PREVALENCE OF GALLBLADDER STONES AND THE ASSOCIATED RISK FACTORS AMONG TYPE 2 DIABETES MELLITUS PATIENTS - A CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELAGAVI.

By

REG. NO. BG0116015

Dissertation

Submitted to the
KLE Academy of Higher Education and Research,
Belagavi, Karnataka.

In partial fulfillment
of the requirements for the degree of

M.D.
in
GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI, KARNATAKA.

APRIL - 2019

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

ENDORSEMENT

This is to certify that the dissertation entitled **"PREVALENCE OF GALLBLADDER STONES AND THE ASSOCIATED RISK FACTORS AMONG TYPE 2 DIABETES MELLITUS PATIENTS - A CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELAGAVI"** is a bonafide research work done by **(REG. NO. BG0116015)** .

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LIST OF ABBREVIATIONS

ADA	American Diabetes Association
ATP	Adult Treatment Panel
BC	Before Christ
BMI	Body Mass Index
CCK	Cholecystokinin
CHD	Coronary Heart Disease
CI	Confidence Interval
CT	Computed Tomography
DAN	Diabetic Autonomic Neuropathy
DM	Diabetes Mellitus
DN	Diabetic Neuropathy
GDM	Gestational Diabetes Mellitus
GI	Gastro Intestinal
HDL	High Density Lipoprotein
ICMR	Indian Council of Medical Research
IDPP	Indian Diabetes Prevention Programme
IGT	Impaired Glucose Tolerance
LDL	Low Density Lipoprotein
LPL	Lipo-Protein Lipase

MRI	Magnetic Resonance Imaging
NIDDM	Non Insulin Dependent Diabetes Mellitus
OGGT	Oral Glucose Tolerance Test
OR	Odds Ratio
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
T2DM	Type 2 Diabetes Mellitus
TGF	Transforming Growth Factor
TZD	Thiazolidinedione
VLDL	Very Low Density Lipoprotein
WHR	Waist to Hip Ratio

ABSTRACT

Background and Objectives

Diabetes mellitus refers to a group of metabolic disorders that share the phenotype of hyperglycemia. Diabetes related complications affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease. An altered glucose metabolism may increase the risk of cholelithiasis in certain subjects. The objective of the present study was to study the prevalence of gallbladder stones and the associated risk factors among type 2 diabetes mellitus patients.

Materials and Methods

The study was done on 200 patients of type 2 diabetes mellitus, admitted in KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi over a period of one year from January 2017 to December 2017. A thorough medical history was obtained, clinical examination and investigations were performed on the study subjects. Ultrasonography of abdomen was done with special reference to gallbladder and gallstones. The statistical analysis was done using SPSS version 20.0 software. The chi square test and the multiple logistic regression analysis were performed.

Results

The prevalence of gallbladder stones was 33.50%, with 67 type 2 diabetes mellitus patients having asymptomatic gallstones out of the total 200 study subjects. The mean age of the patients with gallstones was 54.67 ± 11.91 years. Out of the 67 patients who were positive for the asymptomatic gallstones, there were 29 males and

38 females. The association of prevalence of gallstones was found to be statistically significant with the BMI, HbA1c, diabetic autonomic neuropathy, total cholesterol, triglyceride and low density lipoprotein. In the patients with gallstones, the mean BMI was 34.39 ± 6.68 kg/m^2 and mean HbA1c was 9.67 ± 2.16%. The mean total cholesterol, triglyceride and low density lipoprotein levels in the patients with gallstones were 225.55 ± 48.38 mg/dl, 207.64 ± 42.4 mg/dl and 144.23 ± 50.17 mg/dl respectively.

Conclusion

In the present study the prevalence of gallbladder stones was 33.50%, with 67 type 2 diabetes mellitus patients having asymptomatic gallstones out of the total 200 study subjects. BMI, HbA1c, diabetic autonomic neuropathy, total cholesterol, triglycerides and low density lipoprotein were found to be significantly associated with gallstone formation in the patients with type 2 diabetes mellitus. This knowledge may provide an early interventional opportunity to implement adequate preventive measures and the consequent morbidity and mortality can be prevented to a greater extent.

Key words Type 2 diabetes mellitus, ultrasonography, gallstones.

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INTRODUCTION

Diabetes mellitus refers to a group of metabolic disorders that share the phenotype of hyperglycemia. The worldwide prevalence of diabetes mellitus has risen dramatically over the past two decades. Diabetes related complications affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease.[1] An altered glucose metabolism may increase the risk of cholelithiasis in certain subjects.[2]

Diabetics with autonomic neuropathy tend to have stasis of bile in the gall bladders along with poor contraction ability in response to fatty meals, thus predisposing these patients to various forms of gall bladder disease.[3]

Diabetics could form cholesterol gallstones more frequently because of a reduced gallbladder contraction and increased biliary cholesterol secretion.[4] A meta-analysis study suggested that there is a strong association between diabetes mellitus and the prevalence of gallstone disease.[5] The incidence of gallstones is higher in type 2 diabetics both in males and females than the non-diabetics.[6]

Female gender, raised total cholesterol and high BMI are risk factors for asymptomatic gallstones in middle aged and elderly patients with type 2 diabetes mellitus.[7]

Mean gallbladder volume is significantly increased in type 2 diabetic patients as compared to non-diabetic healthy subjects.[8]

Poor control of diabetes, hypercholesterolemia and diabetic autonomic neuropathy are important factors for the development of gallbladder disease[9].

Recent studies suggest that, the association between gallstone formation and diabetes can be explained by chronic hyperglycaemia, decrease in gallbladder motility and associated obesity as risk factors in patients with type 2 diabetes mellitus.[10,11]

Many of the diabetes related complications can be prevented or delayed with early detection and aggressive glycemic control.[1]

The present study will be undertaken to have more knowledge about the prevalence of gallbladder stones and the risk factors associated with them in type 2 diabetes mellitus patients, as there is paucity of literature on such study done in this region. This knowledge may provide an early interventional opportunity to implement adequate preventive measures.

OBJECTIVES

1. To study the prevalence of gallbladder stones among type 2 diabetes mellitus patients admitted in KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi.
2. To study the risk factors associated with gallbladder stones among type 2 diabetes mellitus patients -
    a) High Body Mass Index (BMI).
    b) Poor control of diabetes.
    c) Duration of diabetes.

REVIEW OF LITERATURE

Diabetes mellitus

Diabetes mellitus (DM) is a chronic disorder characterized by abnormal metabolic regulation as well as by the potential for vascular and neuropathic complications. Diabetes comprises a cluster of heterogeneous disorders with elevated blood glucose levels as a common diagnostic feature.[12]

Diabetes can affect every system in the body. Hyperglycaemia results in both acute and long-term problems.[13]

Historical Review

Demetrius of Apameia introduced the term 'Diabetes' in the 2nd century BC[14]. Descriptions of abnormal polyuria were recorded as early as 1500 BC in the Egyptian Papyrus Ebers which is an ancient written document of medical knowledge. The early Egyptians, Indians, and Asians noted the sweet taste of urine[14,15,16].

Stanley Benedict, in 1907 developed a test for glycosuria using a copper reagent with a carbonate base. In 1913, Ivar Bang pioneered a method to test blood glucose levels whereby blood proteins were fixed to filter paper and the filtrate was used to measure glucose using copper sulphate and potassium chloride.[17]

In 1979, the National Diabetes Data Group and the World Health Organization developed diagnostic criteria for the diagnosis of diabetes that involved measuring glucose tolerance using an oral glucose tolerance test (OGTT).[18]

Epidemiology

The global burden due to diabetes is mostly contributed by type 2 diabetes which constitutes 80% to 95% of the total diabetic population[19]. Diabetes Mellitus (DM) is the most common metabolic disease which is prevalent in every part of the world and is a major public health challenge of the twenty-first century[19].

Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035. The prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population.[1]

Nauru has the highest prevalence of diabetes (30.9%) and will continue to be so in 2030 (33.4%). Nearly 70% of the people with diabetes live in developing countries. The largest numbers are in the Indian subcontinent and China.[19]

The prevalence of diabetes in India in 1970's was 2.3% in urban and 1.5% in rural areas, as shown by the multi-centric study by the Indian Council of Medical Research (ICMR). In 2000s, the prevalence has risen to 12% to 19% in urban areas and to 4% to 9% in rural areas. The Indian Diabetes Prevention Programme-1 (IDPP-1) has shown an annual incidence of approximately 18% among subjects with Impaired Glucose Tolerance (IGT).[19]

Table 1: Etiologic classification of diabetes mellitus.

	Etiologic classification of diabetes mellitus[1]
1.	**Type 1 diabetes.**
	A. Immune-mediated
	B. Idiopathic
2.	**Type 2 diabetes.**
3.	**Other specific types of diabetes**
	A. Genetic defects of beta cell development or function characterized by mutations.
	B. Genetic defects in insulin action.
	C. Diseases of the exocrine pancreas.
	D. Endocrinopathies.
	E. Drug or chemical induced.
	F. Infections.
	G. Other genetic syndromes sometimes associated with diabetes.
4.	**Gestational diabetes mellitus (GDM).**

Risk factors for type 2 diabetes mellitus[1]

1) Family history of diabetes (i.e., parent or sibling with type 2 diabetes).
2) Obesity (BMI ≥25 kg/m^2 or ethnically relevant definition for overweight).
3) Physical inactivity.
4) Race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
5) Previously identified with Impaired Fasting Glucose (IFG), IGT, or an HbA1c of 5.7-6.4%
6) History of GDM or delivery of baby >4 kg.
7) Hypertension (blood pressure ≥140/90 mmHg)
8) High Density Lipoprotein (HDL) level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L).
9) Polycystic ovary syndrome or acanthosis nigricans.
10) History of cardiovascular disease.

Screening for Type 2 Diabetes Mellitus[1]

Screening test for type 2 DM is recommended because

1) A large number of individuals who meet the current criteria for DM are asymptomatic and unaware that they have the disorder.
2) Epidemiologic studies suggest that type 2 DM may be present for up to a decade before diagnosis.
3) Some individuals with type 2 DM have one or more diabetes-specific complications at the time of their diagnosis.
4) Treatment of type 2 DM may favourably alter the natural history of DM, and the diagnosis of pre-diabetes should spur efforts for diabetes prevention.

The American Diabetes Association (ADA) recommends screening all individuals >45 years every 3 years and screening individuals at an earlier age if they are overweight (BMI >25 kg/m2 or ethnically relevant definition for overweight) and have one additional risk factor for diabetes. The use of the Fasting Plasma Glucose or the HbA1c as a screening test for type 2 DM is recommended.

The criteria for the diagnosis of diabetes[1]

1) Symptoms of diabetes plus Random Plasma Glucose ≥200mg/dl.

or

2) Fasting Plasma Glucose ≥ 126mg/dl.

or

3) Postprandial Plasma Glucose ≥ 200mg/dl.

or

4) Hemoglobin A1c ≥ 6.5%

or

5) 2-h Plasma Glucose ≥ 200 mg/dL during an oral glucose tolerance test.

- Random is defined as without regard to time since the last meal.
- Fasting is defined as no caloric intake for at least 8 h.
- HbA1c test should be performed in a laboratory using a method approved by the National Glycohemoglobin Standardization Program and correlated to the reference assay of the Diabetes Control and Complications Trial.
- Point of care HbA1c should not be used for diagnostic purposes.
- The 2-h plasma glucose test should be performed using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water.

Table 2: The relationship between HbA1c and estimated average glucose levels during the preceding 3 months[12]

	Estimated average glucose level	
HbA1c (%)	**mg/dL**	**mmol/L**
5	97	5.4
6	126	7.0
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.4
11	269	14.9
12	298	16.5

Table 3: Recommended glycemic targets for adults with diabetes[1]

Treatment Goals for Adults with Diabetes	
Index	**Goal**
Glycemic control	
HbA1c	<7.0%
Preprandial capillary plasma glucose	4.4–7.2 mmol/L (80–130 mg/dL)
Peak postprandial capillary plasma glucose	<10.0 mmol/L (<180 mg/dL)
Blood pressure	<140/90 mmHg
Lipids	
Low-density lipoprotein	<2.6 mmol/L (100 mg/dL)
High-density lipoprotein	>1 mmol/L (40 mg/dL) in men >1.3 mmol/L (50mg/dL) in women
Triglycerides	<1.7 mmol/L (150 mg/dL)

Diabetes related complications[1]

The four theories of hyperglycemia leading to the chronic complications of Diabetes Mellitus.

1. Increased intracellular glucose leads to the formation of advanced glycosylation end products, which bind to a cell surface receptor. This leads to accelerated atherosclerosis, glomerular dysfunction, endothelial dysfunction, and altered extracellular matrix composition.

2. Hyperglycemia increases glucose metabolism via the sorbitol pathway related to the enzyme aldose reductase.
3. Hyperglycemia increases the formation of diacylglycerol, leading to activation of protein kinase C, which alters the transcription of genes for fibronectin, type IV collagen, contractile proteins, and extracellular matrix proteins in endothelial cells and neurons.
4. Hyperglycemia increases the flux through the hexosamine pathway, which generates fructose-6-phosphate, leading to altered function by glycosylation of proteins such as endothelial nitric oxide synthase or by changes in gene expression of Transforming Growth Factor β (TGF-β) or plasminogen activator inhibitor-1.[1]

Table 4: Chronic complications of diabetes mellitus.[1]

	Microvascular
1	Eye disease
	Retinopathy (non-proliferative/proliferative)
	Macular edema
2	Neuropathy
	Sensory and motor (mono and polyneuropathy)
	Autonomic
3	Nephropathy (albuminuria and declining renal function)
	Macrovascular
1	Coronary heart disease
2	Peripheral arterial disease
3	Cerebrovascular disease
	Others
1	Gastrointestinal (gastroparesis, diarrhea)
2	Genitourinary (uropathy/sexual dysfunction)
3	Dermatologic
4	Infectious
5	Cataracts
6	Glaucoma
7	Cheiroarthropathy
8	Periodontal disease
9	Hearing loss

Gallbladder Anatomy[20]

The gallbladder is a flask-shaped, blind-ending diverticulum attached to the bile duct by the cystic duct. It stores and concentrates bile. In life, it is grey–blue in colour and is usually firmly attached by connective tissue to the inferior surface of the right lobe of the liver.

In the adult, the gallbladder is between 7 and 10 cm long, with a resting volume of about 25 ml and a capacity of up to 50 ml.

The gallbladder is described as having a fundus, body and neck. The body of the gallbladder normally lies in contact with the visceral surface of the liver. The cystic duct drains the gallbladder into the common bile duct. In adults, it is usually between 2 and 4 cm long and has a luminal diameter of 2–3 mm. The common hepatic duct descends approximately 3 cm before being joined obliquely on its right by the cystic duct to form the common bile duct.

Innervation[20]

The gallbladder and the extrahepatic biliary tree are innervated by branches from the hepatic plexus. Gallbladder contraction occurs in response to Cholecystokinin (CCK) and parasympathetic (vagal) stimulation. Expulsion of gallbladder contents is under neuroendocrine control. Fat in the duodenum causes the release of CCK by intestinal neuroendocrine cells, which stimulates the gallbladder to contract because muscle cells in its walls bear surface receptors for CCK.

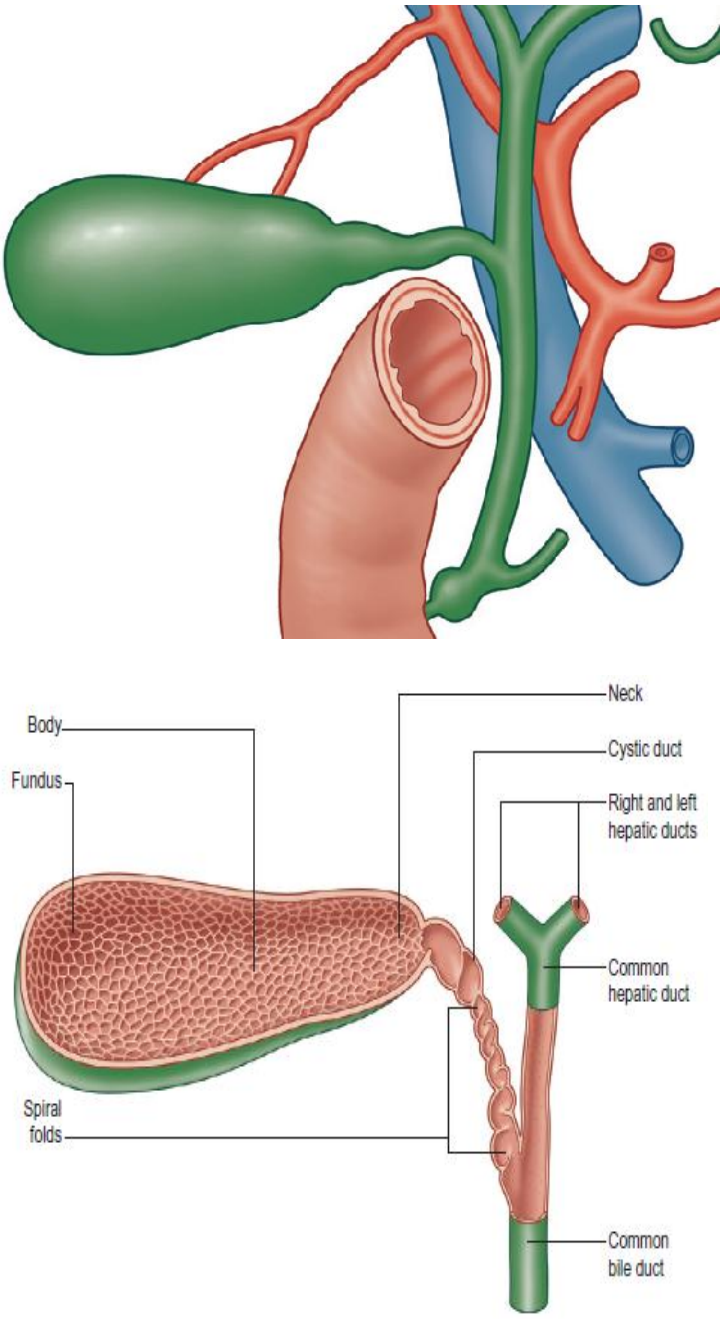


Figure 1: Gallbladder anatomy with external and internal features

Patients with diabetes mellitus have long been considered to be at increased risk of developing gallstones because hypertriglyceridemia and obesity.[21]

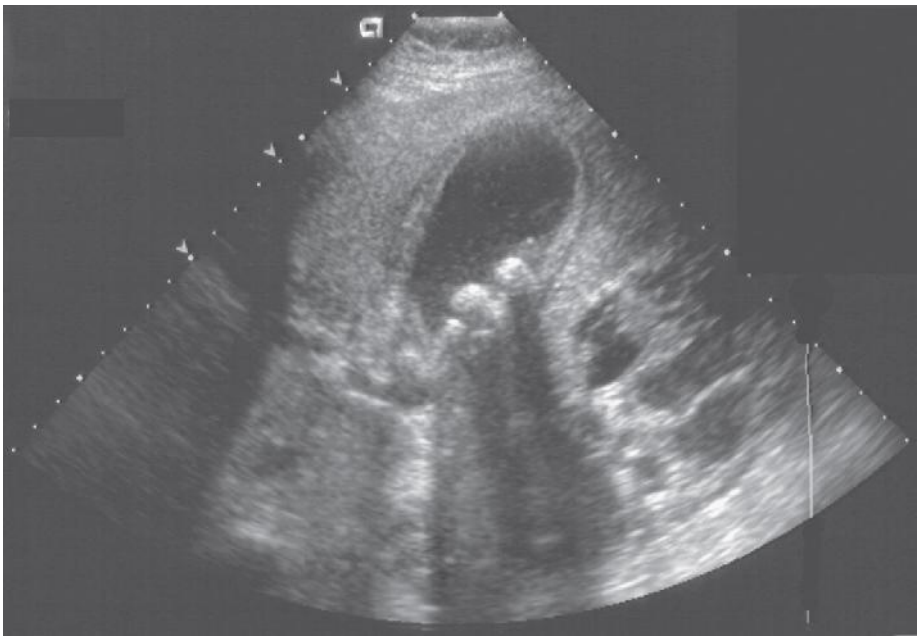


Figure 2: Ultrasound image showing multiple gallstones with thickened gallbladder

Hepatic insulin resistance promotes hepatic secretion of biliary cholesterol by increasing expression of the hepatic cholesterol transporters Abcg5 and Abcg8 through the forkhead transcription factor FoxO1 pathway. It also reduces expression of the bile salt synthetic enzymes, particularly oxysterol 7α-hydroxylase, thereby resulting in a lithogenic bile salt profile.[21]

Gallbladder hypomotility could precede gallstone formation. Gallbladder stasis induced by the hypofunctioning gallbladder could provide the time necessary to accommodate nucleation of cholesterol crystals and growth of gallstones within the mucin gel in the gallbladder.[21]

It has been attributed that the formation of gallbladder stones is due to cholecystomegaly and impaired gall bladder contraction, mainly due to autonomic neuropathy seen in diabetics.[22]

Diabetic autonomic neuropathy of the alimentary canal takes several forms [23]:

a) Esophagopathy
b) Gastroparesis
c) Enteropathy
d) Biliary tract disorders.

