that the crude prevalence of diabetes and hypertension was 7.5 and 25.3% and prevalence is high in middle and old age across all geographical and sociodemographic groups in India. Hypertension prevalence was higher than previously thought.[15]

- Mohamed Berraho et al. performed a cross-sectional study. The study reports that hypertension is a very common co-morbidity among Moroccan patients with type diabetes. Therefore, we found a positive association of hypertension with age, BMI, and duration of diabetes. Of those who had been diagnosed hypertensive, 38.8% were not aware of their hypertension at the time of the study. Of 227 type 2 diabetic patients who were aware of having hypertension, we found a lack (17.2%) of adequately controlled blood pressure.[16]

- Zhehui Wang et. performed a cross-sectional study on a total of 14,422 participants aged 18–98 years were collected (men = 5827, 40.7%). The prevalence was 22.7% for hypertension, 7.0% for diabetes, and 3.8% for diabetes with hypertension complications, respectively. Older age, women, higher educational level, unmarried status, and obesity (central obesity) were associated with increased risk of hypertension and diabetes. We did not find significant multiplicative interaction of diabetes and hypertension on CVDs but observed a synergisticadditivee interaction on coronary heart disease (SI, 1.43; 95% CI, 1.03–1.97; RERI, 1.94; 95% CI, 0.05–3.83; AP, 0.26; 95% CI, 0.06–0.46).20 [17]

- Roberto Carlos et. all (2016) performed a cross-sectional study on 7164 older adults. Of 7164 older adults, 54.8% were women, and their mean age was 70.6 years with a mean frailty index score of 0.175. The prevalence of diabetes was of 22.2%, and 37.3% for hypertension. An independent association between diabetes, hypertension, or both conditions (coefficients 0.28, 0.4, and 0.63, respectively, P< 0.001) with frailty was found. Having any diabetic complication was significantly associated with frailty with a coefficient of 0.55 (95% CI 0.45–0.65, P< 0.001) in the adjusted model. The number of years since diagnosis was also associated with frailty for both conditions.[18]

- Mingyue Xue1(2020) A total of 643,439 subjects participating in the national physical examination have been recruited in this cross-sectional study. After excluding unqualified subjects, 30,507 adults with T2DM were included in the final analysis. 21,355 and 9,152 subjects were randomly assigned to the model developing group and validation group, respectively, with a ratio of 7:3. The potential risk factors used in this study to assess hypertension in patients with T2DM included questionnaire investigation and physical measurement variables.[19]

- Drabo P Y et all reported a 3-year survey concerning diabetes associated with hypertension in 260 diabetic patients at Ouagadougou in France. This association has been found in 29% of the cases. The patients were male subjects 57% of them and 71 more 50 years old. Other vascular risk factors have been observed: obesity (53%), smoking (15%), and hyperuricemia (23%). Hypercholesterolemia and hypertriglyceridemia were observed respectively in 1% and 1.3% of the cases. Many complications arise during the survey: retinopathy in 51% of the patients, nephropathy for 35% and 12% with renal failure, and macroangiopathy in 55% of the patients. The treatment was based on diuretics and calcic inhibitors. The results on the control of blood pressure were excellent but the high cost of this management is an important restrictive factor.[20]

- Dianjianyi Sun, et al performed a population-based prospective cohort study that sought to investigate the bidirectional causal relations of T2D with hypertension, systolic and diastolic blood pressure (BP) using Mendelian randomization (MR) analysis. A total of 318 664 individuals were included in the study and drew the conclusion that T2D may causally affect hypertension, whereas the relationship between hypertension to T2D is unlikely to be causal. These findings suggest the importance of keeping an optimal glycaemic profile in general populations, and BP screening and monitoring, especially systolic BP in patients with T2D.24.[21]

- Shriraam, Vanishree, et all performed a study on 502 participants including 212 (42.2%) men and 290 (57.8%) women. Diabetes and hypertension were prevalent in the indigenous population at 7.4% and 36.5%, respectively. In this study, 68% of cases of hypertension and 62% of cases of diabetes were brand-new diagnoses. Age, female sex, abdominal and generalized obesity, and diabetes were risk factors for hypertension, while diabetes and abdominal obesity were risk factors for hypertension.[22]

- Yonas Akalu et all performed an institution-based cross-sectional study that was employed on 378 T2DM patients in Ethiopia. Data were collected using an interviewer-administered questionnaire. The prevalence of hypertension among T2DM patients was 59.5% (95% CI: 54.5-64.5). Stage 1 hypertension was found to be the most common (30.95%). The study concluded that there is a high prevalence of hypertension in diabetes patients and the majority had poor blood pressure control.[23]

- Tsimihodimos V, et all conducted a study on 1770 subjects who participated in the first follow up out of which 1753 returned for the second follow-up. At the 3 examinations, 16% to 46% of the study subjects were hypertensive; among them, the prevalence of diabetes mellitus (20%–39%) was significantly higher than that among normotensive subjects ($P<0.0001$ for all 3 data sets; Among subjects who were normotensive at baseline (n=1876), the study concluded that out of 1770 patients 108 became hypertensive at 3.25 years; another 107 subjects who were normotensive at both baseline and 3.25 years were found to be hypertensive at 7 years, and 28 other subjects who were normotensive at baseline and missed examination 2 were hypertensive at examination 3. Thus, a total of 243 subjects converted to hypertension during the 7-year follow-up, yielding a crude conversion rate of 2% per year [24]

- H Alsadoon et al Conducted a cross-sectional and retrospective study in 2017, and data from 1252 adults with T2DM were collected from the rural and urban populations of Bangladesh. Cross-sectional data were collected from patients via history examination and questionnaire, and retrospective data were collected from patients' past medical records. The study concluded that the mean duration of diabetes was 10.86 and there is a strong relationship between hypertension and diabetes **[**25**]**

- Azzam Nosayba et all investigated in a retrospective cross-sectional study among diabetic patients in Jordan in 1485 patients out of which 598 were males and 887 were females and their ages ranged from 18 to 96 years with a mean (SD) of 58.57. The study concluded that HTN was found to be highly associated with T2DM in Jordan with an approximate prevalence of 80% of the participated T2DM patients.[26]

- Kotiso Kehabtimer et all conducted a study on a total of 200 cases with both type 2 diabetes and hypertension and 186 controls with only type 2 diabetes, but no hypertension. The mean (±SD) age was 60.3 (± 9.9) years for cases and 55.3 (±11.3) years for controls. Among the participants, almost half of the cases and controls (47.3%) were females, The median (IQR) reported duration of DM from the diagnosis was 15 (9, 20) years in cases and 10 (6, 17) years in controls. One-third of the cases and about a quarter of the controls reported a family history of HTN. Over two-thirds, (68.5%) of the cases and a half (50.5%) of the controls reported using insulin. This study also revealed that there is a sedentary activity of ≥ 4 hours/day in the majority (62.0%) of the cases and in less than half (43.0%) of the controls. The result of the multivariable analysis identified obesity, sedentary activity, stress scores, the interaction of diabetes duration with insulin use, serum creatinine of >1.1 mg/dl, age, government employee, and family history of hypertension as independent determinants of hypertension among people with T2DM.[27]

- Rupasinghe D et all conducted a cross-sectional study on diabetic clinics of a tertiary care hospital from August 2020 to August 2021. The source population included all adult patients with type 2 diabetes. Data collection was done using a structured interviewer-administered questionnaire. A total of 610 patients were included in the study. The mean age of participants was 57.37 (±11.32) years. The overall prevalence of hypertension among diabetic patients was 39.84%. Age, physical activity, family history of hypertension, smoking status, BMI, sedentary lifestyle, stress level, and serum creatinine were independent determinants of hypertension among people with type 2 diabetes mellitus. The overall prevalence of hypertension among diabetic patients was found to be 39.84%[28]