The commonly cited reasons for the increased prevalence of gall stone disease in diabetics include[23]:

a) Decreased gall bladder motility.
b) Decreased postprandial cholecystokinin (CCK) release.
c) Decreased sensitivity of gall bladder smooth muscle to CCK.
d) Decreased number of CCK receptors in the gallbladder wall.

Pathogenesis of diabetic cholecystoparesis:

Neural control of gallbladder emptying is mediated by both parasympathetic and sympathetic innervations. The former increases gallbladder contractility and the latter causes relaxation. Meal-related release of CCK causes gallbladder contraction. The motility defects of gallstone patients are manifested by increased fasting volume, decreased ejection fraction, decreased rate of ejection, and increased residual volume of the gall bladder[24]. Hahn et al. suggested that impairment of gall bladder motility complicated by autonomic neuropathy causes stasis and results in cholesterol gall stone crystal formation and gall stone growth.[25]

The frequency of large gallbladders was higher among the diabetic than the non diabetic individuals. The findings reported in a study by Gitelson et al., suggest that a search for diabetes is justified in patients with a large gallbladder. In some of the cases studied in the past, the finding of a large gallbladder on cholecystography gave the first clue leading to the detection of previously unsuspected diabetes.[25]

The exact mechanisms for the impairment in post-prandial gall-bladder emptying in diabetics are not known. It is reported that in Non Insulin Dependent Diabetes Mellitus (NIDDM) patients with gallstones, fasting serum insulin and daily average insulin levels are higher than in NIDDM patients without gallstones. Several studies have recently pointed to the effect of blood glucose concentrations in the regulation of gastrointestinal motility both in healthy subjects and in diabetics. In healthy volunteers acute hyperglycemia dose-dependently inhibits Cholecystokinin (CCK) and meal-stimulated gall-bladder emptying, as well as CCK-stimulated pancreatic polypeptide secretion, suggesting impaired cholinergic activity during hyperglycemia. Pazzi et al., reviewed gall bladder motor function in diabetes and proposed that the mechanism of gall bladder emptying abnormalities may represent a manifestation of denervation caused by visceral neuropathy, a decreased sensitivity of smooth muscle of the gall bladder to plasma cholecystokinin, and/or decreased cholecystokinin receptors in the gall bladder wall[26].

In healthy subjects, acute hyperglycemia and also euglycemic hyperinsulinaemia have been shown to reduce basal duodenal bilirubin output and inhibit gall-bladder emptying stimulated by infusion of low-dose CCK, producing plasma CCK levels similar to those seen after a low-fat meal. This inhibitory effect was more pronounced during hyperglycemia than during euglycemic hyperinsulinaemia.[26]

Gallbladder Disease and Diabetes Mellitus

Recent studies suggest that, the association between gallstone formation and diabetes can be explained by chronic hyperglycaemia, decrease in gallbladder motility and associated obesity as risk factors in patients with type 2 diabetes mellitus.[10, 11]

Poor control of diabetes, hypercholesterolemia and diabetic autonomic neuropathy are important factors for the development of gallbladder disease.

In a study conducted on 50 cases of type 2 diabetes mellitus and 25 healthy controls, it was found that 34% of type 2 diabetics had gallstones.[9] Diabetics could form cholesterol gallstones more frequently because of a reduced gallbladder contraction and increased biliary cholesterol secretion.[4]

In another study gallstones were seen in 25.2% of diabetic patients. Gallstone was higher in patients with increased duration of diabetes, in patients with BMI more than 25kg/m, with increased cholesterol and triglycerides levels and with high level of HbA1C.[27]

These risk factors were also confirmed in the study conducted by Chapman et al., which also found a statistically significant association between increased age, BMI, triglycerides, LDL, alcohol intake and family history of gallstone disease.[28]

In a study conducted by Saxena et al., 29% of patients of type 2 DM had gallstones and 67.5% of diabetics with gallstones were females.[29]

Various modifiable and non modifiable risk factors are correlated with the association of type 2 diabetes mellitus and gall stones. Among the non modifiable risk factors family history of gall stone disease and duration of diabetes was positively

correlated. Among modifiable risk factors which were found to be significant were BMI and sedentary life style. Importance of these observation lies in respect to early identification and control of the modifiable risk factor.[30, 31]

In a study done by Kaur M et al., the prevalence of gallbladder disease among the diabetes was 45%[31]. The studies done by Elmehdawi RR et al.[32], Gupta RS et al.[33], also showed significant increase in the incidence of gallbladder disease in diabetic patients. Chhabra A et al., which also reports 34% prevalence of gallstones in patients of type 2 diabetes mellitus.[9] Another study done by Al-Kayatt et al.[34] in 2012 also reported a prevalence of gallstones in type 2 diabetes mellitus to be 33%. The Goyel K. study focused on the magnitude of the asymptomatic gallstones in patients of type 2 diabetes mellitus in New Delhi and found about 31% had asymptomatic gallstone disease.[35]

Other studies from different countries showed different figures. In Taiwan, Liu CM showed the prevalence of gallstones in diabetic patients was 14.4% [36]. Pagliarulo M. et al. from Italy showed a prevalence of 24.8% [37], Agunloye A.M. et al. from Nigeria showed the prevalence of asymptomatic gallstone disease in patients of type 2 diabetes mellitus to be 17.5%[38]. Such variation in the prevalence of gallbladder stones in type 2 diabetes mellitus patients across the globe could be attributed to the different study designs, geographical variation and the difference in ethnicity of the patients.[39]

Certain studies found that the distribution of asymptomatic gallstone disease according to the increasing age was statistically significant. A study done by Coelho JC et al. found an average age of 59.9 years in the patients with gallstones[40]. Sodhi J.S. et al.[41] showed that the prevalence of the gallstones in type 2 diabetes mellitus patients increased with the increasing age with a peak in the sixth decade. Another

study by Khalaf SK[27] revealed that the peak prevalence of the gallstones was in the age group of 40-49 years and these results were in agreement with other studies done in Iran by Rasheed K[42] and Idris S.A. et al.[43].

The study done by Khare et al.[7] showed that 65.38% of the diabetic patients with gallstones were females and only 34.61% subjects were males. They found this association to be statistically significant. The female gender association with the increased prevalence of the gallstones in patients of type 2 diabetes mellitus was also found in the other studies done by Anmar HA[6] and Saxena R. et al.[29] which showed that 67.05% of the diabetic patients with gallstone disease were females. The rationale offered for the increased prevalence of the gallbladder stones in the female patients of type 2 diabetes mellitus is that, the women especially those in the reproductive age group are 2–3 times more predisposed to develop gallstones than those in the non-reproductive age group. This is due to the high estrogen levels which causes bile super-saturation with cholesterol.[44]

A high level of HbA1c reflects poor control of diabetes mellitus. The study done by Khalaf et al.[27] reported a mean HbA1c level of 11.01 ± 2.1%.

It is a known fact that the longer the duration of diabetes mellitus, more are the complications of the diabetes. The studies done by Agunloye A.M. et al.[38], Al-Bayati S. et al.[45] and Olokoba A.B et al.[46] all suggested that an increase in the duration of diabetes mellitus was associated with an increased prevalence of gallstones.

Complications of cholelithiasis in diabetics

Cholecystitis in the diabetics is a severe disease as it may present unexpectedly and advance rapidly.[47] Diabetics are at increased risk of developing emphysematous cholecystitis, a rare condition with a 30-fold increased risk of gangrene and threefold increase of both perforation and death.[48] This led to a general consensus that prophylactic cholecystectomy should be performed in the diabetic patients with asymptomatic gallstones. But many later studies including Walsh DB et al[49]., found no difference in the rates of complications between the diabetics, a difference which was not statistically remarkable. However, recent evidence-based studies challenged this approach and concluded that prophylactic cholecystectomy is not justified in diabetic patients with asymptomatic gallstones. It is inferred that, as in the general population, asymptomatic cholelithiasis in diabetics should be managed expectantly and preemptive surgery should not be routinely performed. A "watch-and-wait" approach is advised for asymptomatic cholelithiasis in the diabetics when found, and surgical therapy when symptoms specific to cholelithiasis ensue.[50]

Since gall bladder abnormalities may be asymptomatic in diabetic patients, gall bladder ultrasonography should be considered in the management of diabetic patients, to facilitate proactive management of gall bladder complications and its attendant morbidity/mortality. Ultrasonography is cheap and usually readily available, and does not utilise ionising radiation.[51]

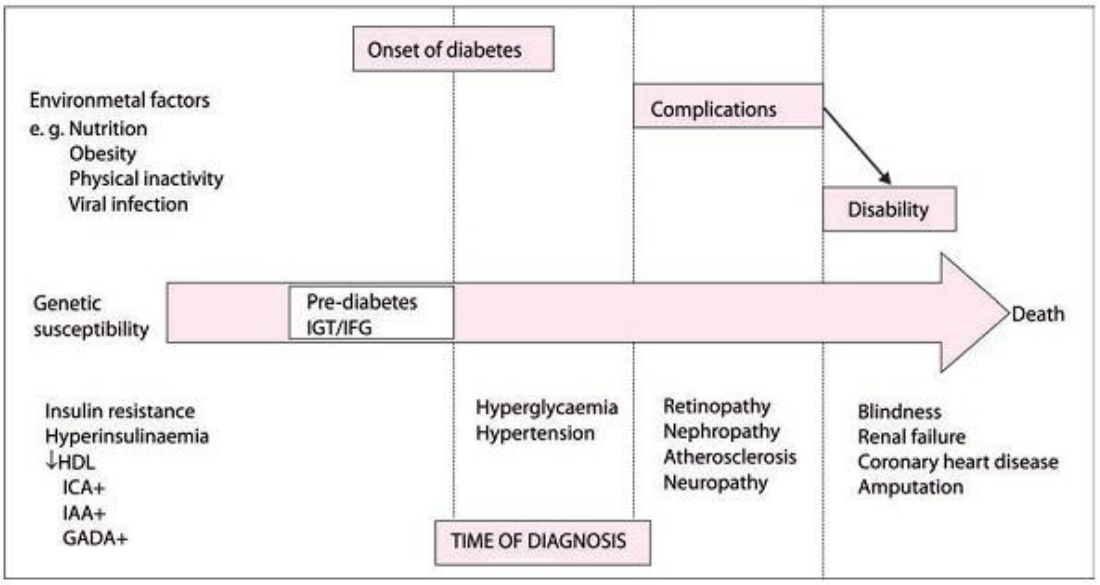


Figure 3:Natural history of complications of diabetes mellitus[19]

Type 2 diabetes constitutes about 98% of diabetic population in India. Age, obesity, lack of physical activity, and family history of diabetes are the predisposing factors for type 2 diabetes. Other risk factors are hypertension, dyslipidemia, and past history of gestational diabetes mellitus (GDM). A vast majority of patients of type 2 diabetes remain asymptomatic for many years and directly present with features of longterm complications like neuropathy (tingling, numbness, paraesthesia of lower limbs), retinopathy or even nephropathy.[19]

Many of the diabetes related complications can be prevented or delayed with early detection and aggressive glycemic control. Diabetic neuropathy occurs in ~50% of individuals with long-standing type 1 and type 2 DM. It may manifest as polyneuropathy, mononeuropathy, and/or autonomic neuropathy. As with other complications of DM, the development of neuropathy correlates with the duration of diabetes and glycemic control. Additional risk factors are body mass index (BMI) (the greater the BMI, the greater the risk of neuropathy) and smoking, elevated triglycerides and hypertension. [1]

Diabetic Neuropathy

Diabetic neuropathy (DN) is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes.

The prevalence of neuropathy increases with the duration of diabetes mellitus. The incidence of DN in India is not well known but in a study from South India 19.1% type 2 diabetic patients had peripheral neuropathy. According to an estimate, two-thirds of the diabetic patients have clinical or subclinical neuropathy.[19]

Table 5: Classification of Diabetic Neuropathies.[19]

	Classification of Diabetic Neuropathies
1.	**Symmetrical Polyneuropathies**
	- Distal sensory or sensorimotor polyneuropathy
	- Large-fibre neuropathy
	- Small-fibre neuropathy
	- Autonomic neuropathy
2.	**Asymmetrical Neuropathies**
	- Cranial neuropathy (single or multiple)
	- Truncal neuropathy (thoracic radiculopathy)
	- Lumbosacral radiculopathy (asymmetrical proximal motor neuropathy)
	- Limb mononeuropathy (single or multiple)
	- Entrapment neuropathy
3.	**Combinations**
	- Polyradiculoneuropathy
	- Diabetic neuropathic cachexia
	- Symmetrical polyneuropathies

Diabetic Autonomic Neuropathy

Individuals with long-standing type 2 DM may develop signs of autonomic dysfunction involving the cholinergic, noradrenergic, and peptidergic (peptides such as pancreatic polypeptide, substance P, etc.) systems. DM-related autonomic neuropathy can involve multiple systems, including the cardiovascular, gastrointestinal, genitourinary, sudomotor, and metabolic systems.[1]

Autonomic neuropathies affecting the cardiovascular system cause a resting tachycardia and orthostatic hypotension. Reports of sudden death have also been attributed to autonomic neuropathy. Gastroparesis and bladder emptying abnormalities are often caused by the autonomic neuropathy seen in DM Hyperhidrosis of the upper extremities and anhidrosis of the lower extremities result from sympathetic nervous system dysfunction. Anhidrosis of the feet can promote dry skin with cracking, which increases the risk of foot ulcers.[1]

Autonomic neuropathy may reduce counterregulatory hormone release (especially catecholamines), leading to an inability to sense hypoglycemia appropriately (hypoglycemia unawareness), thereby subjecting the patient to the risk of severe hypoglycemia and complicating efforts to improve glycemic control.[1] Diabetic Autonomic Neuropathy (DAN) is typically assessed by focusing on symptoms or dysfunction attributable to a specific organ system. Cardiac Autonomic Neuropathy is the most prominent focus because of the life threatening consequences of this complication and the availability of direct tests of cardiovascular autonomic function. However, neuropathies involving other organ systems should also be considered in the optimal care of patients with diabetes.

Clinical manifestations of diabetic autonomic neuropathy[23]

1) Cardiovascular
    - Resting tachycardia
    - Exercise intolerance
    - Orthostatic hypotension
    - Silent myocardial ischemia
2) GI
    - Esophageal dysmotility
    - Gastroparesis diabeticorum
    - Constipation
    - Diarrhea
    - Fecal incontinence
3) Genitourinary
    - Neurogenic bladder (diabetic cystopathy)
    - Erectile dysfunction
    - Retrograde ejaculation
    - Female sexual dysfunction (e.g., loss of vaginal lubrication)
4) Metabolic
    - Hypoglycemia unawareness
    - Hypoglycemia-associated autonomic failure
5) Sudomotor
    - Anhidrosis
    - Heat intolerance
    - Gustatory sweating
    - Dry skin

6) Pupillary
    - Pupillomotor function impairment (e.g., decreased diameter of dark adapted pupil)
    - Argyll-Robertson pupil.

The differential diagnosis of DAN involves excluding the following conditions:[23]

1. Pure autonomic failure (formerly called idiopathic orthostatic hypotension)
2. Multiple system atrophy with autonomic failure (formerly called Shy-Drager syndrome)
3. Addison's disease and hypopituitarism.
4. Pheochromocytoma.
5. Hypovolemia.
6. Medications, with anticholinergic or sympatholytic effects (insulin, vasodilators, sympathetic blockers)
7. Peripheral autonomic neuropathies (e.g., amyloid neuropathy, idiopathic autonomic neuropathy)

Gastro Intestinal (GI) autonomic neuropathy[23]

GI symptoms are relatively common among patients with diabetes and often reflect diabetic GI autonomic neuropathy. It should be noted, however, that although GI symptoms are common, symptoms may be more likely due to other factors than to autonomic dysfunction.

GI manifestations of DAN are diverse, and symptoms and pathogenic mechanisms have been categorized according to which section of the GI tract is affected:

1) Esophageal enteropathy (disordered peristalsis, abnormal lower esophageal sphincter function).
2) Gastroparesis diabeticorum (nonobstructive impairment of gastric propulsive activity; brady/tachygastria, pylorospasm).
3) Diarrhea (impaired motility of the small bowel [bacterial overgrowth syndrome], increased motility and secretory activity [pseudocholeretic diarrhea]).
4) Constipation (dysfunction of intrinsic and extrinsic intestinal neurons, decreased or absent gastrocolic reflex).
5) Fecal incontinence (abnormal internal anal sphincter tone, impaired rectal sensation, abnormal external sphincter).
6) Gallbladder atony and enlargement.

A study was conducted on 50 cases of type 2 diabetes mellitus and 25 healthy controls to determine the incidence of gallbladder disorders. In the study 34% of type 2 diabetics had gallstones.[9]

A cross sectional study was conducted on the prevalence and risk factors of asymptomatic gallstones in 100 patients of type 2 diabetes mellitus over a period of one year. The patients were evaluated ultrasonographically. The prevalence rate of asymptomatic gallstones was found to be 26% in type 2 diabetic patients.[7]

The epidemiological associations of gallstone disease was evaluated in a general population sample of 29,584 individuals who were screened for the presence of gallstones by ultrasonography. A higher risk for gallstones among diabetic men and women was evident in the study.

The authors found that increasing age, body mass index and maternal family history of gallstone disease were consistently associated with gallstones.[4]

A study done by Raman P.G. et al.[8] found out that the mean fasting gallbladder volume was significantly larger in diabetic subjects with diabetic autonomic neuropathy than those without neuropathy. Thus there is an increased prevalence of the gallstones in diabetic patients with diabetic autonomic neuropathy which leads to stasis of the bile in the gallbladder and also causes hypomotility of the gallbladder.[8] According to Stone BH et al.[52] the gallbladder emptying was lower in diabetics. Similar findings were reported by Gaur C et al.[53] and Yang CC et al.[54]. Kayacetin E et al.[55] showed that the gallbladder ejection fraction was significantly reduced in the patients with autonomic neuropathy as compared to the patients without autonomic neuropathy.

Lipids in Patients With Type 2 Diabetes

Obesity, insulin resistance and Type 2 DM are frequently accompanied by dyslipidemia characterized by elevated plasma levels of TG, low HDL-C, variable levels of LDL-C, and increased levels of small dense LDL. A rise in the levels of total cholesterol, triglycerides and low density lipoprotein was associated with increased prevalence of gallstones.

In insulin-resistant patients who progress to type 2 diabetes mellitus, dyslipidemia is common. In addition to increased Very Low Density Lipoprotein (VLDL) production, insulin resistance can also result in decreased (LPL) Lipoprotein Lipase activity, resulting in reduced catabolism of chylomicrons and VLDLs and more severe hypertriglyceridemia type 2 diabetes have been reported to be associated with variably reduced LPL activity. This may be due in part to the effects of tissue insulin resistance leading to reduced transcription of LPL in skeletal muscle and adipose, as well as to increased production of the LPL inhibitor ApoC-III by the liver.

The in LPL activity often contributes to the dyslipidemia seen in these patients.[1] Increased hepatic secretion of large triglyceride-rich VLDL and impaired clearance of VLDL appears to be of central importance in the pathophysiology of this dyslipidemia. Each of these dyslipidemic features is associated with an increased risk of cardiovascular disease. Clinical trials have shown significant improvement in coronary artery disease after diabetic dyslipidemia treatment.

Pathophysiology of Diabetic dyslipidemia

Patients with Non Insulin-Dependent Diabetes Mellitus (NIDDM) also have altered lipoproteins. Obesity and insulin resistance are contributing factors. Characteristically, these patients have elevated triglycerides, increased VLDL cholesterol, and reduced HDL cholesterol.

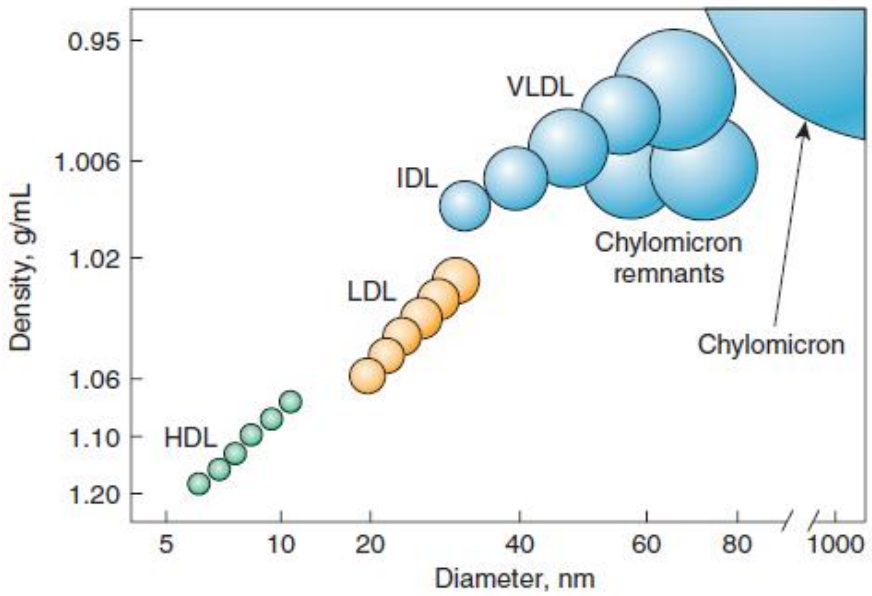


Figure 4: The density and size distribution of the major classes of lipoprotein particles.[1]

Lipoproteins are classified by density and size, which are inversely related.[1]

Table 6: ATP III Classification of LDL, Total, and HDL Cholesterol and Triglycerides (mg/dL) [56]

LDL Cholesterol – Primary Target of Therapy	
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
>190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
>240	High
HDL Cholesterol	
<40	Low
>60	High
Serum Triglycerides	
<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high

Altered metabolism of triglyceride-rich lipoproteins is crucial in the pathophysiology of the atherogenic dyslipidemia of diabetes. Alterations include both increased hepatic secretion of VLDL and impaired clearance of VLDL and intestinally derived chylomicrons. These include cholesterol enriched Intermediate density lipoproteins (IDLs), are particularly atherogenic in humans. Plasma residence time of these LDL particles may be prolonged because of their relatively reduced affinity for LDL receptors.[57]

The reductions in HDL associated with type 2 diabetes and insulin resistance are multifactorial, but a major factor appears to be increased transfer of cholesterol from HDL to triglyceride rich lipoproteins, with reciprocal transfer of triglyceride to HDL. Triglyceride-rich HDL particles are hydrolyzed by hepatic lipase and, as a result, are rapidly catabolised and cleared from plasma.

In insulin resistance and type 2 diabetes, increased efflux of free fatty acids from adipose tissue and impaired insulin mediated skeletal muscle uptake of free fatty acids increase fatty acid flux to the liver. The fact that free fatty acid levels are elevated in individuals with impaired glucose tolerance suggests that insulin resistance associated with elevated free fatty acid levels occurs before the onset of hyperglycemia.[57]

A cluster of interrelated plasma lipid and lipoprotein abnormalities associated with alterations in VLDL metabolism contribute to the risk for atherosclerosis and Coronary Heart Disease (CHD) in the majority of patients with type 2 diabetes. Insulin resistance plays a key role in the development of diabetic dyslipidemia.[57]

Each of the lipid abnormalities (low HDL, small dense LDL, and elevated triglycerides) is associated with an increased risk of CHD. Features of this dyslipidemia can be improved by a variety of therapeutic modalities, including weight loss and physical activity, and the use of statins, fibrates, nicotinic acid, and Thiozolidinediones (TZD). Additionally, evidence from angiographic trials indicates that reduction in small dense LDL particles can contribute significantly to reduced coronary disease progression observed with these treatments.[57]

The study done by Tao-Hsin-Tung[58] which had a mean total cholesterol level of 220 ± 20.5 mg/dl and was significantly associated with the gallstone disease in patients with type 2 diabetes mellitus. A study done by Khalaf SK[27] had a mean total cholesterol level of 272 ± 46.0 mg/dl, mean low density lipoprotein levels of 114 ± 44.40 mg/dl and a mean triglyceride levels of 254.04 ± 144.40 mg/dl in the gallstone positive patients and the association was maintained after the multivariate logistic regression analysis was done. A study done by Chhabra A. et al.[9] reported that a mean total serum cholesterol level in the diabetic patients with gallstones was 177.15 ± 32.69 mg/dl.

BMI, Obesity and Type 2 Diabetes Mellitus.

Obesity is a state of excess adipose tissue mass. Although not a direct measure of adiposity, the most widely used method to gauge obesity is the body mass index (BMI), which is equal to weight/height^2 (in kg/m^2) Other approaches to quantifying obesity include anthropometry (skinfold thickness), densitometry (underwater weighing), computed tomography (CT) or magnetic resonance imaging (MRI), and electrical impedance.[1]

BMI of 30 is most commonly used as a threshold for obesity in both men and women. Most but not all large-scale epidemiologic studies suggest that all-cause, metabolic, cancer, and cardiovascular morbidity begin to rise (albeit at a slow rate) when BMIs are ≥25. Most authorities use the term overweight (rather than obese) to describe individuals with BMIs between 25 and 30.[1]

The distribution of adipose tissue in different anatomic depots also has substantial implications for morbidity. Specifically, intra abdominal and abdominal subcutaneous fat have more significance than subcutaneous fat present in the buttocks and lower extremities. This distinction is most easily made clinically by determining the waist-to-hip ratio, with a ratio >0.9 in women and >1.0 in men being abnormal. Obesity, however, is a major risk factor for diabetes, and as many as 80% of patients with type 2 diabetes mellitus are obese.[1]

In a study done by Kaur M et al.[31], higher BMI was significantly related to gall stone disease and BMI was >25kg/m^2 in 80% patients with diabetes and gallstones. A study done by A. B. Olokoba et al.[46] who found that the diabetic patients had a significantly higher mean BMI than the controls.

A study done by Khare et al.[7] showed a statistically significant association between high BMI and an increased prevalence of gallstones. The mean BMI was 27.77 ± 3.2 kg/m^2. The study done by Elmehdawi R.R.[32] had a mean BMI of 34.78 ± 6.2 kg/m^2 in the diabetic population with gallstones. Tao-Hsin-Tung et al.[58] also studied the correlation of BMI and the prevalence of the gallstones in the diabetic population. They found that BMI was significantly associated with gallstones in the patients of type 2 diabetes mellitus. The mean BMI was 26.57 ± 1.07 kg/m^2.

Table 7: Classification of adults according to BMI.[59]

CLASSIFICATION	BMI	RISK OF COMORBIDITIES
Underweight	< 18.50	Low (but risk of other clinical problems increased)
Normal range	18.50-24.99	Average
Overweight:	≥25.00	
Pre-obese	25.00-29.99	Increased
Obese class I	30.00-34.99	Moderate
Obese class II	35.00-39.99	Severe
Obese class III	≥40.00	Very severe

The most widely used criteria for body weight quantification are :[59]

1) Body mass index (Quetelet's index)

   Weight (kg)/Height^2(m)

2) Ponderal index

   Height (cm)/Cube root of body weight (kg)

3) Brocca index

   = Height (cm) *minus* 100

   For example, if a person's height is 160 cm,

   his ideal weight is (160-100) = 60 kg

4) Corpulence index

   Actual weight/Desirable weight

   This should not exceed 1.2

Waist circumference and waist to hip ratio (WHR)[59]

Waist circumference is measured at the mid-point between the lower border of the rib cage and the iliac crest. It is a convenient and simple measurement that is unrelated to height, correlates closely with BMI and WHR and is an approximate index of intra-abdominal fat mass and total body fat. Changes in waist circumference reflect changes in risk factors for cardiovascular disease and other forms of chronic diseases. There is an increased risk of metabolic complications for men with a waist circumference ≥ 102 cm, and women with a waist circumference ≥ 88 cm. Over the past 10 years or so, it has become accepted that a high WHR (> 1.0 in men and > 0.85 in women) indicates abdominal fat accumulation.[59]

Type 2 Diabetes Mellitus (T2DM) comprises about 90%–95% of all diabetes cases, and its prevalence has been steadily increasing. Obesity, classified as body mass index (BMI) ≥30 kg/m^2, is a known predictor of T2DM and has become a major public health problem.

After adjusting for a number of characteristics associated with the risk of T2DM, it was found that, compared with normal BMI, overweight and obesity was statistically significantly associated with the risk of being diagnosed with T2DM among individuals without any other prior evidence of T2DM.

Other studies have also examined the association between BMI and risk of T2DM using nationally representative samples. Using the data from the 2001 Behavioral Risk Factor Surveillance System, Mokdad et al. also found statistically significant and increasingly larger Odds Ratios for T2DM among overweight adults (1.59, 95% CI: 1.46–1.73), adults with BMI between 30 and 39.9 kg/m2 (3.44, 95%

CI: 3.17–3.74), and adults with BMI ≥ 40 kg/m2 (7.37, 95% CI: 6.39–8.50) relative to adults with normal BMI.[60]

The overall relative risk of non-insulin-dependent T2DM among women with BMI ≥ 29.9 kg/m^2 relative to women with BMI ≤ 20.1 kg/m^2 in the 1986–1994 cohort was 11.2 (95% CI: 7.9–15.9)[61]. According to the Nurses Health Study, the adjusted relative risk of T2DM associated with each 5-unit increment in BMI ranged from 1.55 (95% CI: 1.36–1.77) to 2.36 (95% CI: 1.83–3.04) among women, depending on the participants race/ethnicity[62].

The Diabetes Prevention Program (DPP) is a large randomized clinical trial that ran from 1996 to 2001 (average follow-up: 2.8 years) and that enrolled individuals at higher risk for T2DM (all subjects had impaired glucose tolerance at baseline). The incidence of T2DM was 58% lower (95% CI: 48–66%) among subjects who were assigned to the lifestyle-modification program (with a goal of at least a 7% weight loss of the baseline body weight) than those in the placebo group [63].

Additionally, weight loss among subjects in the lifestyle-modification program was significantly and independently associated with reductions in blood glucose from pre-diabetic to normal levels[64]. Weight loss was also associated with long term benefit in a follow-up study of the DPP program, which found that the 10-year cumulative incidence of Type 2 DM among participants in the lifestyle-modification program was lower compared with those treated with metformin or in the placebo group.[65]

The risk of developing T2DM for individuals who were overweight or obese was about 1.5–5 times higher than for individuals with normal BMI.[66] Obesity is

associated with increased saturation of bile with cholesterol in both men and women.[64]

Hyperinsulinaemia, associated with obesity, may be responsible for the cholesterol saturation in bile. Insulin increases the activity of HMG-CoA reductase, the rate-limiting enzyme for cholesterol synthesis in the liver.[67] Insulin also activates low-density lipoprotein (LDL) receptors in the liver, and thereby increasing cholesterol excretion in the bile.[59] In fact hyperinsulinaemia has been shown to be associated with increased risk of gallstones in several studies.[68,69,70.]

METHODOLOGY

The study was done on 200 patients of Type 2 Diabetes Mellitus, admitted in KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi over a period of one year from January 2017 to December 2017.

All the patients who were enrolled in the study were explained the nature of the study and a written and informed consent was taken from all the study subjects. The study protocol was approved by the ethical committee of the KAHER.

Inclusion criteria:

All the patients of type 2 diabetes mellitus with 5 years or more than 5 years duration of diabetes mellitus admitted in General Medicine wards of KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi.

Exclusion criteria:

1) The patients of type 2 diabetes mellitus who have undergone cholecystectomy.
2) Type 2 diabetics with acute complications.
3) The patients of type 1 diabetes mellitus .

Study design : Cross sectional study.

Study population: 200 patients of type 2 diabetes mellitus admitted in KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi.

Sample size: 200 patients of type 2 diabetes mellitus.

Sample size is calculated using the formula

$$\mathbf{n=4pq/d^2}$$

where,

p=34 based on the review article[9].

q=66

d=7.

n=4x34x66/7x7

n=183

On calculation the sample size is 183, which is rounded off to 200 by taking 17 extra cases.

The criteria for the diagnosis of diabetes was,

1) Random blood glucose > 200 mg/dl.
2) Fasting blood glucose > 126 mg/dl.
3) Postprandial blood glucose > 200 mg/dl.

The patients were informed the details of the study and after they fit into the inclusion criteria, they were invited to sign the consent form. After taking the written informed consent from the patients, a detailed history including age, sex and duration of diabetes was taken. Leading questions were put forth to assess the diabetes related complications. Details regarding treatment history with the details of the anti-diabetic medications were recorded as per the proforma.

A detailed physical examination was performed recording the pulse rate in supine position and standing position. Blood pressure was also recorded in both supine and standing positions. The heart rate variability according to body position and the blood pressure variability according to body position was assessed for the

presence of diabetic autonomic neuropathy. The anthropometric measurements like height, weight, hip circumference, waist circumference, hip-waist ratio were recorded. Body Mass Index was calculated using the formula.

BMI = weight (kg)/height^2 (m)

Measurement protocols

Height

It was measured against a vertical board with an attached metric rule and a horizontal headboard was brought in contact with upper most point on the head. It was recorded barefoot, with person standing on a flat surface and weight distributed evenly on both feet and heels together and the head positioned so that the line of vision is perpendicular to the body. The arms were hanging freely by the sides and the head, back; buttocks and heels were in contact with vertical board. The individual was asked to inhale deeply and maintained a full erect position. Top-most point on the head with sufficient pressure to compress the hairs was taken as height

Weight

Weight was recorded without footwear with light clothes worn on body, standing straight on the centre of weighing machine with body weight evenly distributed between both feet by the ISI certified weighing machine.

Waist circumference

It was measured in cms with a flexible measuring tape, midway between the inferior margin of the last rib and crest of ilium in the horizontal plane, at the end of expiration, to the nearest of .1 cm. The tape did not compress the underlying soft tissues.

Hip circumference

It was also measured in cms with a flexible measuring tape at the level of maximum extension of buttocks (greater trochanter) bilaterally in the horizontal plane with the subject standing with arms at the sides and feet together with light clothes over the body.

Haematological and biochemical investigations like Hb, Total leucocyte count, Differential leucocyte count, Fasting blood sugar, Post-prandial blood sugar, HbA1c, Blood urea, Serum creatinine, Lipid profile, routine urine examination results were recorded.

Ultrasonography of abdomen was done with GE Healthcare LOGIQ P7 ultrasound machine with 3 – 5 MHz transducer. With special reference to gallbladder and gallstones, the ultrasonography was performed.

Parameters that were recorded:

1) Gallbladder wall - Thickened/ Normal.
2) Gallbladder – Empty/ Filled/ Distended.
3) Gallstones – Absent/ Present- Multiple/ Solitary Size of the largest gallbladder stone.
4) Biliary sludge – Present/ Absent.

Statistical analysis

The obtained data was entered into Excel 2010. It was converted and analysed by SPSS version 20.0 software. The data was analysed by descriptive statistics including the frequency %, mean and SD. The independent 't' test was used to compare the data of the patients with and without gallstone groups with various quantitative parameters.

The chi square test was used to assess the association between the two attributes. The Multiple Logistic Regression Analysis was performed to assess the risk factors of the prevalence of gallstones in terms of the Odds Ratio. The statistical significance was set at 5% level of significance.