- Valenzuela et all conducted a nationwide cross-sectional study between 2012 and 2016 (data analysis was performed in 2021). Participants' lifestyle-related factors—BMI, sleeping hours, alcohol, smoking, and physical activity—were assessed, and the prevalence of hypertension and diabetes was considered. The study was conducted on 451157 participants out of which (33.1% were women, aged 44.5 [SD=9.2] years, 3.2% with diabetes, and 29.3% with hypertension). The study concluded that having diabetes was associated with a higher prevalence of hypertension even after adjusting for all lifestyle-related factors, and people with diabetes and hypertension had a higher prevalence of mild kidney function impairment than people with diabetes alone. However, people with diabetes and an optimal lifestyle—normal weight and sleeping hours, absent-to-little alcohol drinking, nonsmoking, and regular physical activity—presented a prevalence of hypertension comparable with that of those without diabetes (OR=1.00, 95% CI=0.71, 1.32). The study showed that Diabetes is positively and largely independently associated with hypertension risk.[29]

- Nazarzadeh M et all performed A Cross-sectional study on 145 939 participants (88 500 [60·6%] men and 57 429 [39·4%] women from 19 randomized controlled trials were included in the one-stage individual participant data meta-analysis. 22 trials were included in the individual participant data network meta-analysis. After a median follow-up of 4·5 years (IQR 2·0), 9883 participants were diagnosed with new-onset type 2 diabetes. Systolic blood pressure reduction by 5 mm Hg reduced the risk of type 2 diabetes across all trials by 11% (hazard ratio 0·89 [95% CI 0·84–0·95]). Investigation of the effects of five major classes of antihypertensive drugs showed that in comparison to the placebo, angiotensin-converting enzyme inhibitors (RR 0·84 [95% 0·76–0·93]) and angiotensin II receptor blockers (RR 0·84 [0·76–0·92]) reduced the risk of new-onset type 2 diabetes; however, the use of β blockers (RR 1·48 [1·27–1·72]) and thiazide diuretics increased this risk, and no material effect was found for calcium channel blockers [30]

AIM AND OBJECTIVE

AIM

The aim of the present study is to determine the association between DMII and Hypertension

OBJECTIVE

- To record the history of DM type II duration.
- To record the history of Hypertension duration.
- To determine the association of DM II with Hypertension.
- To measure the RBS value
- To measure the blood pressure value

METHODS AND MATERIAL

TYPE OF STUDY – Cross-sectional Study.

PLACE OF STUDY - The study was performed in the Department of Physiology at Integral Institute Medical Science & Research, Lucknow (U.P.).

Duration of Study- 6 months. (february2023 to July2023)

INCLUSION CRITERIA

1. Subjects with diagnosed Diabetes and hypertension as per WHO norms.

2. Subjects (male & female).

3. Age group from 40 and 80 years of age

4. Subject who had signed the Informed consent form.

EXCLUSION CRITERIA

1. Terminal patients

2. Patients with cognitive impairment

3. Pregnant women

4. Patients less than 40 years

5. Patients with incomplete data will be excluded

RESEARCH QUESTION

Is there any association between type II diabetes mellitus and hypertension?

HYPOTHESIS

NULL HYPOTHESIS H0:

There is no association between type II diabetes mellitus and hypertension

ALTERNATE HYPOTHESIS H1:

There is a positive relationship between type II diabetes mellitus and hypertension.

COLLECTION OF DATA

The study is a questionnaire-based cross-sectional study on the patients attending medicine OPD and IPD of IIMS&R Lucknow.

The data was collected from patients who were willing to sign the informed consent.

Patients RBS was measured using glucometer

Patients blood pressure was measured using sphygmonameter

The purpose of the study and the procedure of the study was fully explained to the patient attending Medicine OPD and IPD.

SAMPLE SIZE

The sample size is calculated using the formula

N =z2 p(1-p)/d2

FOR QUANTITATIVE VARIABLE

P = 7.5%

Z= 1.96 for 95% CI

D2 = 5%

N= sample size in the group

Values (Reference Mother Article – JAMA internal medicine Diabetes and Hypertension in 1.3 Millon Adults

India. A nationally representative study of 1.3Million Adults)

N = 107+10% nonresponse

= 120

The total calculated sample size is 120

RESULTS AND OBSERVATION

STATISTICAL ANALYSIS

The data were entered into an MS EXCEL spreadsheet and were analyzed by using (SPSS) -22 trial version. Means and standard deviation were applied in the study. To test the normality Kolmogorov-Smirnov test was applied.

To check the significance of the study spearman's rank correlation coefficient and Mann-Whitney U test is applied.

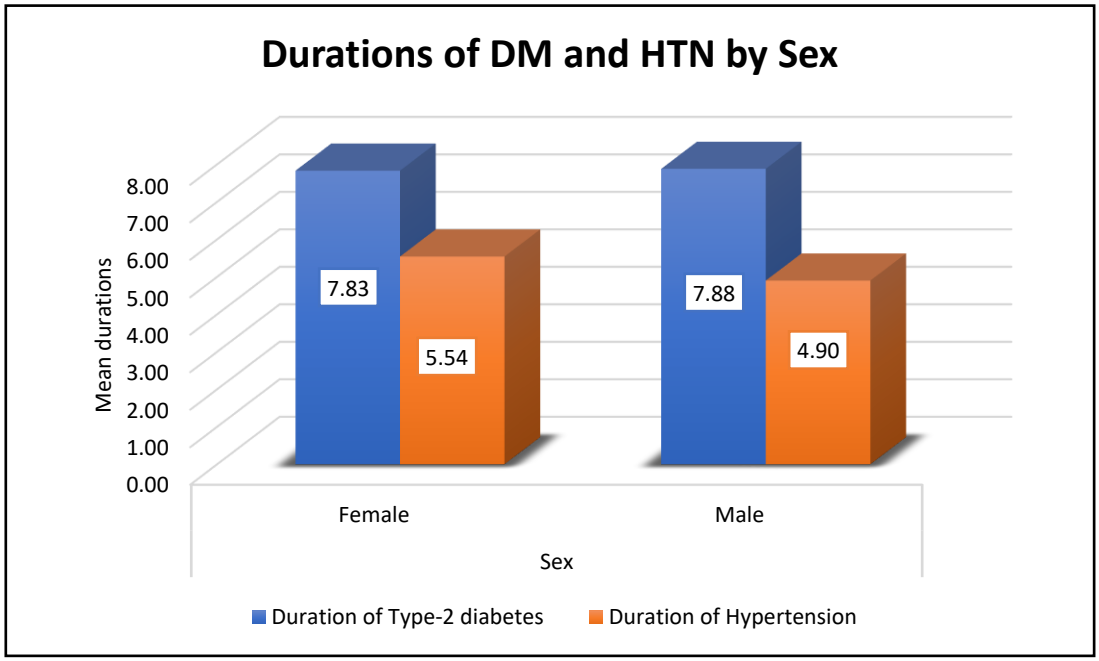
Table 1: Description of variables

Age	Mean = 53.83 years Standard deviation = 10.44
Type-2 DM duration	Mean = 7.85 years Standard deviation = 6.94
HTN duration	Mean = 5.27 years Standard deviation = 5.92
Random BS	Mean = 301.83 Standard deviation = 120.24
Systolic BP	Mean = 153.91 Standard deviation = 18.92
Diastolic BP	Mean = 85.97 Standard deviation = 11.07
Gender	Female N (%) = 70 (58.3) Male N (%) = 50 (41.7)
Location	Rural N (%) = 81 (67.5) Urban N (%) = 39 (32.5)
Socio-economic status	Low N (%) = 68 (56.7) Middle N (%) = 42 (35.0) Upper N (%) = 10 (8.3)
Tobacco intake	No N (%) = 66 (55.0) Yes N (%) = 54 (45.0)
Alcohol intake	No N (%) = 102 (85.0) Yes N (%) = 18 (15.0)
Vegetarian diet intake	No N (%) = 93 (77.5) Yes N (%) = 27 (22.5)
Non-vegetarian diet intake	No N (%) = 100 (83.3) Yes N (%) = 20 (16.7)
DM medication	No N (%) = 90 (75.0) Yes N (%) = 30 (25.0)
Insulin	No N (%) = 95 (79.2) Yes N (%) = 25 (20.8)
HTN medication	No N (%) = 90 (75.0) Yes N (%) = 30 (25.0)

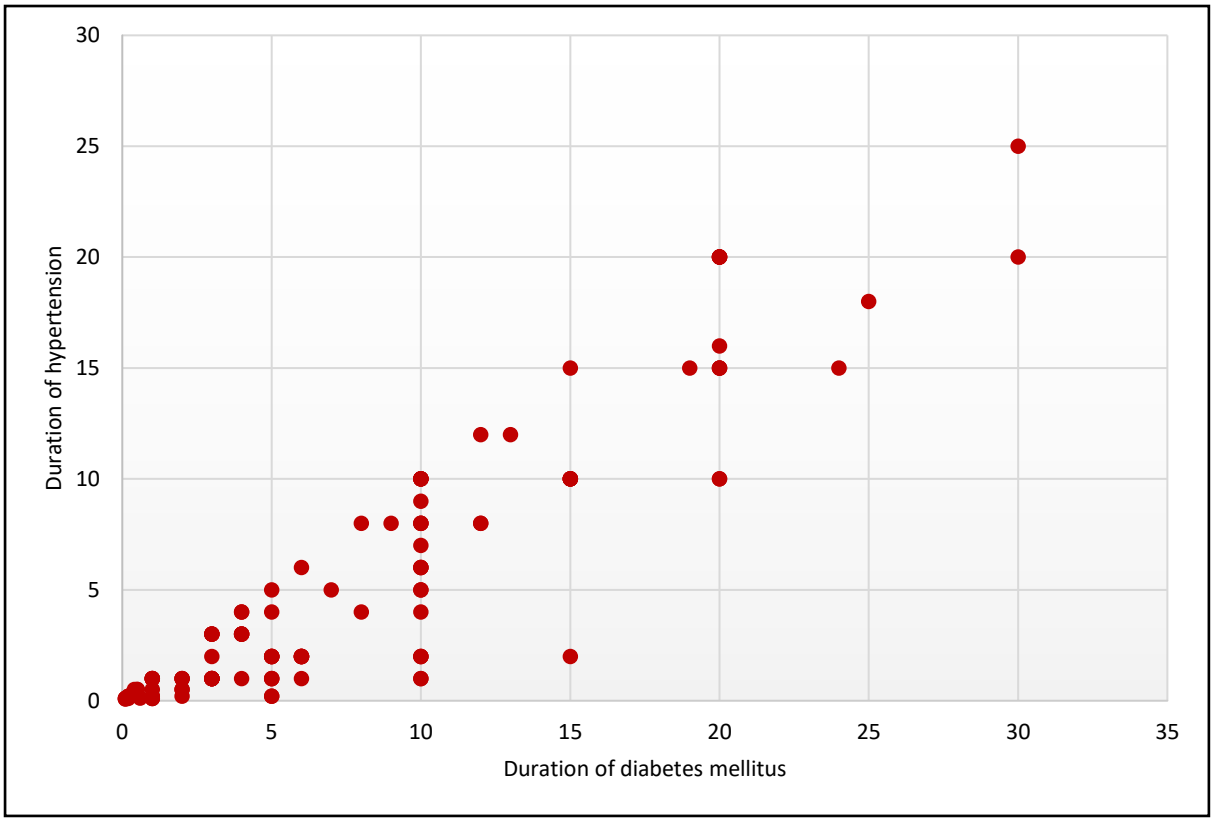
Table 1 represents the description of different variables related to the demographic profile and clinical profile of the respondents. The results suggest that the mean duration of type 2 DM was 7.85 years ± 6.94 whereas the mean duration of HTN was 5.27 years ± 5.92. The mean of random blood sugar was observed to be 301.83 ± 120.24. The mean systolic BP was 153.9 ± 18.92, whereas the mean diastolic BP was 85.97 ± 11.07. Most of the patients were females (N = 70, 58.3%) and belonged to rural areas (N = 81, 67.5%). The socioeconomic status of the respondents was majorly low (N = 68, 56.7%). However, the major portion of the population did not take tobacco (N = 66, 55.0%), alcohol (N = 102, 85.0%), vegetarian diet (N = 93, 77.5%), non-vegetarian diet (N = 100, 83.3%). DM medication (N = 90, 75.0), insulin (N = 95, 79.2%), and hypertension medication (N = 90, 75.0%) was not given to a larger portion of the population. Moreover, we performed a Mann-Whitney U test to compare the duration of type 2 diabetes and hypertension across sex. The results interpret that both durations of type-2 diabetes ($M_f = 7.83$, $M_m = 7.88$; $p > 0.05$) and hypertension ($M_f = 5.54$, $M_m = 4.90$; $p > 0.05$) are not significantly distributed across sex, as presented in Table 2 (Fig. 1).

Table 2: Comparison of duration of type-2 diabetes and hypertension by sex

Durations	**Sex**		**p-value**
	Female **Mean (SD)**	**Male** **Mean (SD)**	
Type-2 diabetes	7.83 (7.13)	7.88 (6.74)	0.771
Hypertension	5.54 (5.88)	4.90 (6.02)	0.686



Further, the aim of the study was to determine the relationship between type 2 diabetes and hypertension. To examine this, we applied Spearman's rho correlation as both the durations were not normally distributed ($p > 0.05$). the results from Table 3 suggest that the duration of type-2 diabetes is strongly and positively correlated with the duration of hypertension (coefficient = 0.895, $p < 0.05$), which could possibly be depicted from the scatterplot (Fig. 2) (with an increase in type 2 diabetes, an increase in years could be observed in hypertension).



As a part of additional analysis, we wanted to observe which demographic and clinical factors could possibly influence the duration of type 2 diabetes and hypertension. For this purpose, we employed the use of multiple linear regression (MLR) where duration of diabetes mellitus and hypertension were taken as dependent variables for model 1 and 2 respectively and age, sex, and tobacco intake as independent variables (Table 4). To validate the results of MLR, a set of assumptions were performed including Durbin-Watson (D-W) statistic for autocorrelation, Variance Inflation Factor (VIF) for multicollinearity, histogram for normal residuals (Fig. 3 and Fig. 5), and a scatter plot for homoscedastic residuals (Fig. 4 and Fig. 6). Moreover, a coefficient of determination and F-statistic by ANOVA table were stated to prove the model fitting.

Now, the results are summarized as follows:

- For model 1, a negligible autocorrelation (D-W statistic = 1.238) was observed with a VIF values of 1.012, 1.058, and 1.054 for age, sex and tobacco intake respectively showing that multicollinearity is absent in the data. From the plots, residuals were normally distributed (Fig. 3) as well as had a constant variance or homoscedastic (Fig. 4). Further, the model fit was significant ($F = 14.966$, $p < 0.05$) and almost 28% variation in duration of diabetes mellitus was explained by age, sex, and tobacco intake.

- Age ($B = 0.321$, $p < 0.05$) and tobacco intake ($B = 2.816$, $p < 0.05$) were positive and significant predictors of duration of diabetes mellitus. That means, one year increase in the age would lead to an increase of 0.321 years in the duration of diabetes mellitus whereas tobacco intake would increase the duration of diabetes mellitus by 2.816 times. Model 1 can be represented as:

$$Duration\ of\ DM = -11.394 + 0.321 \times age + 1.217 \times sex + 2.816 \times tobacco\ intake + \in$$

- For model 2, a negligible autocorrelation (D-W statistic = 1.331) was observed with a VIF values of 1.012, 1.058, and 1.054 for age, sex and tobacco intake respectively showing that multicollinearity is absent in the data. From the plots, residuals were normally distributed (Fig. 5) as well as had a constant variance or homoscedastic (Fig. 6). Further, the model fit was significant ($F = 12.375$, $p < 0.05$) and almost 24% variation in duration of hypertension was explained by age, sex, and tobacco intake.