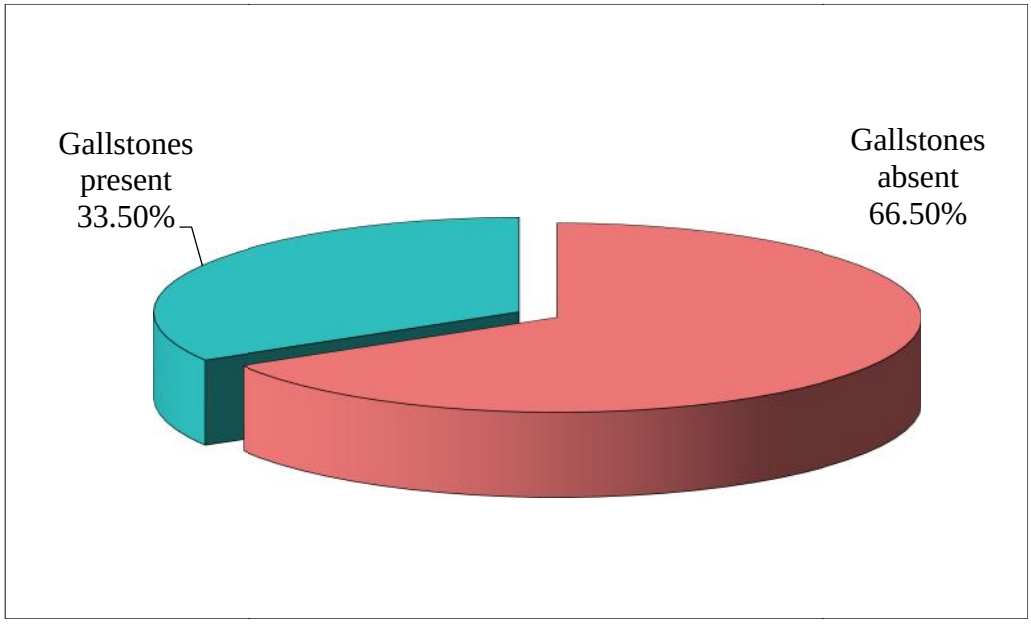
RESULTS

The present study titled '**Prevalence of gallbladder stones and the associated risk factors among type 2 diabetes mellitus patients - A cross sectional study at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi.'** was carried out in the Department of General Medicine, KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi. During the study period of one year from January 2017 to December 2017, a total of 200 subjects were studied. The final results of the study are presented here.

Table 8: Prevalence of gallstones

Prevalence of gallstones	No. of patients	% of patients
Gallstones present	67	33.50 %
Gallstones absent	133	66.50 %
Total	200	100.00 %

Graph 1: Prevalence of gallstones



The prevalence of gallbladder stones in the present study is 33.50%. The study included a total of 200 patients and 67 of them had asymptomatic gallstones.

Table 9: Age groups wise distribution

Age groups	No. of patients	% of patients
30 - 39 years	10	5.00
40 - 49 years	29	14.50
50 - 59 years	90	45.00
60 - 69 years	61	30.50
70 - 79 years	10	5.00
Total	**200**	**100.00**

The maximum number of study subjects were in the age group of 50 – 59 years (45%). The youngest patient was 35 years old and the oldest patient was 79 years old in the present study.

Graph 2: Age groups wise distribution

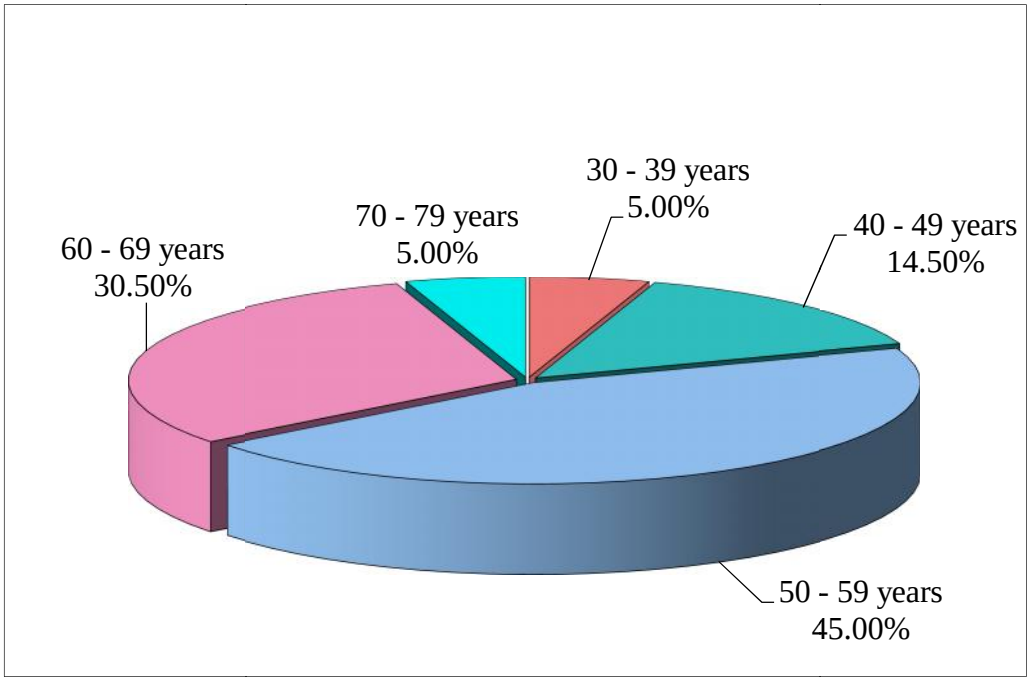


Table 10: Age groups wise distribution of patients with gallstones

Age groups	No. of patients with gallstones	% of patients with gallstones
30 – 39 years	10	14.93 %
40 – 49 years	14	20.90 %
50 – 59 years	23	34.33 %
60 – 69 years	12	17.91 %
70 – 79 years	08	11.94 %
Total	67	100 %

The above table represents the age groups wise distribution of patients with gallstones. The maximum number (23) of patients with gallstones were present in the group of 50 – 59 years of age. The least number (08) of patients with gallstones were present in the group of 70 – 79 years of age.

Graph 3: Age groups wise distribution of patients with gallstones

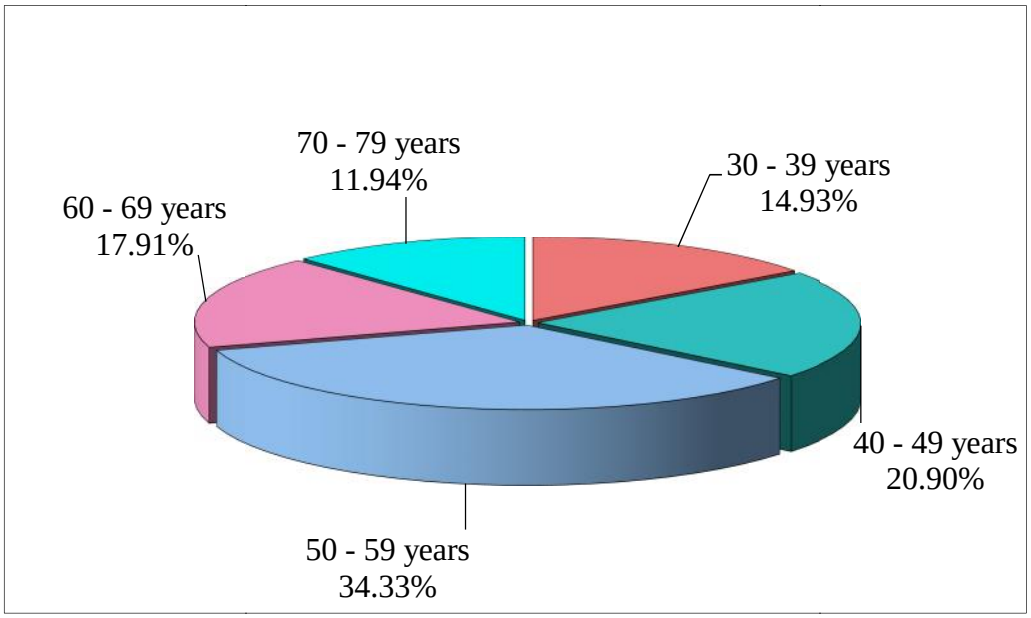


Table 11: Gender wise distribution

Gender	No. of patients	% of patients
Male	96	48.00
Female	104	52.00
Total	200	100.00

The above table depicts the distribution of the study subjects according to their gender. Out of the total 200 study subjects, 96 (48%) were males and the remaining 104 (52%) were females.

Graph 4: Gender wise distribution

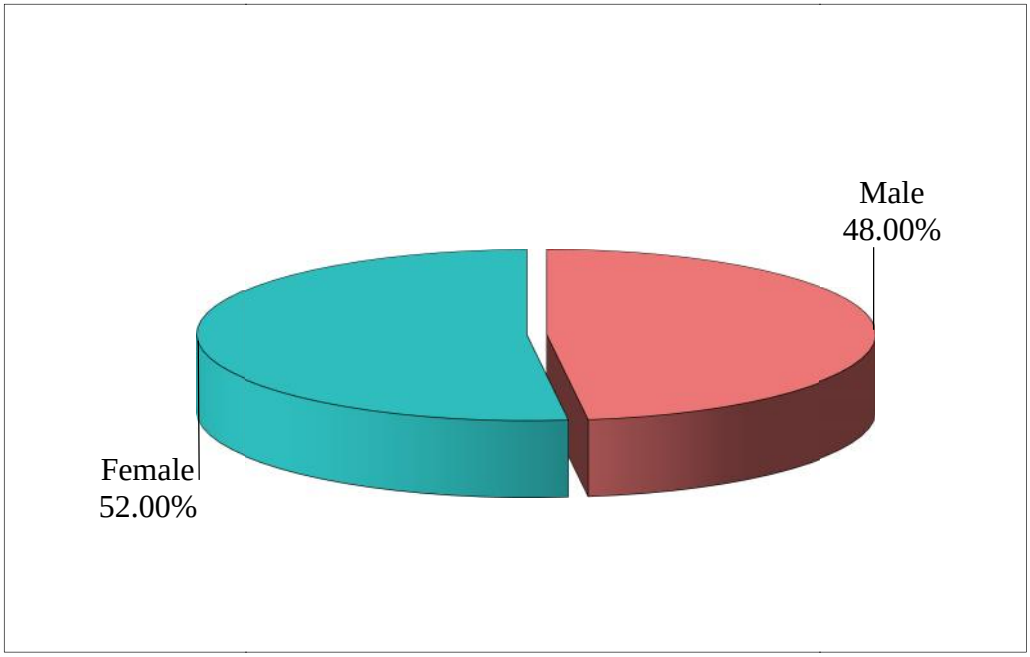


Table 12: Association between gender and prevalence of gallstones

Gender	Gallstones absent	%	Gallstones present	%	Total	%
Male	67	69.79	29	30.21	96	48.00
Female	66	63.46	38	36.54	104	52.00
Total	133	66.50	67	33.50	200	100.00
Chi-square=0.8979 p=0.3434						

The percentage of patients with gallstones was found to be higher among females than the males in our study group. However the difference was not found to be statistically significant.

Graph 5: Association between gender and prevalence of gallstones

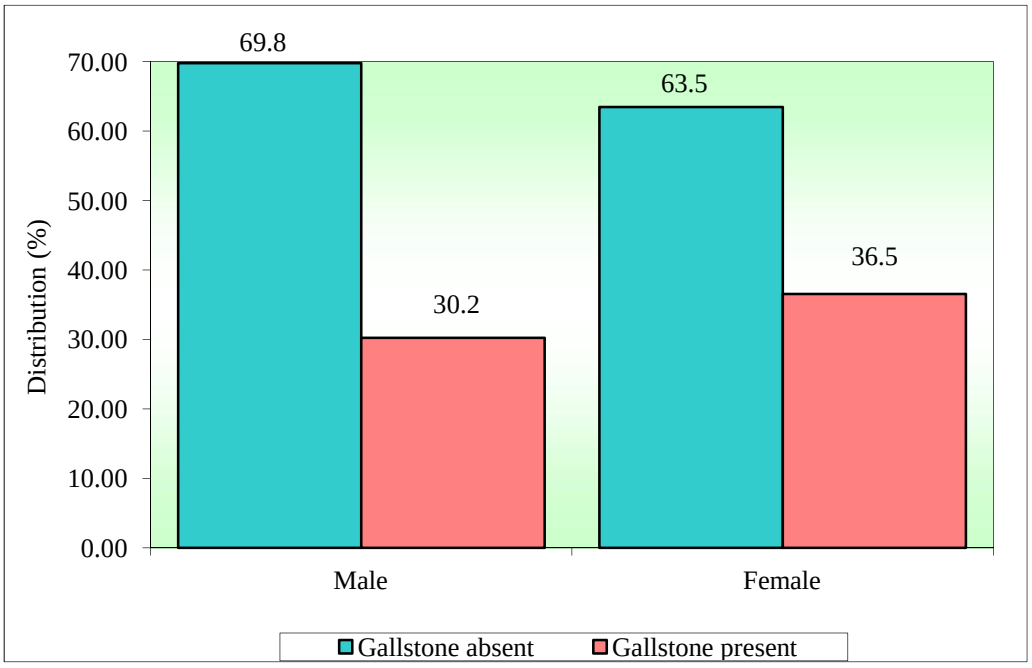


Table 13: Duration of diabetes wise distribution

Duration of diabetes	No. of patients	% of patients
05 - 09 years	67	33.50
10 - 15 years	85	42.50
>15 years	48	24.00
Total	200	100.00

The maximum number of subjects (85) were present in the duration group of 10 – 15 years, which comprised of 42.5% of the total study subjects.

Graph 6: Duration of diabetes wise distribution

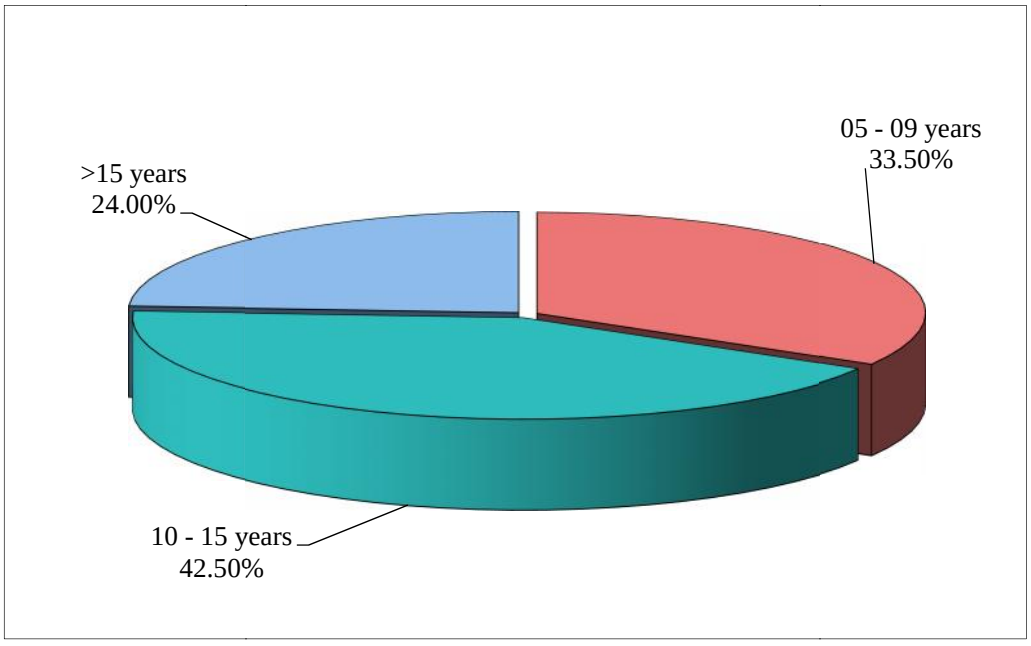


Table 14: Association between duration of diabetes and prevalence of gallstones

Duration of diabetes	Gallstones absent	%	Gallstones present	%	Total	%
05 - 09 years	49	73.13	18	26.87	67	33.50
10 - 15 years	56	65.88	29	34.12	85	42.50
>15 years	28	58.33	20	41.67	48	24.00
Total	133	66.50	67	33.50	200	100.00
Chi-square=2.7753 p=0.2497						

In the present study the association between the duration of diabetes and the prevalence of gallstones was not found to be statistically significant.

Graph 7: Association between duration of diabetes and prevalence of gallstones

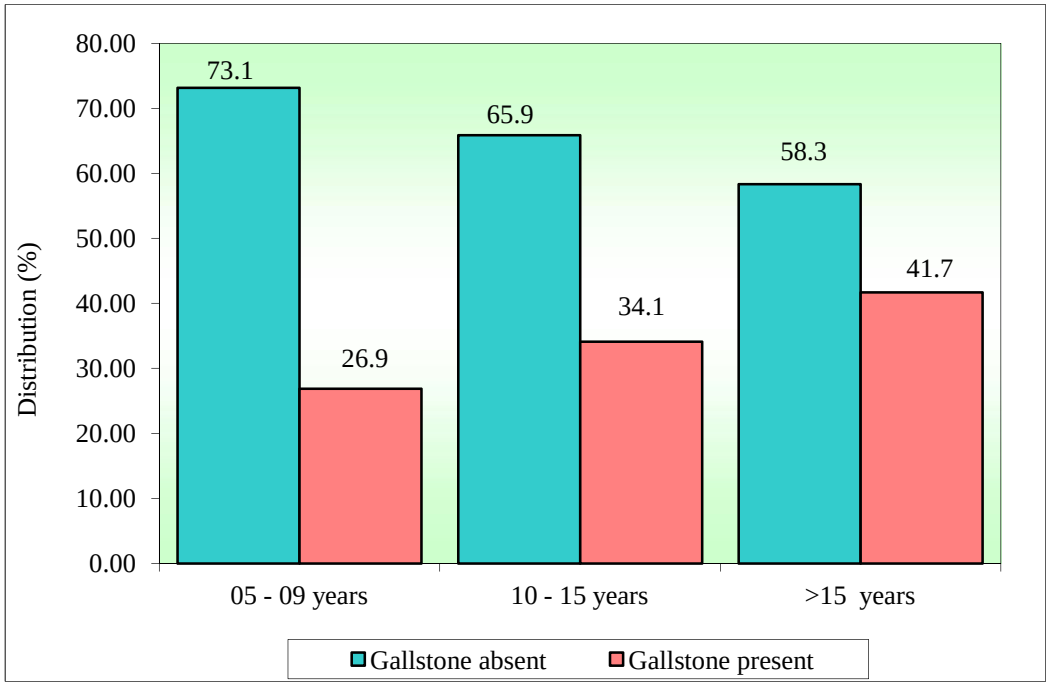


Table 15: BMI groups wise distribution

BMI groups	No. of patients	% of patients
18.5-24.9 kg/m^2	30	15.00
25-29.9 kg/m^2	85	42.50
30-34.9 kg/m^2	46	23.00
35-39.9 kg/m^2	17	8.50
≥40 kg/m^2	22	11.00
Total	200	100.00

Maximum number of the study subjects (85) belonged to the BMI range of 25 – 29.9 kg/m^2 in the present study. The group of BMI 35 – 39.9 kg/m^2 was found to have the least number of study subjects (17).