- Age ($B = 0.249$, $p < 0.05$) and tobacco intake ($B = 2.437$, $p < 0.05$) were positive and significant predictors of duration of hypertension. That means, one year increase in the age would lead to an increase of 0.249 years in the duration of hypertension whereas tobacco intake would increase the duration of hypertension by 2.437 times. Model 2 can be represented as:

$$Duration\ of\ HTN = -10.186 + 0.249 \times age + .672 \times sex + 2.437 \times tobaccan\ o\ intake + \in$$

Table 4: Regression models for DM and HTN

Models	Durbin-Watson statistic	VIF	F-statistic (p-value)	R-square	B (p-value)
Model 1[a]					
Constant	1.238	-	14.966* (0.000)	0.279	-11.394* (0.000)
Age		1.012			0.321* (0.000)
Sex		1.058			1.217 (0.287)
Tobacco intake		1.054			2.816* (0.014)
Model 2[b]					
Constant	1.331	-	12.375* (0.000)	0.242	-10.186* (0.000)
Age		1.012			0.249* (0.000)
Sex		1.058			1.672 (0.095)
Tobacco intake		1.054			2.437* (0.015)

[a] $Duration\ of\ DM = \beta_0 + \beta_1 \times age + \beta_2 \times sex + \beta_3 \times tobacco\ intake + \in$

[b] $Duration\ of\ HTN = \beta_0 + \beta_1 \times age + \beta_2 \times sex + \beta_3 \times tobacco\ intake + \in$

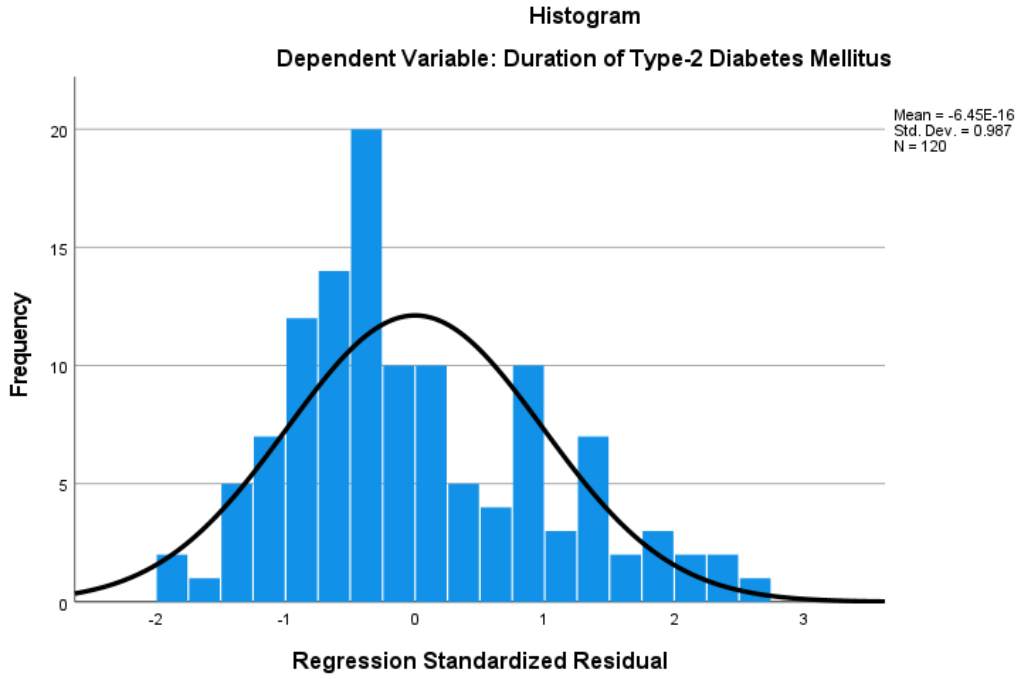


Fig. 3: Histogram showing the distribution of standardized residuals.

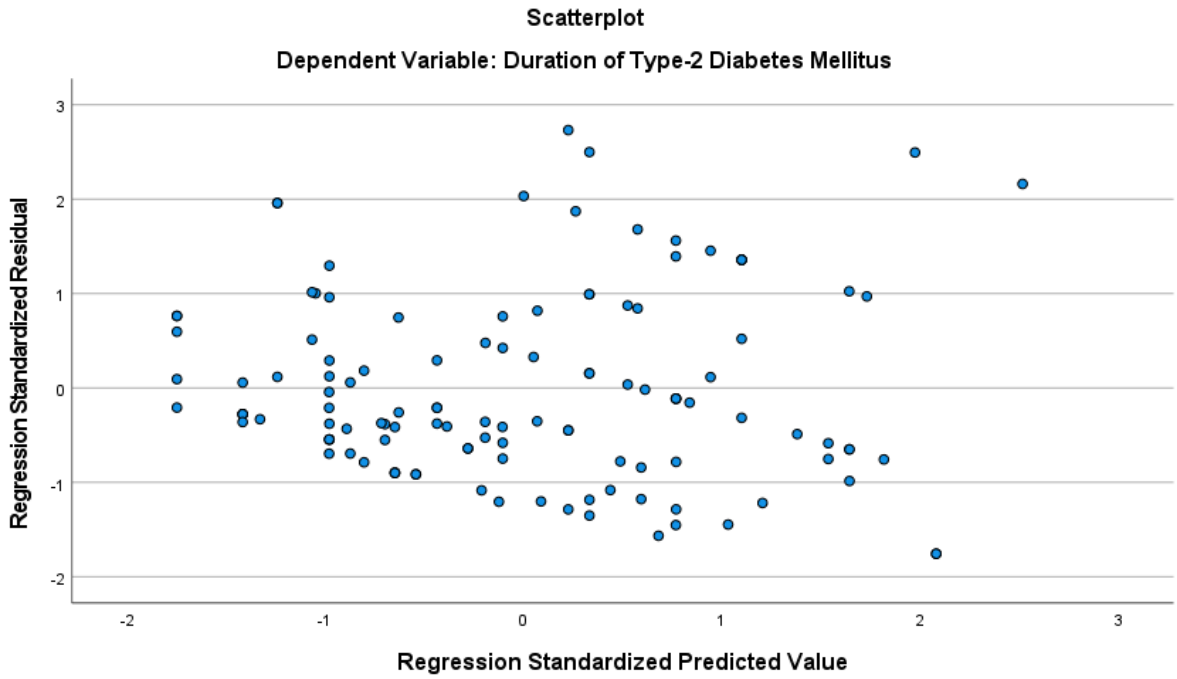


Fig. 4: Scatter plot showing correlation between standardized residuals and standardized predicted values

Model 2 charts:

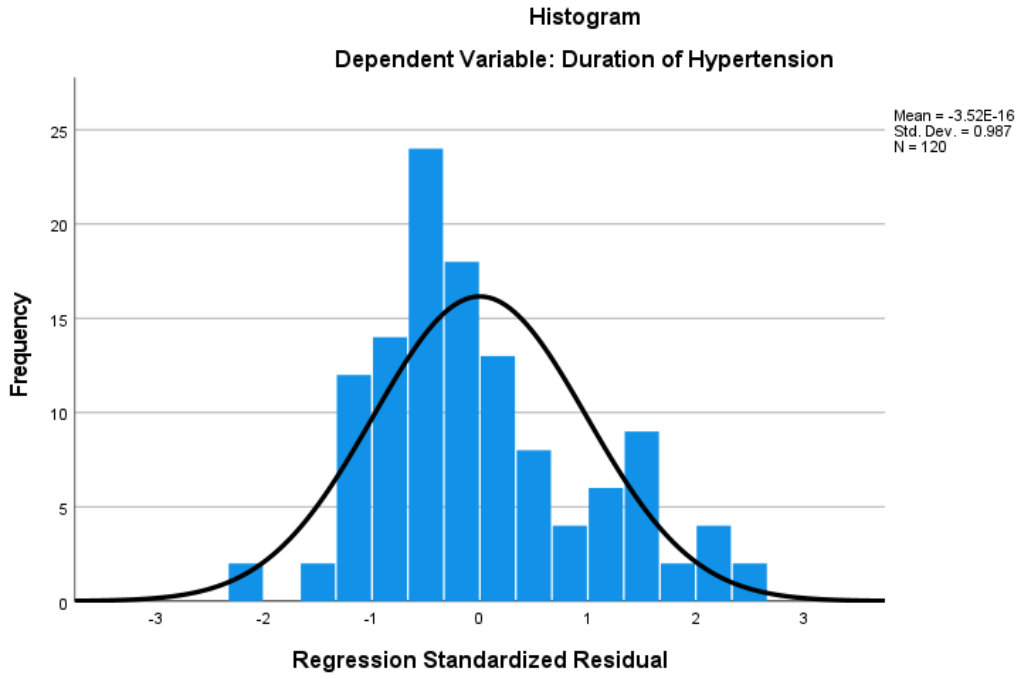


Fig. 5: Histogram showing the distribution of standardized residuals.

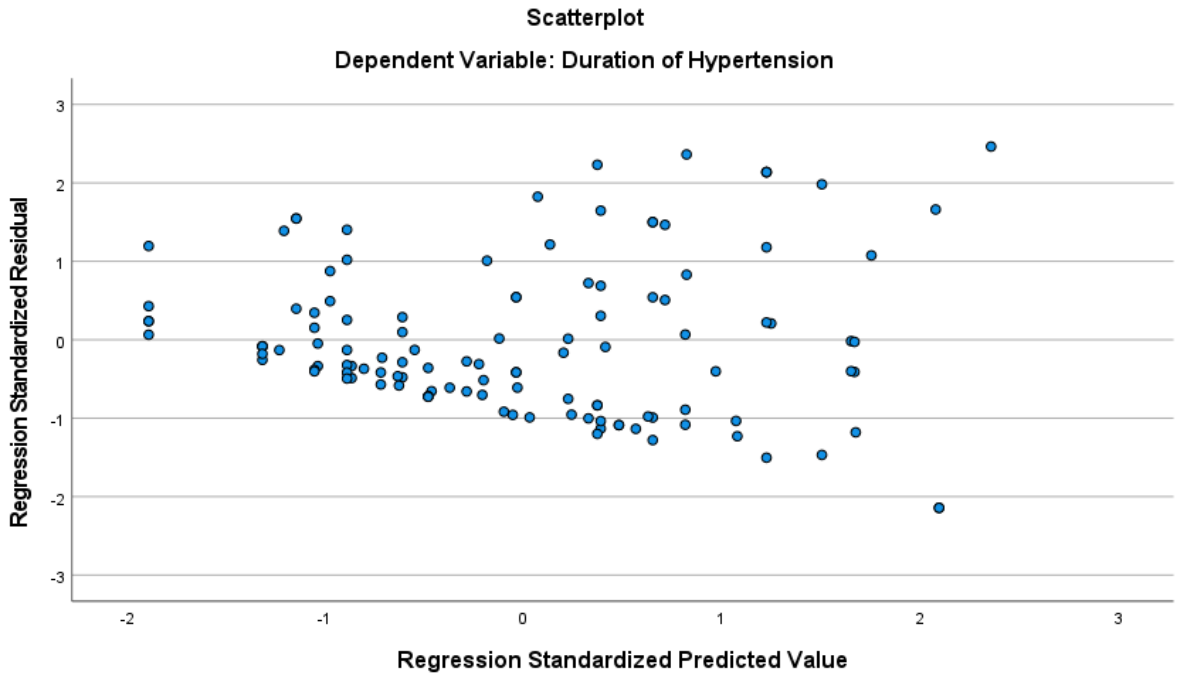


Fig. 6: Scatter plot showing correlation between standardized residuals and standardized predicted values

Statistical Tools Employed –

Mean: To obtain the mean, the individual observations were first added together and then divided by the number of observations. The operation of adding together or summation is denoted by the sign Σ.

$$\bar{X} = \frac{\sum X_i}{n}$$

n = number of observations

x_i = value of x (for ith observation)

$\bar{X}$ = mean of n observations

Standard Deviation: It is denoted by the Greek letter σ. If a sample is more than 30 then.

$$\sigma = \sqrt{\frac{\Sigma(X - \overline{X})^2}{n}}$$

When sample in less than 30 then.

$$\sigma = \sqrt{\frac{\Sigma(X - \overline{X})^2}{n-1}}$$

Test for Normality (Kolmogorov-Smirnov Test): For testing for normality of the distribution, samples are standardized and compared with a standard normal distribution. This test is less powerful for testing normality than the Shapiro–Wilk test or Anderson–Darling test. However, it can be considered over Shapiro–Wilk test in situations where the sample size is larger. Also, Shapiro–Wilk test is known not to work well in samples with many identical values.

Correlation: Correlation is a bivariate analysis that measures the strength of association between two variables and the direction of the relationship. In terms of the strength of relationship, the value of the correlation coefficient varies between +1 and -1. A value of ± 1 indicates a perfect degree of association between the two variables. As the correlation coefficient value goes towards 0, the relationship between the two variables will be weaker. The direction of the relationship is indicated by the sign of the coefficient; a '+' sign indicates a positive relationship and a '–'sign indicates a negative relationship.

Spearman's rank correlation coefficient is often denoted by the Greek letter ρ. It is a nonparametric measure of rank correlation (statistical dependence between the rankings of two variables). It assesses how well the relationship between two variables can be described using a monotonic (whether linear or not) function. If there are no repeated data values, a perfect Spearman correlation of +1 or −1 occurs when each of the variables is a perfect monotone function of the other. Intuitively, the Spearman correlation between two variables will be high when observations have a similar rank between the two variables, and low when observations have a dissimilar rank between the two variables. Spearman's coefficient is appropriate for both continuous and discrete ordinal variables.

$$\rho = 1 - \frac{6 \sum {d_i}^2}{n(n^2 - 1)}$$

ρ = Spearman rank correlation coefficient

n = number of observations

d_i = difference between the two ranks of each observation

Mann Whitney U test: It is often considered the non-parametric alternative to the independent t-test. It is used to compare differences between two independent groups when the dependent variable is either ordinal or continuous, but not normally distributed.

Assumptions:

- The dependent variable should be measured on an ordinal scale or a continuous scale.
- The independent variable should be two categorical groups.
- Observations should be independent. In other words, there should be no relationship between the two groups or within each group.
- Observations are not normally distributed. However, they should follow the same shape (i.e., both are bell-shaped and skewed left).

$$U_x = n_x n_y + \frac{n_x(n_x + 1)}{2} - R_x$$

$$U_y = n_x n_y + \frac{n_y(n_y + 1)}{2} - R_y$$

Now, $U = \min(U_x, U_y)$ is the Mann-Whitney U statistic

n_x is the number of samples drawn from population X

n_y is the number of samples drawn from population Y

R_x is the sum of ranks attributed to population X

R_y is the sum of ranks attributed to population Y

Regression Assumptions –

- There should be a linear and additive relationship between dependent (response) variable and independent (predictor) variable(s). A linear relationship suggests that a change in response Y due to one unit change in X is constant, regardless of the value of X. An additive relationship suggests that the effect of X on Y is independent of other variables.
- There should be no correlation between the residual (error) terms. Absence of this phenomenon is known as Autocorrelation.
- The independent variables should not be correlated. Absence of this phenomenon is known as multicollinearity.
- The error terms must have constant variance. This phenomenon is known as homoskedasticity. The presence of non-constant variance is referred to heteroskedasticity.
- The error terms must be normally distributed.