Graph 8: BMI groups wise distribution

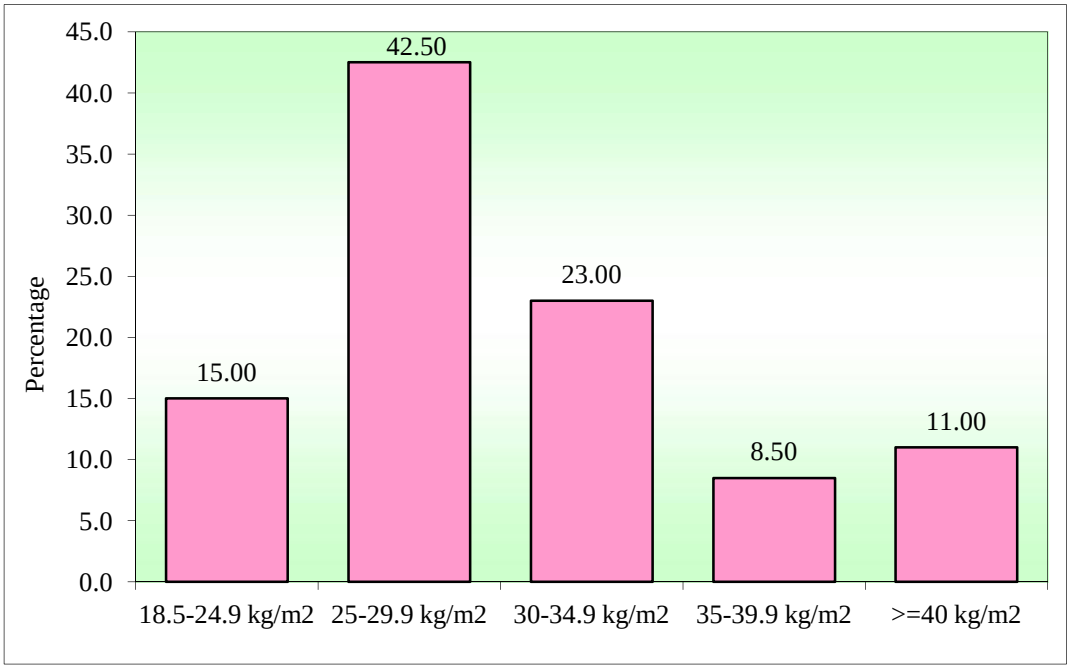


Table 16: Association between BMI groups and prevalence of gallstones

BMI groups	Gallstones absent	%	Gallstones present	%	Total	%
18.5-24.9 kg/m^2	24	80.00	6	20.00	30	15.00
25-29.9 kg/m^2	69	81.18	16	18.82	85	42.50
30-34.9 kg/m^2	35	76.09	11	23.91	46	23.00
35-39.9 kg/m^2	4	23.53	13	76.47	17	8.50
>=40 kg/m^2	1	4.55	21	95.45	22	11.00
Total	133	66.50	67	33.50	200	100.00
Chi-square=64.5666 p=0.0001*						

*p<0.05

The above table depicts the association between BMI and the prevalence of the gallstones. As the BMI increases the risk of developing gallstones increases as shown by our study. The above association is statistically significant in the present study.

Graph 9: Association between BMI groups and prevalence of gallstones

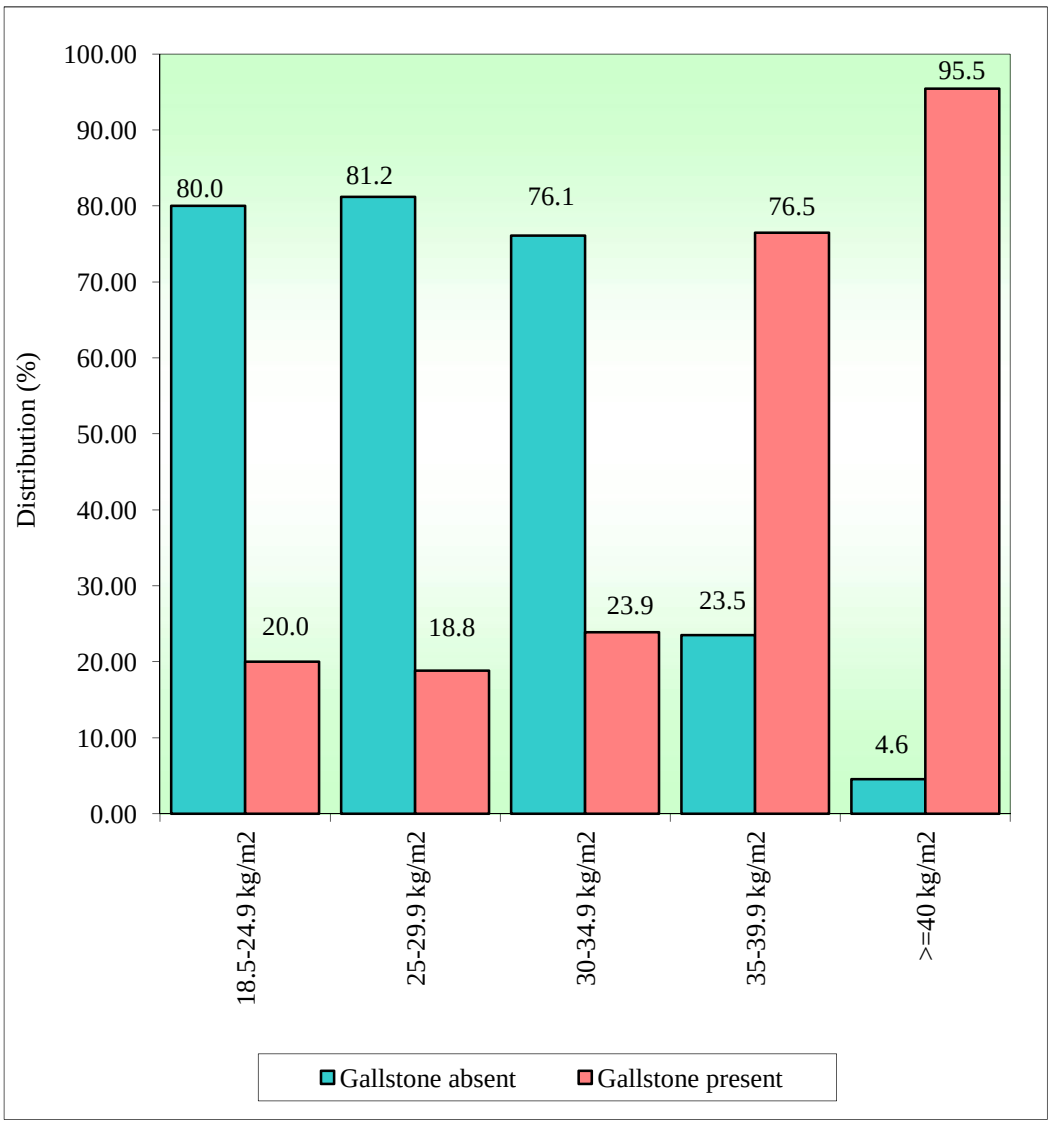
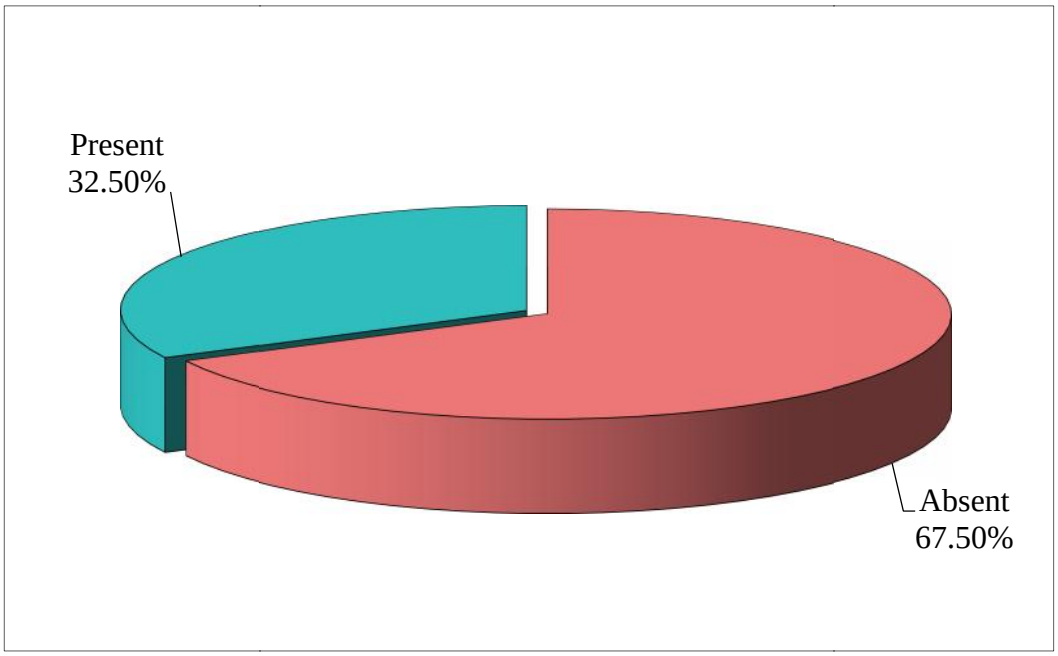


Table 17: Diabetic autonomic neuropathy wise distribution

Diabetic autonomic neuropathy	No. of patients	% of patients
Absent	135	67.50
Present	65	32.50
Total	200	100.00

In the present study, diabetic autonomic neuropathy was present in 65 members of our study group, which consists of 32.5% of the total study subjects.

Graph 10: Diabetic autonomic neuropathy wise distribution



The above pie-chart depicts the percentages of the study subjects with and without diabetic autonomic neuropathy. Presence of DAN is shown in blue and absence is shown in red.

Table 18: Association between Diabetic autonomic neuropathy and prevalence of gallstones

Diabetic autonomic neuropathy	Gallstones absent	%	Gallstones present	%	Total	%
Absent	115	85.19	20	14.81	135	67.50
Present	18	27.69	47	72.31	65	32.50
Total	133	66.50	67	33.50	200	100.00
Chi-square=65.0996 p=0.0001*						

*p<0.05

The above table shows that the association between diabetic autonomic neuropathy and the prevalence of gallstones is statistically significant. In the present study the number of patients with diabetic autonomic neuropathy and gallstones is 47.

Graph 11: Association between Diabetic autonomic neuropathy and prevalence of gallstones

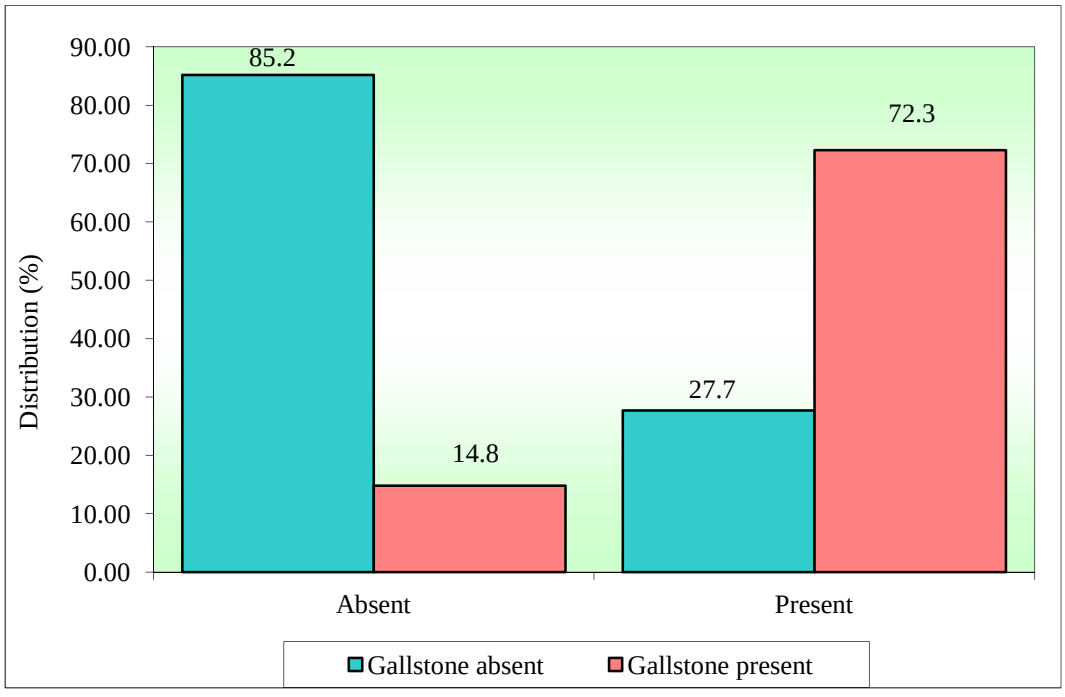


Table 19: HbA1c wise distribution

HbA1c	No. of patients	% of patients
6.5-7.9 %	58	29.00
08 to 9.9 %	89	44.50
≥10 %	53	26.50
Total	200	100.00

This table shows the distribution of the study subjects based on their HbA1c levels. Maximum number of patients belonged to the group of study subjects having HbA1c range of 08 to 9.9 %, which consists of 44.5% of the total study subjects.

Graph 12: HbA1c wise distribution

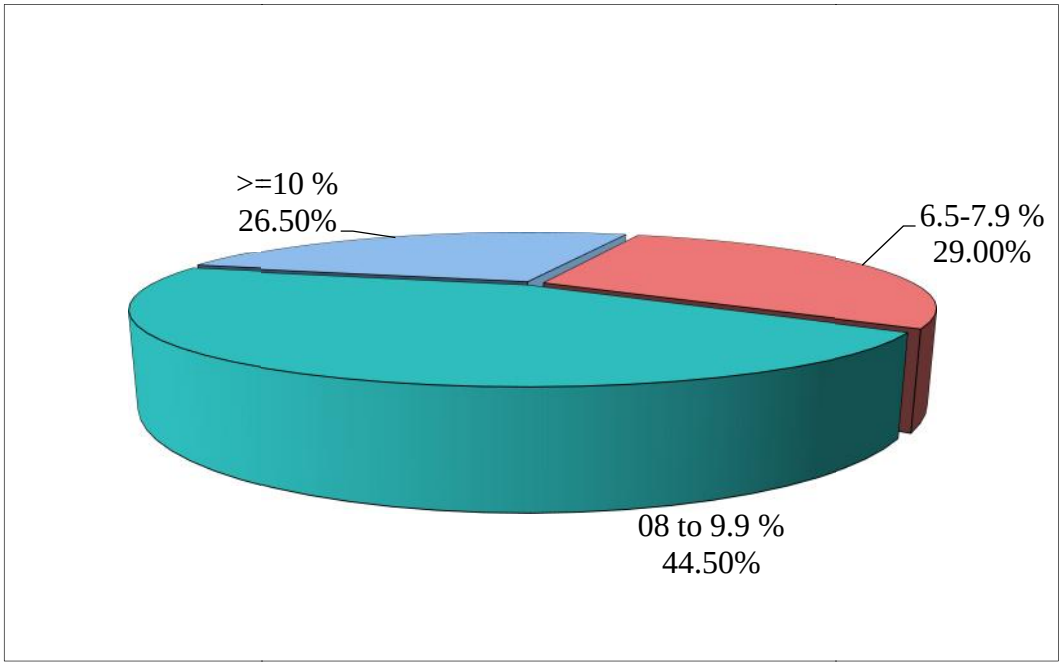


Table 20: Association between HbA1c and prevalence of gallstones

HbA1c	Gallstones absent	%	Gallstones present	%	Total	%
6.5-7.9 %	38	65.52	20	34.48	58	29.00
08 to 9.9 %	67	75.28	22	24.72	89	44.50
≥10 %	28	52.83	25	47.17	53	26.50
Total	133	66.50	67	33.50	200	100.00
Chi-square=7.5511 p=0.0229*						

*p<0.05

The above table shows the association between HbA1c and the prevalence of gallstones. It is evident from the chart that the prevalence of gallstones increases with the increase in the HbA1c of the study subjects. The association is statistically significant.

Graph 13: Association between HbA1c and prevalence of gallstones

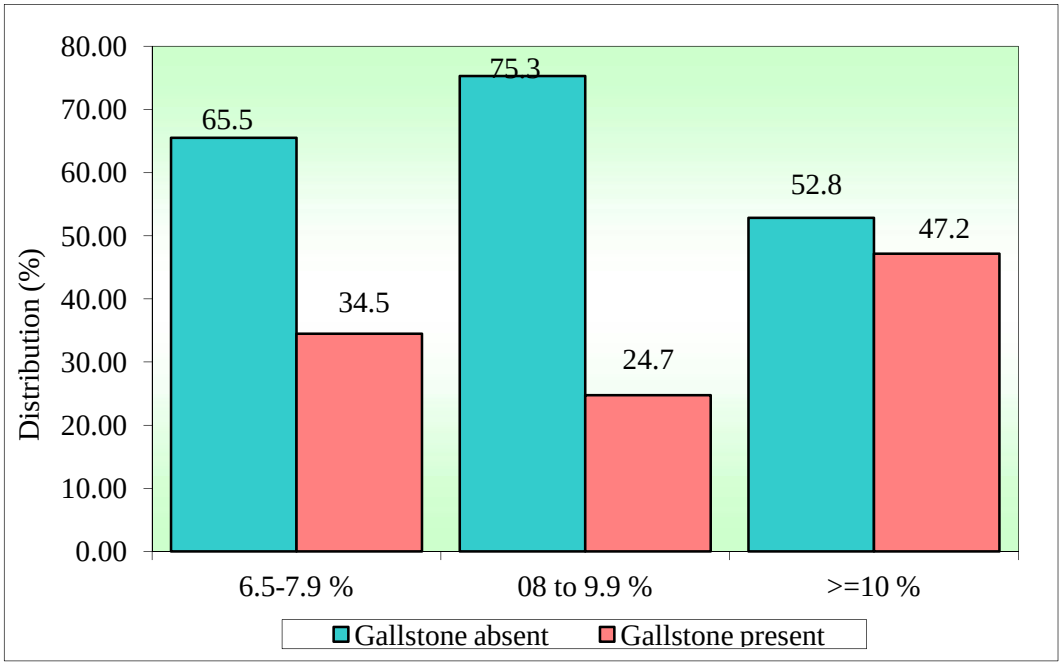


Table 21: Total cholesterol wise distribution

Total cholesterol	No. of patients	% of patients
< 200 mg/dl	104	52.00
≥200 mg/dl	96	48.00
Total	200	100.00

This is the table showing the distribution of the study subjects by their levels of total cholesterol. 104 (52%) of the patients had total cholesterol of < 200 mg/dl and 96 (48%) of patients had ≥ 200mg/dl out of the 200 total patients enrolled in the study.