Table 4 results interpret that both durations of type-2 diabetes ($M_f = 7.83$, $M_m = 7.88$; $p > 0.05$) and hypertension ($M_f = 5.54$, $M_m = 4.90$; $p > 0.05$) is not significantly distributed across sex.

DISCUSSION

Diabetes Mellitus is a metabolic syndrome characterized by hyperglycemia resulting in macrovascular complications along with high blood pressure.

There were 120 patients in the study. After analyzing the data and through Spearman's rank test and Mann-Whitney U test the value of p was >0.005 which showed there is a strong and positive correlation between Diabetes Mellitus type II and Hypertension.

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Tatsumi Yukako et al through their study obtained the same results which were conducted in Japan. The study showed there is a positive correlation between diabetes mellitus type II and hypertension and together both increase the risk factor for cardiovascular disease.[31]

A study conducted by **Azzam Al Nosayba et al** and found that HTN is most common in patients with Type II Diabetes Mellitus with a prevalence of 80%. Both Type II Diabetes Mellitus and HTN are associated with CKD and CVS.[32]

Zibaeenezhad et al conducted a study on 1799 patients and reported that there is a strong positive association between DM and HTN which later develops risk factors like major adverse cardiovascular events in patients of diabetes mellitus type II.[33]

Similar study conducted by Ziyad S. Almalki et all conducted a hospital based Cross sectional study on 1178 patients and concluded out of 1178 patients 846 (71.8%) had hypertension. The extent of uncontrolled hypertension amoung patients with diabetes was found to be high.[14]

A cross-sectional study titled "DM type II-induced Hypertension" by **Omer Abdelbagi e**t **al.** discovered that DMII is more frequently linked to hypertension. 854 (47.5%) of the 1973 patients who participated in the study had DMII and hypertension. This study's findings indicated a relationship between diabetes mellitus and hypertension that is favorable.[13]

Roberto Carlos et. al (2016) performed a cross-sectional study on 7164 older adults. Of 7164 older adults, 54.8% were women, and their mean age was 70.6 years with a mean frailty index score of 0.175. The prevalence of diabetes was of 22.2%, and 37.3% for hypertension. An independent association between diabetes, hypertension, or both conditions (coefficients 0.28, 0.4, and 0.63, respectively, P< 0.001) with frailty was found. Having any diabetic complication was significantly associated with frailty with a coefficient of 0.55 (95% CI 0.45–0.65, P< 0.001) in the adjusted model.[18]

The study conducted by **Kemche Beryl et al** on diabetics from the Yaoundé Central Hospital and the Etoug-Ebe Baptist Health Centre has a significant prevalence of hypertension (prevalence of 86.2%). Additionally, it emphasized how the nature of important risk factors changed as hypertension progressed, with the exception of how long diabetes persisted at each stage. Waist-to-hip ratio, waist circumference, smoking, and feeding rates were risk variables that might be changed. Gender, age, and diabetes duration were risk variables that could not be changed. Patients who have had diabetes for more than nine years should therefore receive extra attention. The early detection of normotensive diabetics who smoke and/or consume diets high in salt should also be a top priority. Patients older than 40 and/or with abnormal blood pressure should receive special attention when they are stage 1 hypertensive diabetes.[33]

CONCLUSION

The present study concluded that Diabetes Mellitus Type II is associated with Hypertension

We can apply our results and its interpretation in prevention and detection of hypertension in diabetes mellitus induced patient.

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ANNEXURE

ANNEXURE 1(A)

INFORMED CONSENT FORM (FOR CASE)

1. I **SANCHITA SINGH** MSC third-year student medical physiology IIMS&R Lucknow.
2. I am not associated with your treating doctor panel.
3. There will be no charges /fees/any consideration given or taken for the study.
4. Your identity will be confidential and information and result of your history examination will not be revealed to any other except you if u desire.
5. The study has nothing to do with your treatment and is not going to hamper if you refuse to participate.
6. The study has nothing to do with your current treatment but may improve the knowledge and understanding of disease process and that knowledge may or not be helpful in future.
7. After knowing the all above detail would you like to participate in our study? Yes/ No

Name of the patient Signature of the Research Scholar

Signature:

CONSENT FORM

I……aged…….W/O,D/O,S/O…….R/O……

……here with state that I have been duly informed about the study titled **"A STUDY OF DIABETES MELLITUS II INDUCED HYPERTENSION ."** , its prospects and consequences. I hereby give informed and written consent for the collection of my blood sample for the above said study only.

Signature/thumb impression of the patient:

Signature/thumb impression of the witness: Signature of research scholar:

ANNEXURE 1(B)

INFORMED CONSENT FORM (FOR CONTROL)

1. I SANCHITA SINGH M.SC third year student medical physiology IIMS&R Lucknow.
2. I am not associated with your treating doctor's panel
3. There will be no charges/fees/any consideration given or taken for the study.
4. Your identity will be confidential and the information and result of your history examination will not be revealed to any other except you if u desire.
5. The study is not going to hamper if you refuse to participate.
6. The study will/will not be beneficial for you but may improve the knowledge and understanding of the disease process and that knowledge may or may not be helpful in future.
7. After knowing the all above detail would you like to participate in our study? Yes/ No

Name of the subject Signature of the Research Scholar

Signature:

CONSENT FORM

I……aged…….W/O,D/O,S/O…….R/O……
……here with state that I have been duly informed about the study titled **"A STUDY OF DIABETES MELLITUS II INDUCED HYPERTENSION."**, its prospects and consequences. I hereby give informed and written consent for the collection of my blood sample for the above said study only.

Signature/thumb impression of the patient :

Signature/thumb impression of the witness: Signature of research scholar:

अनुलग्नक I (ए)

सूचित सहमति फॉर्म (मामले के लिए)

1. मैं संचिता सिंह एमएससी थर्ड ईयर स्टूडेंट मेडिकल फिजियोलॉजी आईआईएमएस आर लखनऊ।
2. मैं आपके ट्रीटिंग डॉक्टर पैनल से जुड़ा नहीं हूं।

3. अध्ययन के लिए कोई शुल्क /शुल्क /दिया गया या दिया गया कोई विचार नहीं होगा।

4. आपकी पहचान गोपनीय होगी और जानकारी और आपके इतिहास की परीक्षा का परिणाम किसी अन्य के अलावा आपके लिए नहीं होगा यदि आप चाहते हैं।

5. अध्ययन का आपके उपचार से कोई लेना -देना नहीं है और यदि आप भाग लेने से इनकार करते हैं तो आप बाधा नहीं डालेंगे।

6. अध्ययन का आपके वर्तमान उपचार से कोई लेना -देना नहीं है, लेकिन रोग प्रक्रिया के ज्ञान और समझ में सुधार हो सकता है और यह ज्ञान भविष्य में सहायक हो सकता है या नहीं।

7. उपरोक्त सभी विस्तार को जानने के बाद क्या आप हमारे अध्ययन में भाग लेना चाहेंगे? हां नहीं

रोगी का नाम: अनुसंधान विद्वान का हस्ताक्षर

हस्ताक्षर:

सहमति पत्र

मैं..... आयु .....
पुत्री/पुत्र/पत्नी.....पता.....
.....। यहाँ राज्य के साथ कि मुझे "ए स्टडी ऑफ मायोपिया और मेडिकल छात्रों में इसके संबद्ध जोखिम कारक" शीर्षक से अध्ययन के बारे में विधिवत जानकारी दी गई है। , इसकी संभावनाएं और परिणाम। मैंने अनुसंधान कार्य के विवरण को बहुत अच्छी तरह से जाना है और मैं उसी के लिए अपनी सहमति देता हूं।

रोगी के हस्ताक्षर/अंगूठे की छाप:

गवाह के हस्ताक्षर/अंगूठे की छाप: अनुसंधान विद्वान के हस्ताक्षर:

अनुलग्नक I (बी)

सूचित सहमति फॉर्म (नियंत्रण के लिए)

1. मैं संचिता सिंह एमएससी थर्ड ईयर स्टूडेंट मेडिकल फिजियोलॉजी आईआईएमएस आर लखनऊ।
2. मैं आपके ट्रीटिंग डॉक्टर पैनल से जुड़ा नहीं हूं।

3. अध्ययन के लिए कोई शुल्क /शुल्क /दिया गया या दिया गया कोई विचार नहीं होगा।

4. आपकी पहचान गोपनीय होगी और जानकारी और आपके इतिहास की परीक्षा का परिणाम किसी अन्य के अलावा आपके लिए नहीं होगा यदि आप चाहते हैं।

5. अध्ययन का आपके उपचार से कोई लेना -देना नहीं है और यदि आप भाग लेने से इनकार करते हैं तो आप बाधा नहीं डालेंगे।

6. अध्ययन का आपके वर्तमान उपचार से कोई लेना -देना नहीं है, लेकिन रोग प्रक्रिया के ज्ञान और समझ में सुधार हो सकता है और यह ज्ञान भविष्य में सहायक हो सकता है या नहीं।

7. उपरोक्त सभी विस्तार को जानने के बाद क्या आप हमारे अध्ययन में भाग लेना चाहेंगे? हां नहीं

रोगी का नाम: अनुसंधान विद्वान का हस्ताक्षर

हस्ताक्षर:

सहमति पत्र

मैं..... आयु .....
पुत्री/पुत्र/पत्नी.....पता.....
.....। यहाँ राज्य के साथ कि मुझे "ए स्टडी ऑफ मायोपिया और मेडिकल छात्रों में इसके संबद्ध जोखिम कारक" शीर्षक से अध्ययन के बारे में विधिवत जानकारी दी गई है। , इसकी संभावनाएं और परिणाम। मैंने अनुसंधान कार्य के विवरण को बहुत अच्छी तरह से जाना है और मैं उसी के लिए अपनी सहमति देता हूं।

रोगी के हस्ताक्षर/अंगूठे की छाप:

गवाह के हस्ताक्षर/अंगूठे की छाप: अनुसंधान विद्वान के हस्ताक्षर

INFORMATION SHEET (FOR CASES)

I, SANCHITA SINGH of Medical Physiology am a

research scholar in IIMS&R. I am not associated with

your treating doctor panel.

You are diagnosed with diabetes mellitus type II-associated hypertension.

For this study, I will take a history of patients with diabetes mellitus type II.

I will also measure your blood pressure with

Sphygmomanometer.You will be neither charged

for any of the above tests nor paid.

Your identity will be kept confidential and information and result will not be revealed to any other except you if you, so desire.

The result of this test may or may not be helpful for your treatment but may improve theknowledge and understanding of disease and the knowledge may be helpful in the future.

After having the all above information would you like to participate in our study? YES NO

CASE REPORT PERFORMA

Registration No/Date: OPD

IPDName (in capital):

Father Name/Husband's Name:

Mother Name:

Date of Birth:

Age:

Sex: Male

Female Marital status:

Permanent Address:

Current Address:

Mobile no:

Category: GEN OBC SC ST

Nationality

Mather Tongue:

Social/Economical Status: Annual income (approx.)

Educational level: Uneducated / Metric

/Graduate / Postgraduate / PhD .

Vegetarian / Non-Vegetarian:

Physical Activity: Sedentary / Moderate / Active

III DEMOGRAPHIC

1. **Age:** **years**
2. **Sex:** **Male** ☐ **Female** ☐

3. **Religion:**

4. **Height:** **Cm**

5. **Weight:** **Kg**

I.INCLUSION AND EXCLUSION

CRITERIA

INCLUSION CRITERIA

1. Subject with hypertension and diabetes.

2. Subject male & female.

EXCLUSION CRITERIA

1. pregnant females.

2. Subject with age less than 40

3. Terminal patients.

The subject is eligible for the study, if all **INCLUSION** criteria are **YES** and all **EXCLUSION**

criteria are **NO**

INVESTIGATORS

STATEMENT

I have verified the data entered in the case report form and have determined that it is complete,accurate, and compatible with the source documents.

Investigator's name Investigator's signature

Date

Family history

1. Mother **2. Father**

a) Mother suffers from diabetic Disorders: b) Father suffers from diabetic.

Yes, No Unknown **Yes, No Unknown**

3. No. of siblings: ☐

How many of them suffering from diabetic ? ☐

III. **MEDICAL HISTORY**

HYPERTENSION : ☐

	Yes	No
1. MILD HYPERTENSION:	☐	☐
2. MODERATE HYPERTENSION:	☐	☐
3. SEVERE HYPERTENSION:	☐	☐

1. Treatment: ☐ ☐

If yes, specify:

- Duration of treatment:

3. Patient complications; - ☐ **Low** **Fair** ☐ **High**

ETHICAL CLEARENCE

INSTITUTIONAL ETHICS COMMITTEE (IEC)

IIMS&R INTEGRAL UNIVERSITY, LUCKNOW

IEC/IIMS&R/2023/11

CERTIFICATE

This is to certify that research work entitled **"Type II Diabetes Mellitus Associated Hypertension"** submitted by **Sanchita Singh** for ethical approval before the Institutional Ethics Committee IIMS&R. The above mentioned research work has been approved by Institutional Ethics Committee, IIMS&R with consensus in the meeting held on **30th December 2022**.

Dr.Q.S.Ahmed
(Member Secretary)
IRC/IEC
IIMS &R

S.NO	AGE	SEX	LOCATION	SOCIO ECONOMIC STATUS	T2DM	HTN	RBS	SystolicBP	DiastolicBP	TOBACCO	ALCOHOL	VEG DIET	NON VEG DIET	ON DM MEDICATION	INSULIN	ON HTN MEDICATION
1	80	2	1	1	30	25	364	160	70	1	1	1	1	1	1	1
2	80	1	1	1	5	0.2	365	180	100	0	0	0	0	0	0	0
3	80	1	1	2	5	0.2	365	160	100	0	0	0	0	0	0	0
4	75	1	2	3	8	8	356	180	100	0	0	0	0	0	0	0
5	72	2	1	1	10	4	210	173	80	1	1	1	1	1	1	1
6	70	1	1	2	30	20	225	154	92	1	0	0	0	0	0	0
7	70	2	1	1	20	20	460	160	100	1	0	0	0	0	0	0
8	70	2	1	1	10	2	160	135	85	1	0	0	0	0	0	0
9	68	1	2	2	3	3	150	187	94	0	0	0	0	0	0	0
10	67	2	1	1	10	10	550	180	100	1	0	0	0	0	0	0
11	66	2	2	3	10	1	170	150	80	0	0	0	0	0	0	0
12	65	1	1	2	10	10	200	180	80	1	0	0	0	0	0	0
13	65	1	2	1	10	8	324	150	70	0	0	0	0	0	0	0
14	65	1	1	3	9	8	180	166	88	1	0	0	0	0	0	0
15	65	1	2	2	6	2	260	140	90	0	1	1	1	1	1	1
16	65	2	2	1	5	2	255	120	60	1	1	1	1	1	1	1
17	65	1	1	1	3	3	164	140	90	0	0	0	0	0	0	0
18	65	2	1	1	3	1	132	136	82	0	0	0	0	0	0	0
19	62	2	1	1	20	20	288	150	90	1	0	0	0	0	0	0
20	62	2	1	2	12	12	250	140	80	1	0	0	0	0	0	0
21	61	2	2	2	1	0.2	193	180	100	0	0	0	0	0	0	0
22	60	1	1	1	24	15	388	160	70	0	0	0	0	0	0	0
23	60	1	1	1	20	20	2OO	166	82	1	0	0	0	0	0	0
24	60	1	1	1	20	20	300	160	88	1	0	0	0	0	0	0
25	60	1	1	1	20	20	300	160	86	1	0	0	0	0	0	0
26	60	2	1	1	20	15	500	190	100	1	0	0	0	0	0	0
27	60	1	1	2	20	10	300	160	80	1	0	0	0	0	0	0
28	60	2	1	1	20	10	460	150	90	0	0	0	0	0	0	0
29	60	2	2	2	19	15	180	140	80	1	0	0	0	0	0	0
30	60	1	1	1	15	15	385	136	82	1	0	0	0	0	0	0
31	60	1	2	1	15	10	160	160	100	0	0	0	0	0	0	0
32	60	2	2	1	10	10	300	140	70	1	0	0	0	0	0	0
33	60	2	1	1	10	2	360	160	90	1	0	0	0	0	0	0
34	60	1	1	1	10	1	360	140	50	1	0	0	0	0	0	0
35	60	2	1	1	2	0.5	339	160	80	1	1	1	1	1	1	1
36	60	1	2	1	2	0.5	207	144	74	0	0	0	0	0	0	0
37	60	1	1	1	1	1	172	154	96	0	0	0	0	0	0	0
38	59	2	1	2	1	1	600	140	80	1	1	1	1	1	1	1
39	58	2	1	1	5	1	365	140	90	1	0	0	0	0	0	0
40	58	2	2	2	3	1	210	160	90	1	0	0	0	0	0	0
41	57	1	1	3	13	12	200	160	62	0	0	0	0	0	0	0
42	57	1	1	1	10	6	190	160	80	1	0	0	0	0	0	0
43	55	1	1	1	10	8	604	140	80	0	0	0	0	0	0	0
44	55	2	1	1	15	2	225	160	90	1	1	1	1	1	1	1
45	55	1	1	2	12	8	150	100	70	0	0	0	0	0	0	0
46	55	2	1	1	10	6	289	160	100	1	1	1	1	1	1	1
47	55	2	1	1	5	5	250	230	120	0	0	0	0	0	0	0
48	55	2	1	2	5	2	565	160	90	0	1	1	1	1	1	1