Graph 14: Total cholesterol wise distribution

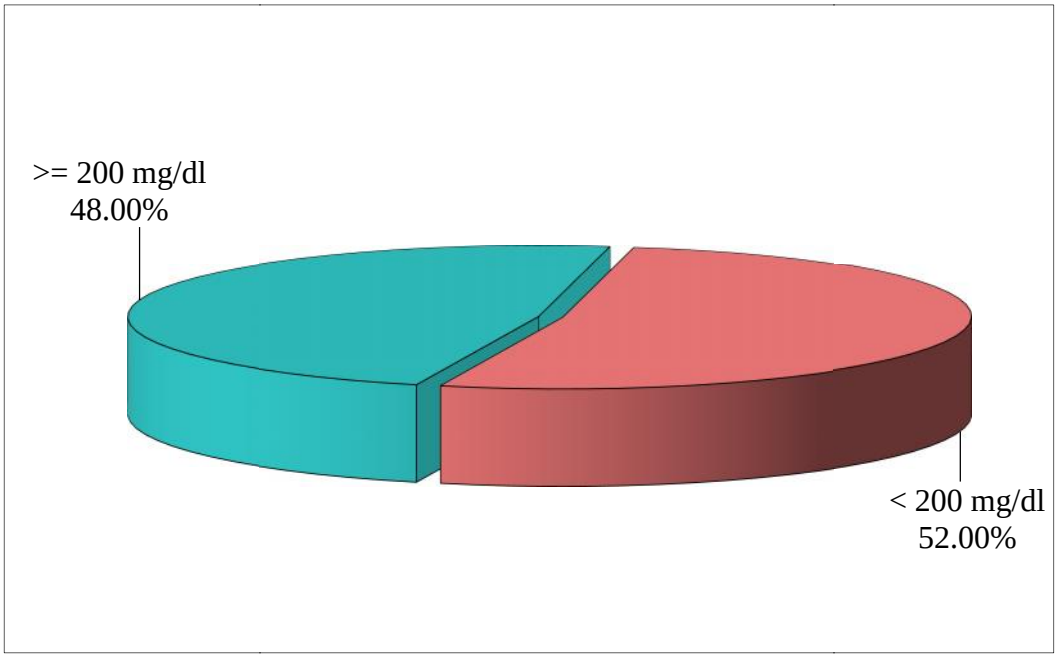


Table 22: Association between Total cholesterol and prevalence of gallstones

Total cholesterol	Gallstones absent	%	Gallstones present	%	Total	%
< 200 mg/dl	83	79.81	21	20.19	104	52.00
≥ 200 mg/dl	50	52.08	46	47.92	96	48.00
Total	133	66.50	67	33.50	200	100.00
Chi-square=17.2238 p=0.0001*						

*p<0.05

This shows the association between total cholesterol and prevalence of gallstones. There were a total of 21 patients with with gallstones and cholesterol levels < 200mg/dl and 46 patients with gallstones and a total cholesterol level of ≥ 200mg/dl. So as the level of total cholesterol increases, the number of patients with gallstones also rises. This association is found to be statistically significant.

Graph 15: Association between Total cholesterol and prevalence of gallstones

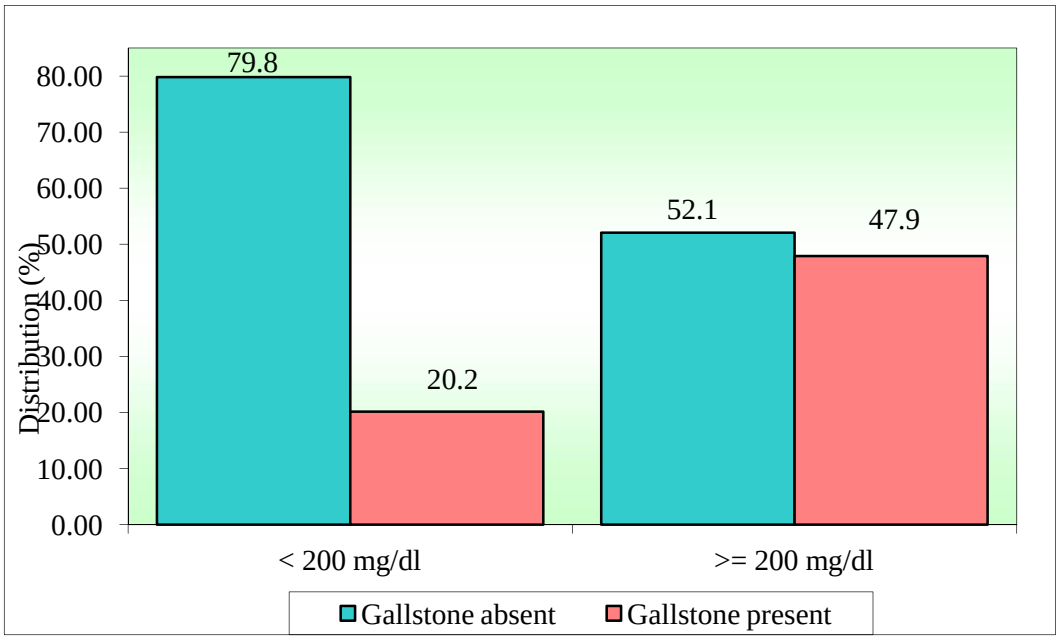


Table 23: Triglycerides wise distribution

Triglycerides	No. of patients	% of patients
< 150 mg/dl	15	7.50
150-200 mg/dl	129	64.50
≥201 mg/dl	56	28.00
Total	200	100.00

This table shows the distribution of the patients according to the triglyceride levels. The group with a triglyceride level of 150 – 200 mg/dl had the maximum number of patients with 129 (64.50%) of the total 200 patients.

Graph 16: Triglycerides wise distribution

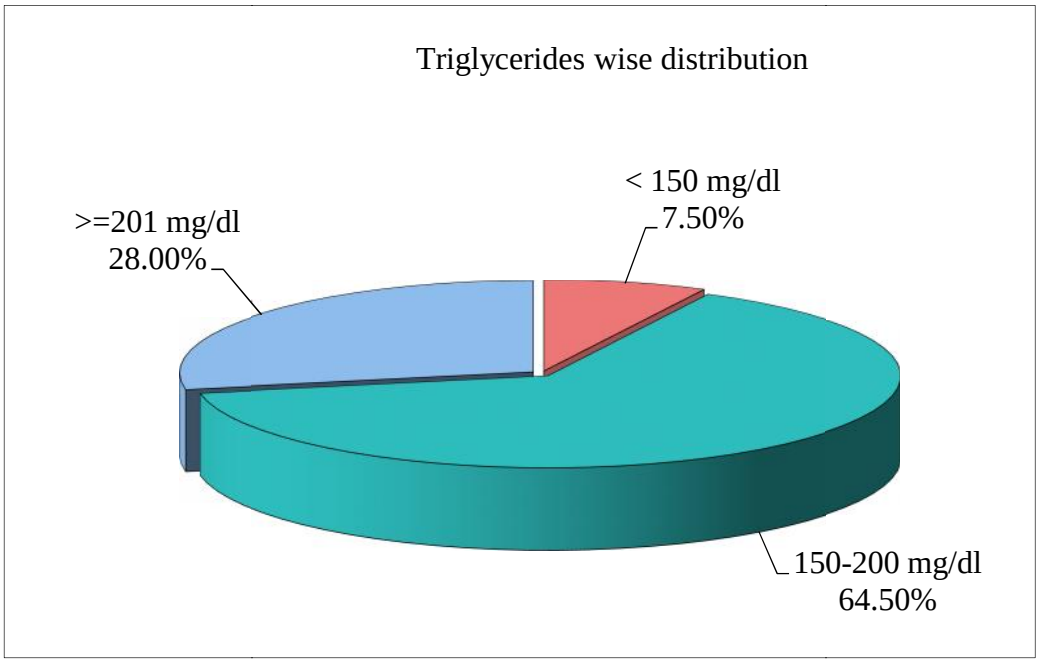


Table 24: Association between Triglycerides and prevalence of gallstones

Triglycerides	Gallstones absent	%	Gallstones present	%	Total	%
< 150 mg/dl	10	66.67	5	33.33	15	7.50
150-200 mg/dl	105	81.40	24	18.60	129	64.50
≥201 mg/dl	18	32.14	38	67.86	56	28.00
Total	133	66.50	67	33.50	200	100.00
Chi-square=42.5204 p=0.0001*						

*p<0.05

This table represents the association between triglycerides and prevalence of gallstones which is statistically significant. The maximum number of the gallstone positive patients belonged to the group with triglyceride level of ≥ 201mg/dl.

Graph 17: Association between Triglycerides and prevalence of gallstones

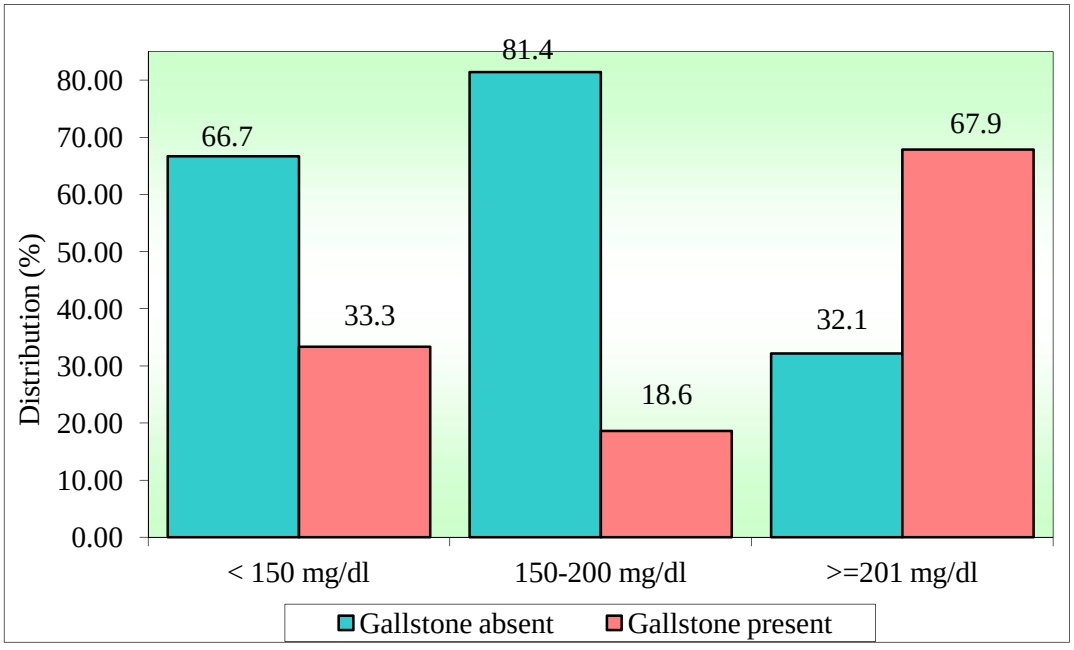


Table 25: LDL wise distribution

LDL	No. of patients	% of patients
<100 mg/dl	40	20.00
100-129 mg/dl	80	40.00
130-160 mg/dl	45	22.50
≥161 mg/dl	35	17.50
Total	200	100.00

The above table shows the distribution of the patients according to the levels of LDL. The maximum number of patients belong to the group of LDL level of 100 – 129 mg/dl, comprising of 80 patients. The group with minimum patients was ≥ 161mg/dl.

Graph 18: LDL wise distribution

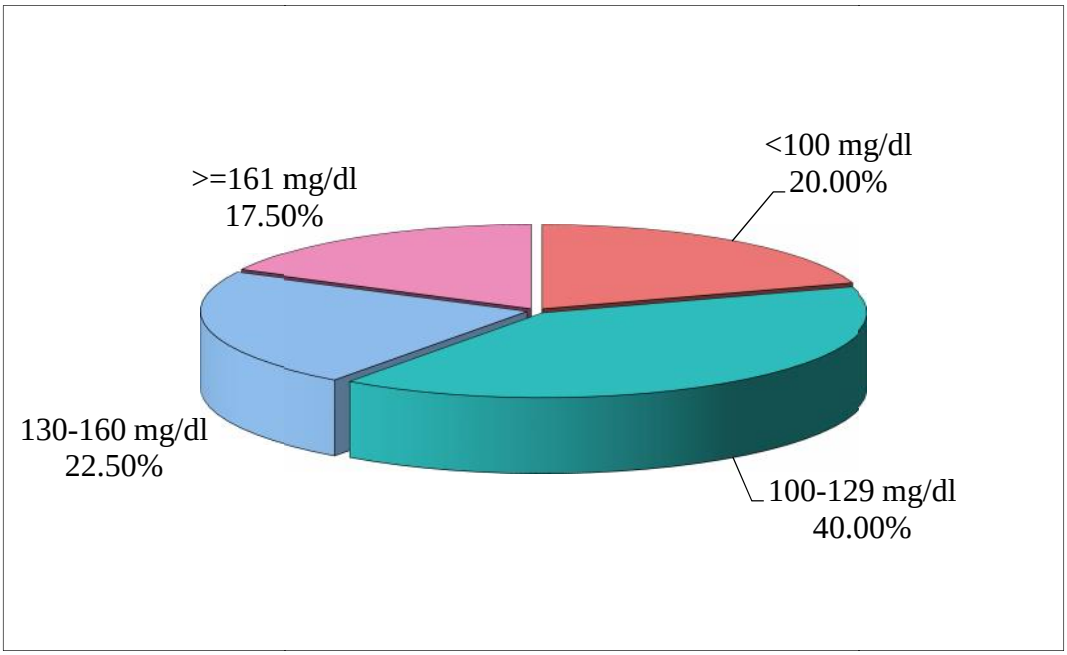


Table 26: Association between LDL and prevalence of gallstones

LDL	Gallstones absent	%	Gallstones present	%	Total	%
<100 mg/dl	26	65.00	14	35.00	40	20.00
100-129 mg/dl	69	86.25	11	13.75	80	40.00
130-160 mg/dl	31	68.89	14	31.11	45	22.50
≥161 mg/dl	7	20.00	28	80.00	35	17.50
Total	133	66.50	67	33.50	200	100.00
Chi-square=48.1340 p=0.0001*						

*p<0.05

The above table shows the association between LDL and prevalence of gallstones. It is evident from the table that as the LDL levels increase there is an increase in the prevalence of gallstones, which is statistically significant.

Graph 19: Association between LDL and prevalence of gallstones

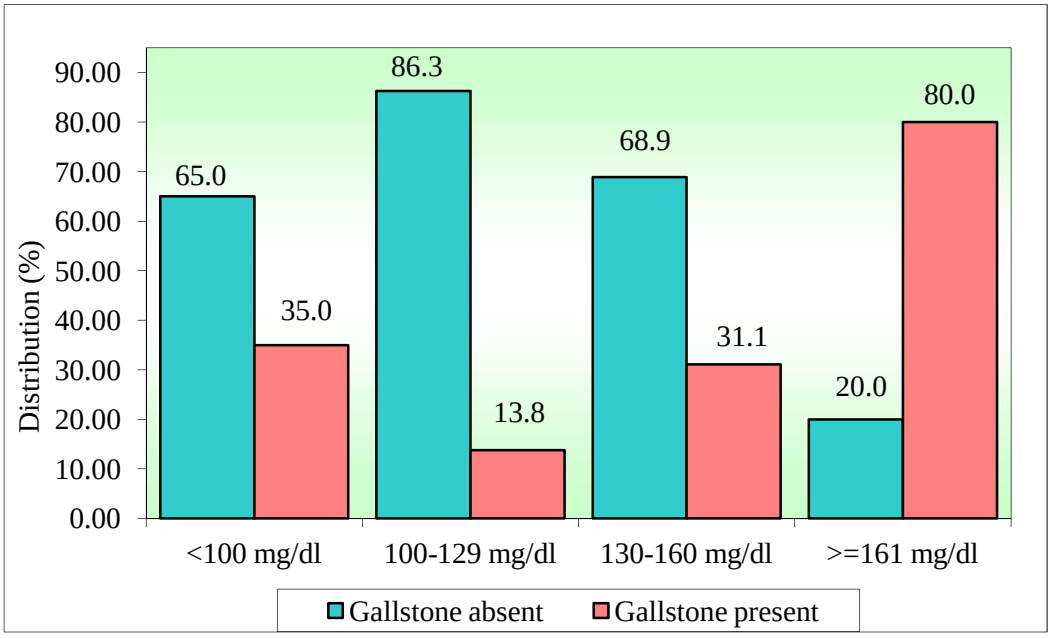


Table 27: HDL wise distribution

HDL	No. of patients	% of patients
<40 mg/dl	81	40.50
40-60 mg/dl	105	52.50
≥61 mg/dl	14	7.00
Total	200	100.00

According to the above table the HDL group with level of 40 – 60 mg/dl has the maximum number of the study subjects i.e. 105 out of 200. The least number of study subjects (14) were found in the group of ≥61mg/dl.

Graph 20: HDL wise distribution

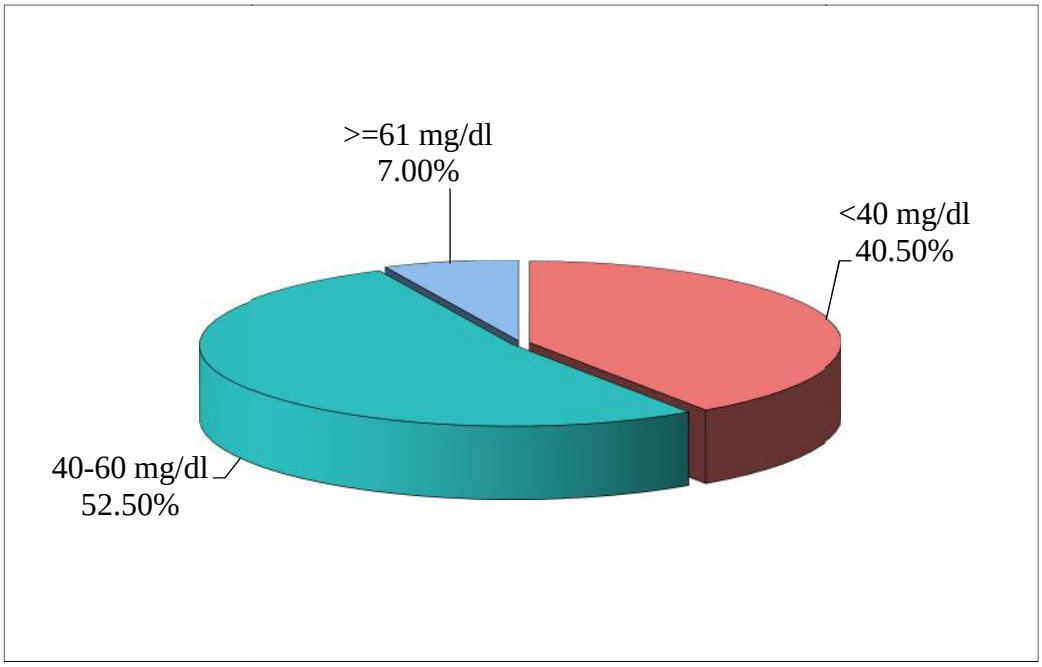


Table 28: Association between HDL and prevalence of gallstones

HDL	Gallstones absent	%	Gallstones present	%	Total	%
<40 mg/dl	49	60.49	32	39.51	81	40.50
40-60 mg/dl	83	79.05	22	20.95	105	52.50
≥61 mg/dl	1	7.14	13	92.86	14	7.00
Total	133	66.50	67	33.50	200	100.00
Chi-square=42.5204 p=0.0001*						

*p<0.05

In the present study the 32 patients with gallstones belonged to the HDL group of < 40mg/dl and 22 of the patients with gallstones belonged to the group 40 – 60 mg/dl. The HDL group of ≥ 61mg/dl contains 13 patients with gallstones.