49	55	1	1	1	4	3	250	160	100	0	0	0	0	0	0	0
50	55	2	1	1	4	1	230	140	80	0	0	0	0	0	0	0
51	55	1	2	2	3	3	600	140	80	0	0	0	0	0	0	0
52	54	1	1	1	20	15	247	140	80	1	0	0	0	0	0	0
53	54	1	1	1	15	10	300	140	80	1	0	0	0	0	0	0
54	54	1	2	2	10	5	439	140	80	0	0	0	0	0	0	0
55	53	1	1	2	5	2	480	160	110	1	0	0	0	0	0	0
56	53	1	1	2	3	1	255	154	86	0	0	0	0	0	0	0
57	52	2	2	2	6	2	234	160	80	1	1	1	1	1	1	1
58	52	2	2	2	3	1	550	168	109	0	0	0	0	0	0	0
59	52	2	1	2	2	0.2	168	140	80	0	0	0	0	0	0	0
60	50	1	2	2	25	18	260	144	84	1	0	0	0	0	0	0
61	50	1	1	2	6	2	360	180	100	1	1	1	1	1	1	1
62	50	2	1	1	5	2	480	160	90	1	0	0	0	0	0	0
63	50	2	1	1	5	2	250	140	80	0	0	0	0	0	0	0
64	50	1	1	1	1	0.1	220	160	90	1	0	0	0	0	0	0
65	50	2	1	1	0.5	0.5	180	140	80	0	0	0	0	0	0	0
66	50	1	1	2	0.4	0.5	300	175	113	0	0	0	0	0	0	0
67	49	2	1	1	5	1	365	140	80	1	0	0	0	0	0	0
68	49	2	2	2	4	3	207	140	80	1	0	0	0	0	0	0
69	48	2	1	2	10	9	300	180	100	0	0	0	0	0	0	0
70	48	1	2	2	10	5	570	180	90	1	0	0	0	0	0	0
71	48	1	1	2	3	1	290	150	88	0	0	0	0	0	0	0
72	48	2	1	1	3	1	230	140	80	1	0	0	0	0	0	0
73	47	1	1	1	0.2	0.2	260	140	80	0	0	0	0	0	0	0
74	46	1	1	2	0.2	0.2	377	180	100	1	0	0	0	0	0	0
75	45	1	2	1	12	8	471	140	90	0	0	0	0	0	0	0
76	45	1	1	1	10	10	200	180	80	0	0	0	0	0	0	0
77	45	1	1	1	6	2	236	140	88	0	0	0	0	0	0	0
78	45	1	1	2	5	4	400	140	90	0	1	1	1	1	1	1
79	45	1	1	1	2	1	322	140	80	0	0	0	0	0	0	0
80	45	1	2	2	1	0.5	195	140	80	0	0	0	0	0	0	0
81	45	1	1	1	1	0.1	250	140	80	0	0	0	0	0	0	0
82	45	1	1	3	0.6	0.12	110	140	70	1	0	0	0	0	0	0
83	45	2	2	1	0.4	0.4	450	140	80	1	0	0	0	0	0	0
84	44	1	2	2	10	7	150	140	80	0	0	0	0	0	0	0
85	44	2	1	1	10	2	230	150	94	1	1	1	1	1	1	1
86	44	1	1	1	7	5	336	152	98	0	0	0	0	0	0	0
87	43	1	1	2	4	3	277	160	100	1	0	0	0	0	0	0
88	42	1	2	2	15	10	244	150	94	0	1	1	1	1	1	1
89	42	1	1	2	15	10	146	140	80	0	0	0	0	0	0	0
90	42	1	1	1	4	4	297	140	96	0	0	0	0	0	0	0
91	41	1	2	1	1	1	222	170	100	0	0	0	0	0	0	0
92	40	2	1	1	6	6	200	120	80	0	0	0	0	0	0	0
93	40	2	1	1	6	2	200	140	80	0	1	1	1	1	1	1
94	40	2	2	1	5	1	247	140	80	0	1	1	1	1	1	1
95	40	2	1	1	4	4	380	160	100	1	1	1	1	1	1	1
96	40	2	1	1	3	3	270	140	70	1	0	0	0	0	0	0
97	40	1	1	1	3	2	225	140	90	1	0	0	0	0	0	0
98	40	1	2	1	3	1	379	140	90	0	0	0	0	0	0	0
99	40	1	1	1	1	1	296	150	80	0	0	0	0	0	0	0

100	40	1	1	1	1	1	500	140	80	0	0	0	0	0	0
101	40	2	1	1	1	0.2	311	130	90	1	0	0	0	0	0
102	40	1	1	1	1	0.1	376	160	80	0	0	0	0	0	0
103	40	1	1	2	0.5	0.5	200	160	80	0	0	0	0	0	0
104	40	1	1	1	0.12	0.12	115	140	70	1	0	0	0	0	0
105	40	2	2	3	0.1	0.1	180	155	75	1	0	0	0	0	0
106	40	1	1	1	0.1	0.1	115	110	70	1	0	0	0	0	0
107	40	1	1	1	0.1	0.08	250	140	80	1	0	0	0	0	0
108	75	1	2	2	10	10	500	180	90	0	0	1	0	1	1
109	40	2	2	2	0.2	0.1	277	140	90	0	0	1	0	1	0
110	63	2	1	1	20	15	300	180	110	0	0	0	1	1	1
111	40	2	2	2	2	1	180	140	90	0	0	1	0	1	0
112	76	1	2	2	20	16	215	140	70	0	0	1	0	1	0
113	49	1	2	2	4	3	470	170	80	0	0	0	1	1	1
114	47	1	1	1	6	1	376	190	90	0	0	1	0	1	0
115	60	1	2	2	10	8	500	190	80	0	0	1	0	1	1
116	66	2	2	2	15	10	500	180	90	0	0	1	0	1	1
117	67	2	2	3	10	6	365	180	90	0	0	1	0	1	1
118	50	1	2	3	6	2	400	190	90	1	0	0	1	1	1
119	55	2	2	3	8	4	430	180	90	0	1	1	0	1	1
120	46	1	2	3	2	1	200	140	80	0	0	1	0	1	0

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