Table 29: Comparison of patients without and with gallstones status with Age, Duration of diabetes, BMI, Waist to Hip Ratio, HbA1c, Total Cholesterol, Triglycerides, LDL and HDL by independent t test

Variables	Without gallstones		With gallstones		|t|-value	p-value
	Mean	SD	Mean	SD		
Age (years)	56.684	6.231	54.672	11.911	1.5705	0.1179
Duration of diabetes (Years)	12.128	4.291	13.037	5.979	1.2343	0.2186
BMI (kg/m^2)	28.548	3.696	34.391	6.689	7.9582	0.0001*
Waist to Hip Ratio	0.852	0.052	0.968	0.056	14.5791	0.0001*
HbA1c (%)	9.020	1.254	9.670	2.160	2.6885	0.0078*
Total Cholesterol (mg/dl)	196.910	25.687	225.552	48.385	5.4731	0.0001*
Triglycerides (mg/dl)	176.398	23.322	207.642	42.405	6.7239	0.0001*
LDL (mg/dl)	116.752	23.957	144.239	50.172	5.2492	0.0001*
HDL (mg/dl)	43.639	7.732	42.806	14.653	0.5268	0.5989

*$p<0.05$

The above table depicts the comparison of patients without and with gallstones status with Age, Duration of diabetes, BMI, Waist to Hip Ratio, HbA1c, Total Cholesterol, Triglycerides, LDL and HDL by independent t test. A significant difference was observed between the patients with and without gallstones with respect to BMI, Waist to Hip Ratio, HbA1c, Total Cholesterol, Triglycerides and LDL at 5% level of significance.

The patients with gallstones have significantly higher BMI, Waist to Hip Ratio, HbA1c, Total Cholesterol, Triglycerides and LDL levels as compared to the patients without gallstones.

Graph 21: Comparison of patients without and with gallstones status with age, Duration of diabetes, BMI, Waist to Hip Ratio, HbA1c, Total Cholesterol, Triglycerides, LDL and HDL by independent t test

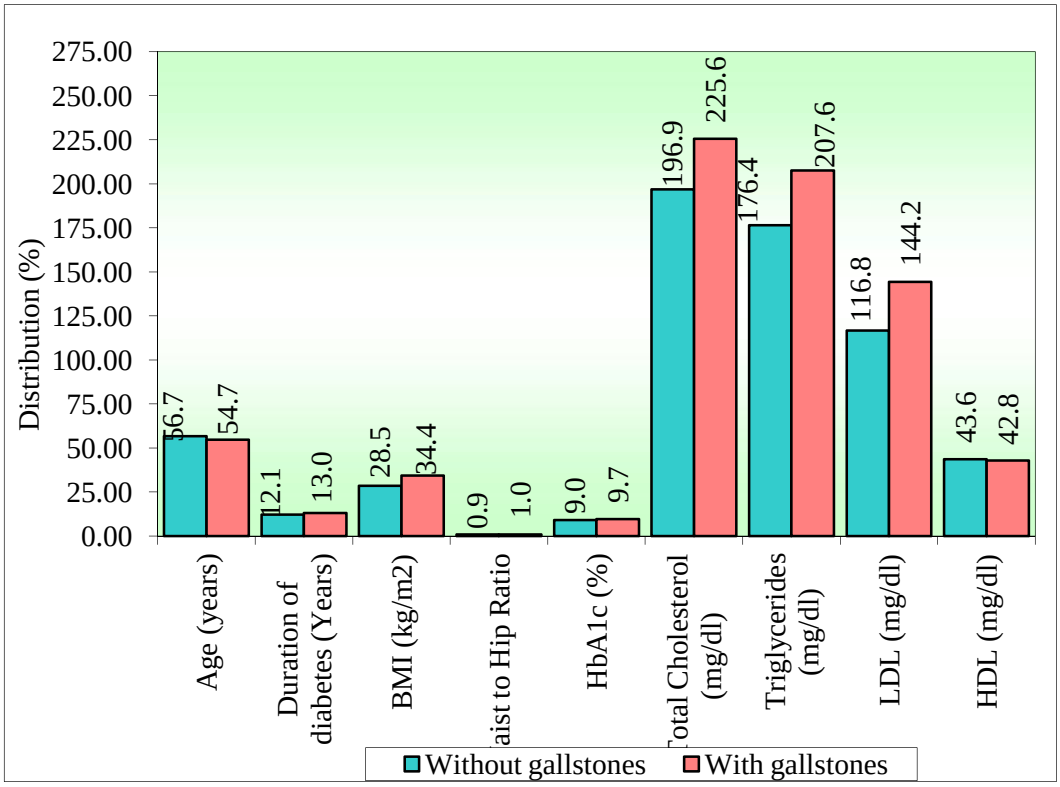


Table 30: Multivariate logistic regression analysis of prevalence of gallstones in the study

Factors	Unadjusted OR	95% CI for OR		p-value	Adjusted OR	95% CI for OR		p-value
		Lower	Upper			Lower	Upper	
Age groups								
30 - 39 years	Reference				Reference			
40 - 49 years	0.93	0.45	1.93	0.853	0.8	0.06	10.21	0.866
50 - 59 years	0.34	0.21	0.55	0.0001*	0.05	0	0.66	0.0230*
60 - 69 years	0.25	0.13	0.46	0.0001*	0.02	0	0.44	0.0120*
70 - 79 years	4	0.85	18.84	0.08	0.3	0.01	6.48	0.441
Gender								
Male	Reference				Reference			
Female	0.58	0.39	0.86	0.0070*	0.24	0.04	1.24	0.088
Duration of diabetes								
05 - 09 years	Reference				Reference			
10 - 15 years	0.52	0.33	0.81	0.0040*	3.8	0.5	28.85	0.197
≥15 years	0.71	0.4	1.27	0.25	1.01	0.09	11.86	0.992
BMI groups								
18.5-24.9 kg/m^2	Reference				Reference			
25-29.9 kg/m^2	0.23	0.14	0.4	0.0001*	0.62	0.09	4.25	0.624
30-34.9 kg/m^2	0.31	0.16	0.62	0.0010*	0.67	0.07	6.27	0.727
35-39.9 kg/m^2	3.25	1.06	9.97	0.0390*	4.84	0.19	123	0.339
≥40 kg/m^2	21	2.83	156.12	0.0030*	234.09	0.35	15570.6	0.1

Diabetic autonomic neuropathy								
Absent	Reference				Reference			
Present	2.61	1.52	4.5	0.0010*	104.11	11.18	969.64	0.0001*
HbA1c								
6.5-7.9 %	0.53	0.31	0.9	0.0200*	5.16	0.9	29.43	0.065
08 to 9.9 %	0.33	0.2	0.53	0.0001*	3.24	0.48	21.85	0.227
≥10 %	Reference				Reference			
Total cholesterol								
< 200 mg/dl	Reference				Reference			
≥ 200 mg/dl	0.92	0.62	1.37	0.683	0.74	0.05	11.31	0.827
Triglycerides								
< 150 mg/dl	Reference				Reference			
150-200 mg/dl	0.23	0.15	0.36	0.0001*	2.79	0.15	52.54	0.494
≥201 mg/dl	2.11	1.21	3.7	0.0090*	85.81	3.29	2235.26	0.0070*
LDL								
<100 mg/dl	Reference				Reference			
100-129 mg/dl	0.16	0.08	0.3	0.0001*	2.34	0.13	43.81	0.569
130-160 mg/dl	0.45	0.24	0.85	0.0140*	7.05	0.14	363.35	0.331
≥161 mg/dl	4	1.75	9.16	0.0010*	353.1	3.47	35895.8	0.0130*
HDL								
<40 mg/dl	0.65	0.42	1.02	0.061	0	0	0.07	0.0010*
40-60 mg/dl	0.27	0.17	0.42	0.0001*	0.01	0	0.26	0.0060*
≥61 mg/dl	Reference				Reference			

*p<0.05

The above table represents the Unadjusted and the Adjusted Odds Ratio (OR) of the prevalence of gallstones with other variables.

The Unadjusted OR of the diabetic patients belonging to the group of BMI 35-39.9 kg/m2 (OR = 3.25, CI 1.06 - 9.97) and BMI of ≥40 kg/m2 (OR = 21.00, CI 2.83 – 156.12) was found to be statistically significant.

The Unadjusted OR of the diabetic patients belonging to the group with the presence of diabetic autonomic neuropathy (OR = 2.61, CI 1.52 – 4.50) was found to be statistically significant.

The Adjusted OR of the diabetic patients belonging to the group with the presence of diabetic autonomic neuropathy (OR = 104.11, CI 11.18 - 969.64) was found to be statistically significant.

The Unadjusted OR of the patients in the triglycerides group of ≥201mg/dl (OR = 2.11, CI 1.21 – 3.76) was found to be statistically significant. The Adjusted OR of the patients in the triglycerides group of ≥201mg/dl (OR = 85.81, CI 3.29 - 2235.26) was found to be statistically significant.

The Unadjusted OR of the patients in the LDL group of ≥161mg/dl (OR = 4.00, CI 1.75 – 9.16) was found to be statistically significant. The Adjusted OR of the patients in the LDL group of ≥161mg/dl (OR = 353.10, CI 3.47 – 35895.8) was found to be statistically significant.

DISCUSSION

Diabetes mellitus is a growing health care problem worldwide and is characterized by many complications. The present study was undertaken to evaluate the prevalence of gallbladder stones and the associated risk factors among type 2 diabetes mellitus patients. It is a one year cross sectional study done at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi.

The prevalence of gallbladder stones was studied in 200 type 2 diabetes mellitus patients in the present study. It was found that the prevalence of gallbladder stones was 33.50%, with 67 type 2 diabetes mellitus patients having asymptomatic gallstones.

The observation of the present study is comparable to a study done by Chhabra A et al., which also reports 34% prevalence of gallstones in patients of type 2 diabetes mellitus.[9] Another study done by Al-Kayatt MK et al.[34] in 2012 also reported a prevalence of gallstones in type 2 diabetes mellitus to be 33%. Similarly the study done by Chapman B.A. et al. found the prevalence to be 32.7% [28]. Guimaraes SVD et al. showed a prevalence of gallstones in type 2 diabetics to be 37.1%[11]. The findings of the study by Elmehdawi RR et al. also showed a significant increase in the presence of gallstones in patients of type 2 diabetes.[32]

Few of the Indian studies done to assess the prevalence of gallstones in type 2 diabetics depicted similar findings. The Goyel K study focused on the magnitude of the asymptomatic gallstones in patients of type 2 diabetes mellitus in New Delhi and found about 31% had asymptomatic gallstone disease.[35] The findings of the study by Raman PG et al.[8] reports the prevalence of the gallstones in diabetics to be 32%.

Saxena R. et al.[29] also studied the patients of type 2 diabetes mellitus and found that 29% of patients had ultrasonographic evidence of gallstones. Gupta RS et al.[33] also reported a significant increase in the presence of gallstones in type 2 diabetes mellitus patients.

Other studies from different countries showed different figures. In Taiwan, the prevalence of gallstones in diabetic patients was 14.4% [36]. Pagliarulo M. et al. from Italy showed a prevalence of 24.8%[37] and Agunloye A.M. et al. from Nigeria showed the prevalence of asymptomatic gallstone disease in patients of type 2 diabetes mellitus to be 17.5% [38].

Such variation in the prevalence of gallbladder stones in type 2 diabetes mellitus patients across the globe could be attributed to the different study designs, geographical variation and the difference in ethnicity of the patients.[39]

In the present study the age group wise distribution of the study subjects with gallstones was as follows. The age group of 30 – 39 years had 10 (14.93%) patients out of 67 patients with gallstones. The age group of 40 – 49 years had 14 (20.90%) patients, 50 – 59 years group had 23 (34.33%) patients, 60 – 69 years group had 12 (17.91%) patients and lastly the age group of 70 – 79 years had 08 (11.94%) patients out of the 67 patients with gallstones. Out of these groups, the age group of 50 – 59 years had maximum number (23) of patients who had asymptomatic gallstones in the present study. The mean age of the patients with gallstones was 54.67 ± 11.91 years. This was in agreement with a study done by Khare S. et al.[7], with the mean age in the study being 53.65 years for the type 2 diabetic patients with gallstones.

A study done by Coelho JC et al. found an average age of 59.9 years in the patients with gallstones[40]. Sodhi J.S. et al.[41] showed that the prevalence of the gallstones in type 2 diabetes mellitus patients increased with the increasing age with a peak in the sixth decade. Another study by Khalaf SK[27] revealed that the peak prevalence of the gallstones was in the age group of 40-49 years and these results were in agreement with other studies done in Iran by Rasheed K.[42] and Idris S.A. et al.[43].

The study done by Kaur M. et al[31] found that the distribution of asymptomatic gallstone disease according to the increasing age was not statistically significant. This finding was in agreement with the findings of study done by Chhabra et al.[9] and Khare et al.[7]. While the other studies done by Elmehdawi et al.[32] and Pagliarulo M. et al.[37], the distribution of the gallstones in the patients of type 2 diabetes mellitus according to the age was statistically significant.

In the present study the distribution of the study subjects according to the gender was as follows. The male patients were 96 (48%) and the female patients were 104 (52%) of the total study subjects. There were 29 males and 38 females who were positive for the asymptomatic gallstones in the present study. The association between the gender and the prevalence of gallbladder stones was not statistically significant in the present study. The study done by Khare et al.[7] showed that 65.38% of the diabetic patients with gallstones were females and only 34.61% subjects were males. They found this association to be statistically significant. The other studies done by Elmehdawi R.R. et al.[32] studied 161 patients of type 2 diabetes mellitus and found that the prevalence of the gallbladder stones was significantly higher in the female patients. The female gender association with the increased prevalence of the

gallstones in patients of type 2 diabetes mellitus was also found in the other studies done by Anmar H.[6] and Saxena R. et al.[29] which showed that majority of the diabetic patients with gallstone disease were females. The rationale offered for the increased prevalence of the gallbladder stones in the female patients of type 2 diabetes mellitus is that, the women especially those in the reproductive age group are 2–3 times more predisposed to develop gallstones than those in the non-reproductive age group. This is due to the high estrogen levels which causes bile super-saturation with cholesterol.[44]

In the present study the distribution of the patients with gallstones according to the BMI groups is as follows. The BMI group of 18 – 24.9 kg/m^2 has 06 patients. The group of 25 – 29.9 kg/m^2 has 16 patients. The group 30 – 34.9 kg/m^2 has 11 patients and the group 35 – 39.9 kg/m^2 has 13 patients. The group of BMI ≥ 40 kg/m^2 has 21 patients with gallstones. The mean BMI of patients with gallstones was 34.39 ± 6.68 kg/m^2. There was an increased prevalence of the gallstones in the patients of type 2 diabetes mellitus with the increase in BMI. The percentage of the patients with significantly high prevalence of gallstones was found to belong to the BMI groups of 35 – 39.9 kg/m^2 and ≥ 40 kg/m^2. Association between BMI groups and prevalence of gallstones was found to be statistically significant (p=0.0001**)**. A study done by Khare et al.[7] showed a statistically significant association between high BMI and an increased prevalence of gallstones. The mean BMI was 27.77 ± 3.2 kg/m^2. The study done by Elmehdawi R.R.[32] had a mean BMI of 34.78 ± 6.2 kg/m^2 in the diabetic population with gallstones. Tao-Hsin-Tung[58] also studied the correlation of BMI and the prevalence of the gallstones in the diabetic population. They found that BMI was significantly associated with gallstones in the patients of type 2 diabetes mellitus. The mean BMI was 26.57 ± 1.07 kg/m^2.

A study by Khalaf SK[27] also showed that an increment in the prevalence of the gallstones in type 2 diabetes mellitus patients with BMI more than 25 kg/m^2 as compared to the patients with BMI less than 25 kg/m^2. This result is similar to the findings of other studies like Al-Bayati et al.[45], and Pagliarulo et al.[37] All these studies found that a high BMI and a high prevalence of gallstones sustained significance of association at multivariate analysis. The study done by Kaur et al.[31] in India reported a higher BMI >25kg/m^2 in patients of type 2 diabetes mellitus with gallstones.

The distribution of the subjects in the present study according to diabetic autonomic neuropathy was as follows. The total number of patients with diabetic autonomic neuropathy was 65 out of the total 200 study subjects. The association between diabetic autonomic neuropathy and the prevalence of the gallstones was found to be statistically significant (p=0.0001**)**. A total of 47 diabetic patients with gallstones were found to have diabetic autonomic neuropathy. A study done by Raman P.G. et al.[8] found out that the mean fasting gallbladder volume was significantly larger in diabetic subjects with diabetic autonomic neuropathy than those without neuropathy. Thus there is an increased prevalence of the gallstones in diabetic patients with diabetic autonomic neuropathy which leads to stasis of the bile in the gallbladder and also causes hypomotility of the gallbladder.[8]

The association of autonomic neuropathy and gallstones in diabetics was also studied by Chhabra A. et al.[9] Their statistical analysis showed a strong association between them. They reported that the mean percentage contractility of the gallbladder was significantly decreased in the patients of type 2 diabetes mellitus. According to Stone et al.[52] the gallbladder emptying was lower in diabetics. Similar findings were reported by Gaur et al.[53] and Yang et al.[54]. Kayacetin et al.[55] showed that the

gallbladder ejection fraction was significantly reduced in the patients with autonomic neuropathy as compared to the patients without autonomic neuropathy.

A high level of HbA1c reflects poor control of diabetes mellitus. The distribution of patients in the present study according to the levels of HbA1c is as follows. The HbA1c group of 6.5 – 7.9% had 58 patients. The group of 8 – 9.9% contains 89 patients and lastly HbA1c group of ≥ 10% had 53 patients. The present study found out that there was a statistically significant association between HbA1c levels and gallstones (p=0.0229**)**. With the increase in HbA1c levels there was a high prevalence of gallstones among type 2 diabetes mellitus patients. The mean HbA1c level in the present study in patients with gallstones was 9.67 ± 2.16%. The findings of the present study were consistent with the findings of the study done by Khare et al.[7] with a mean HbA1c level in patients with type 2 diabetes mellitus and gallstones being 9.72 ± 2.78%. The study done by Khalaf [27] reported a mean HbA1c level of 11.01 ± 2.1%.

It is a known fact that the longer the duration of diabetes mellitus, more are the complications of the diabetes. The distribution of the subjects in the present study according to the duration of diabetes with gallstones is as follows. The group with duration of 5 – 9 years has 18 patients, 10 – 15 years has 29 patients and the group of > 15 years has 20 patients with gallstones. The mean duration of diabetes mellitus in the present study in the patients with gallstones was found to be 13.03 ± 5.97 years. In the present study there was no statistically significant association between the duration of diabetes and the prevalence of the gallstones. This was in agreement with the study done by Elmehdawi R.R et al.[32] which reported that the duration of diabetes mellitus did not affect the prevalence of the gallbladder stones. On the other hand the

findings of the study done by Khalaf SK[27] showed that the duration of diabetes mellitus was strongly associated with an increased frequency of gallstone formation, with 42.04% of the gallstone positive patients having duration of diabetes mellitus of more than 10 years. The studies done by Agunloye A.M. et al.[38], Al-Bayati S. et al.[45] and Olokoba A.B et al.[46] all suggested that an increase in the duration of diabetes mellitus was associated with an increased prevalence of gallstones.

In the present study the levels of total cholesterol, triglycerides and low density lipoprotein were found to be significantly associated with gallstone formation in the patients with type 2 diabetes ($p = 0.0001$**)**. A rise in the levels of total cholesterol, triglycerides and low density lipoprotein was associated with increased prevalence of gallstones. The mean total cholesterol level in the patients with gallstones in the present study was 225.55 ± 48.38 mg/dl. The mean triglyceride level was 207.64 ± 42.4 mg/dl and that of low density lipoprotein was 144.23 ± 50.17 mg/dl.

This was in agreement with the results of the study done by Tao-Hsin-Tung[58] which had a mean total cholesterol level of 220 ± 20.5 mg/dl and was significantly associated with the gallstone disease in patients with type 2 diabetes mellitus. A study done by Khalaf SK[27] had a mean total cholesterol level of 272 ± 46.0 mg/dl, mean low density lipoprotein levels of 114 ± 44.40 mg/dl and a mean triglyceride levels of 254.04 ± 144.40 mg/dl in the gallstone positive patients. They also reported that there was a significant association between the gallstone frequency in diabetic patients and an increased level of total cholesterol and triglycerides and that the association was maintained after the multivariate logistic regression analysis was done.

A study done by Chhabra A. et al.[9] reported that a mean total serum cholesterol level in the diabetic patients with gallstones was 177.15 ± 32.69 mg/dl and it was significantly associated with the gallbladder stones in the patients with type 2 diabetes mellitus.

CONCLUSION

Diabetes mellitus is a growing health care problem worldwide and is characterized by many complications. The present study was undertaken to evaluate the prevalence of gallbladder stones and the associated risk factors among type 2 diabetes mellitus patients. Ultrasonography is a simple and cost effective investigation and can be routinely used in all diabetics for screening of gall bladder diseases. Gallbladder stones are more prevalent among type 2 diabetes patients. The present study was done on 200 type 2 diabetes mellitus patients.

1. The prevalence of gallbladder stones was 33.50%, with 67 type 2 diabetes mellitus patients having asymptomatic gallstones out of the total 200 study subjects.
2. In the present study the age group of 50 – 59 years had maximum number (23) patients with gallstones out of the total 67 type 2 diabetes mellitus patients who had asymptomatic gallstones. The mean age of the patients with gallstones was 54.67 ± 11.91 years.
3. Out of the 67 patients who were positive for the asymptomatic gallstones, there were 29 males and 38 females.
4. There was an increased prevalence of the gallstones in the patients of type 2 diabetes mellitus with the increase in BMI. The percentage of the patients with significantly high prevalence of gallstones was found to belong to the BMI groups of 35 – 39.9 kg/m^2 and ≥ 40 kg/m^2 and was found to be statistically significant (p=0.0001**)**.

5. The total number of patients with diabetic autonomic neuropathy was 65 out of the total 200 study subjects. The association between diabetic autonomic neuropathy and the prevalence of the gallstones was found to be statistically significant (p=0.0001**)**. A total of 47 diabetic patients with gallstones were found to have diabetic autonomic neuropathy.
6. The present study found out that there was a statistically significant association between HbA1c levels and gallstones (p=0.0229**)**. With the increase in HbA1c levels there was a high prevalence of gallstones among type 2 diabetes mellitus patients. The mean HbA1c level in the present study in patients with gallstones was 9.67 ± 2.16%.
7. The mean duration of diabetes mellitus in the present study in the patients with gallstones was found to be 13 ± 5.9 years.
8. In the present study the levels of total cholesterol, triglycerides and low density lipoprotein were found to be significantly associated with gallstone formation in the patients with type 2 diabetes (p = 0.0001). The mean total cholesterol, triglyceride and low density lipoprotein levels in the patients with gallstones were 225.55 ± 48.38 mg/dl, 207.64 ± 42.4 mg/dl and 144.23 ± 50.17 mg/dl respectively.

The present study was undertaken to have more knowledge about the prevalence of gallbladder stones and the risk factors associated with them in type 2 diabetes mellitus patients. This knowledge may provide an early interventional opportunity to implement adequate preventive measures and the consequent morbidity and mortality can be prevented to a greater extent.

SUMMARY

The present study was done on 200 patients of type 2 diabetes mellitus, admitted in KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi over a period of one year from January 2017 to December 2017. A thorough medical history was obtained, clinical examination and investigations were performed on the study subjects. Ultrasonography of abdomen was done with a 3 – 5 MHz transducer, with special reference to gallbladder and gallstones. The obtained data was entered into Excel 2010. It was converted and analysed by SPSS version 20.0 software. The chi square test and the multiple logistic regression analysis were performed.

The prevalence of gallbladder stones was 33.50%, with 67 type 2 diabetes mellitus patients having asymptomatic gallstones out of the total 200 study subjects. The mean age of the patients with gallstones was 54.67 ± 11.91 years. Out of the 67 patients who were positive for the asymptomatic gallstones, there were 29 males and 38 females. The percentage of the patients with significantly high prevalence of gallstones was found to belong to the BMI groups of 35 – 39.9 kg/m^2 and ≥ 40 kg/m^2 and was found to be statistically significant (p=0.0001**)**. The association between diabetic autonomic neuropathy and the prevalence of the gallstones was found to be statistically significant (p=0.0001**)**.

The present study found out that there was a statistically significant association between HbA1c levels and gallstones (p=0.0229**)**. The mean HbA1c level in the present study in patients with gallstones was 9.67 ± 2.16%. The mean duration of diabetes mellitus in the present study in the patients with gallstones was found to be 13 ± 5.9 years. Total cholesterol, triglycerides and low density lipoprotein were

found to be significantly associated with gallstone formation in the patients with type 2 diabetes ($p = 0.0001$).

The mean total cholesterol, triglyceride and low density lipoprotein levels in the patients with gallstones were 225.55 ± 48.38 mg/dl, 207.64 ± 42.4 mg/dl and 144.23 ± 50.17 mg/dl respectively.

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ANNEXURE I – CONSENT FORM

TITLE OF RESEARCH STUDY:

PREVALENCE OF GALLBLADDER STONES AND THE ASSOCIATED RISK FACTORS AMONG TYPE 2 DIABETES MELLITUS PATIENTS - A CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MRC, BELAGAVI.

PRINCIPAL INVESTIGATOR:

INTRODUCTION AND PURPOSE:

Diabetes related complications affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease. An altered glucose metabolism may increase the risk of gallbladder stones in certain subjects.

A meta-analysis study suggested that there is a strong association between diabetes mellitus and the prevalence of gallstone disease. Poor control of diabetes, hypercholesterolemia and diabetic autonomic neuropathy are important factors for the development of gallbladder disease. Many of the diabetes related complications can be prevented or delayed with early detection and aggressive glycaemic control.

The present study will be undertaken to have more knowledge about the prevalence of gallbladder stones and the risk factors associated with them in type 2 diabetes mellitus patients. This knowledge may provide an early interventional opportunity to implement adequate preventive measures.

PROCEDURE:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You may have to give blood and urine samples for the necessary investigations.

RISKS AND BENEFITS:

The only risk and possible discomfort you might get is while taking blood samples for the investigations. It may cause swelling, pain, redness bruising or infection (rarely happens) at the site from where the samples are drawn.

Benefit is recognizing the prevalence of gallbladder stones and the associated risk factors and to prevent their complications.

ALTERNATIVES:

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

PRIVACY AND CONFIDENTIALITY:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

INSTITUTION/SPONSORS/COMPENSATION:

In case of any injury related to the study, treatment will be made available at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. There is no compensation or payment for such medical treatment by law.

You will not be paid/offered any gifts/incentives for participating in the study.

AUTHORIZATION TO PUBLISH THE RESULTS:

The results of the study would be forwarded to the KLE Academy of Higher Education and Research, Belagavi as part of requirement towards the completion of MD degree, review and publishing.

QUESTIONS / CONTACT DETAILS:

In case of the queries during study you may contact following persons.

If you need any further information regarding your rights as a study participant, you may also contact,

DR. GANGA S. PILLI M.D.
Chairman of Institutional Ethics Committee,
Professor, Department of Pathology,
J.N. Medical College, Belagavi.
Mobile: 9480275601

CONSENT STATEMENT.

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this consent form, and have had all the questions answered.

Name of the participant:_____ Signature/Thumb print:_____

Name of the witness:_____ Signature/Thumb print:_____

Investigator name:_____ Signature:_____

Date: Place:

ANNEXURE-II

PROFORMA

NAME: CASE NO.

AGE: IP no.:

SEX:

ADDRESS:

PRESENTING COMPLAINTS:

SPECIFIC QUESTIONS:

a) Giddiness.
b) Tingling numbness in hands and legs.
c) Pain abdomen.
d) Excess of sweating/ absence of sweating.

DETAILS OF DIABETES MELLITUS.

a) Age of onset:
b) Duration of illness:
c) Treatment history:

GENERAL EXAMINATION:

a) Pulse:

Supine –

Standing –

b) Blood Pressure:

Supine –

Standing –

c) Temperature:

d) Peripheral pulses:

e) Anthropometry:

Height –

Weight –

BMI –

Waist circumference –

Hip circumference –

Waist to hip ratio –

SYSTEMIC EXAMINATION:

a) Cardiovascular System.

b) Respiratory System.

c) Nervous System.

d) Per abdomen.

INVESTIGATIONS:

a) Random blood sugar.

b) Fasting blood sugar.

c) Post-prandial blood sugar.

d) HbA1c.

e) Ultrasonography of Abdomen –

1. Gallbladder wall - Thickened/ Normal.

2. Gallbladder – Empty/ Filled/ Distended.

3. Gallstones – Absent/ Present- Multiple/ Solitary

Size of the largest gallbladder stone.

4. Biliary sludge – Present/ Absent.

e) Lipid profile.

f) Complete Blood Count.

g) Blood urea.

h) Serum creatinine.

i) Urine routine & microscopy.

Case number	IP no.	Age (years)	Age groups	Age groups					Sex	History												Examination																		Investigations																																
																	Groups of duration of diabetes			Treatment history		Pulse (/min)		Blood Pressure (mmHg)						BMI Groups															HbA1c Groups			Gallstones						Cholesterol groups				Triglycerides groups					LDL groups						HDL groups		
																																																		Present																				
				30-39 years	40-49 years	50-59 years	60-69 years	70-79 years		Giddiness	Tingling numbness in limbs	Pain abdomen	Excess/Absence of sweating	Age of onset of diabetes (Years)	Duration of diabetes (Years)	Duration Groups	5-9 years	10-15 years	>15 years	Oral drugs	Insulin	Supine	Standing	Supine	Standing	Height (m)	Weight (kg)	BMI (kg/m2)	BMI Groups	16-18.4 (kg/m2)	18.5-24.9 (kg/m2)	25-29.9 (kg/m2)	30-34.9 (kg/m2)	35-39.9 (kg/m2)	≥40 (kg/m2)	Waist circumference (cm)	Hip circumference (cm)	Waist to Hip Ratio	Diabetic Autonomic Neuropathy	Random Blood Sugar (mg/dl)	Fasting blood sugar (mg/dl)	Post-prandial Blood Sugar (mg/dl)	HbA1c (%)	HbA1c Groups	6.5-7.9 (%)	08 to 9.9 (%)	≥10 (%)		Absent	Solitary	Multiple	Total Cholesterol (mg/dl)	Total Cholesterol Group	<200 mg/dl	≥200 mg/dl	Triglycerides (mg/dl)	Triglycerides Groups	<150 mg/dl	150-200 mg/dl	>200 mg/dl	LDL (mg/dl)	LDL Groups	<100 mg/dl	100-129 mg/dl	130-160 mg/dl	>160 mg/dl	HDL (mg/dl)	HDL Groups	<40 mg/dl	40-60 mg/dl	>60 mg/dl
1	781164	65	4	-	-	-	✓	-	M	✓	✓	NO	✓	52	13	2	-	✓	-	✓	✓	98	104	162/100	136/90	1.55	86	36.2	5	-	-	-	-	✓	-	97	103	0.94	P	251	148	222	7.5	1	✓	-	-	P	-	-	✓	168	1	✓	-	158	2	-	✓	-	74	1	✓	-	-	-	62	3	-	-	✓
2	782068	54	3	-	-	✓	-	-	M	✓	NO	NO	✓	48	6	1	✓	-	-	✓	NO	74	85	188/100	180/90	1.69	80	28.2	3	-	-	✓	-	-	-	68	81	0.83	A	229	152	252	9.4	2	-	✓	-	A	✓	-	-	189	1	✓	-	192	2	-	✓	-	98	1	✓	-	-	-	52	2	-	✓	-
3	782079	72	5	-	-	-	-	✓	F	NO	✓	NO	✓	46	26	3	-	-	✓	✓	NO	96	106	156/82	122/70	1.7	80	28	3	-	-	✓	-	-	-	88	92	0.95	P	218	168	248	9.6	2	-	✓	-	P	-	-	✓	158	1	✓	-	164	2	-	✓	-	61	1	✓	-	-	-	64	3	-	-	✓
4	782086	63	4	-	-	-	✓	-	M	✓	✓	NO	✓	45	18	3	-	-	✓	✓	✓	84	88	146/96	110/76	1.72	83	28.2	3	-	-	✓	-	-	-	88	89	0.98	P	185	156	206	9.5	2	-	✓	-	P	-	-	✓	195	1	✓	-	235	3	-	-	✓	120	2	-	✓	-	-	28	1	✓	-	-
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49	782986	56	3	-	-	✓	-	-	M	NO	✓	NO	NO	43	13	2	-	✓	-	✓	NO	65	78	190/100	188/96	1.7	64	22.4	2	-	✓	-	-	-	-	67	79	0.82	A	260	142	256	7.6	1	✓	-	-	A	✓	-	-	186	1	✓	-	192	2	-	✓	-	111	2	-	✓	-	-	36	1	✓	-	-
50	782990	69	4	-	-	-	✓	-	M	✓	NO	NO	NO	47	22	3	-	-	✓	✓	NO	68	74	136/86	110/70	1.58	71	28.6	3	-	-	✓	-	-	-	72	89	0.8	P	216	160	230	10.2	3	-	-	✓	A	✓	-	-	130	1	✓	-	150	2	-	✓	-	62	1	✓	-	-	-	38	1	✓	-	-
51	782992	51	3	-	-	✓	-	-	M	NO	✓	NO	✓	43	8	1	✓	-	-	✓	NO	63	74	136/86	130/80	1.56	83	34.4	4	-	-	-	✓	-	-	96	110	0.87	A	257	176	269	8.5	2	-	✓	-	A	✓	-	-	166	1	✓	-	196	2	-	✓	-	88	1	✓	-	-	-	38	1	✓	-	-
52	782996	49	2	-	✓	-	-	-	F	✓	NO	NO	✓	41	8	1	✓	-	-	✓	NO	73	81	110/70	100/66	1.67	76	27.6	3	-	-	✓	-	-	-	77	88	0.87	A	233	150	276	8.9	2	-	✓	-	A	✓	-	-	154	1	✓	-	166	2	-	✓	-	70	1	✓	-	-	-	50	2	-	✓	-

Case number	IP no.	Age (years)	Age groups	Age groups: 30-39 years	Age groups: 40-49 years	Age groups: 50-59 years	Age groups: 60-69 years	Age groups: 70-79 years	Sex	History: Giddiness	History: Tingling numbness in limbs	History: Pain abdomen	History: Excess/Absence of sweating	History: Age of onset of diabetes (Years)	History: Duration of diabetes (Years)	History: Duration Groups	Groups of duration of diabetes: 5-9 years	Groups of duration of diabetes: 10-15 years	Groups of duration of diabetes: >15 years	Treatment history: Oral drugs	Treatment history: Insulin	Examination: Pulse (/min) Supine	Pulse (/min) Standing	Blood Pressure (mmHg) Supine	Blood Pressure (mmHg) Standing	Height (m)	Weight (kg)	BMI (kg/m2)	BMI Groups	BMI Groups: 16-18.4 (kg/m2)	BMI Groups: 18.5-24.9 (kg/m2)	BMI Groups: 25-29.9 (kg/m2)	BMI Groups: 30-34.9 (kg/m2)	BMI Groups: 35-39.9 (kg/m2)	BMI Groups: ≥40 (kg/m2)	Waist circumference (cm)	Hip circumference (cm)	Waist to Hip Ratio	Diabetic Autonomic Neuropathy	Investigations: Random Blood Sugar (mg/dl)	Fasting blood sugar (mg/dl)	Post-prandial Blood Sugar (mg/dl)	HbA1c (%)	HbA1c Groups	HbA1c Groups: 6.5-7.9 (%)	HbA1c Groups: 08 to 9.9 (%)	HbA1c Groups: ≥10 (%)	Gallstones	Gallstones: Absent	Gallstones: Present: Solitary	Gallstones: Present: Multiple	Total Cholesterol (mg/dl)	Total Cholesterol Group	Cholesterol groups: <200 mg/dl	Cholesterol groups: ≥200 mg/dl	Triglycerides (mg/dl)	Triglycerides Groups	Triglycerides groups: <150 mg/dl	Triglycerides groups: 150-200 mg/dl	Triglycerides groups: >200 mg/dl	LDL (mg/dl)	LDL Groups	LDL groups: <100 mg/dl	LDL groups: 100-129 mg/dl	LDL groups: 130-160 mg/dl	LDL groups: >160 mg/dl	HDL (mg/dl)	HDL Groups	HDL groups: <40 mg/dl	HDL groups: 40-60 mg/dl	HDL groups: >60 mg/dl
53	782999	42	2	-	✓	-	-	-	M	NO	NO	NO	NO	31	11	2	-	✓	-	✓	NO	92	110	136/86	130/80	1.8	90	27.8	3	-	-	✓	-	-	-	92	96	0.95	A	210	130	216	7.2	1	✓	-	-	P	-	✓	-	158	1	✓	-	186	2	-	✓	-	50.8	1	✓	-	-	-	70	3	-	-	✓
54	783006	54	3	-	-	✓	-	-	F	✓	✓	NO	NO	45	9	1	✓	-	-	✓	NO	71	79	122/76	120/70	1.66	70	25.6	3	-	-	✓	-	-	-	72	85	0.84	A	235	149	282	8.8	2	-	✓	-	A	✓	-	-	210	2	-	✓	164	2	-	✓	-	143	3	-	-	✓	-	34	1	✓	-	-
55	783106	78	5	-	-	-	-	✓	F	✓	✓	NO	NO	53	25	3	-	-	✓	NO	✓	96	100	136/86	110/70	1.62	83	32	4	-	-	-	✓	-	-	98	99	0.98	P	216	196	230	6.5	1	✓	-	-	P	-	-	✓	178	1	✓	-	184	2	-	✓	-	120	2	-	✓	-	-	71	3	-	-	✓
56	783168	62	4	-	-	-	✓	-	F	✓	✓	NO	NO	53	9	1	✓	-	-	✓	NO	68	77	158/68	150/60	1.64	80	29.8	3	-	-	✓	-	-	-	74	85	0.87	A	223	147	292	8.9	2	-	✓	-	A	✓	-	-	224	2	-	✓	192	2	-	✓	-	140	3	-	-	✓	-	45	2	-	✓	-
57	783192	56	3	-	-	✓	-	-	F	✓	✓	✓	✓	48	8	1	✓	-	-	✓	NO	74	86	138/96	130/88	1.64	80	30.1	4	-	-	-	✓	-	-	80	89	0.91	A	240	143	238	8.5	2	-	✓	-	A	✓	-	-	218	2	-	✓	168	2	-	✓	-	154	3	-	-	✓	-	30	1	✓	-	-
58	783229	37	1	✓	-	-	-	-	F	✓	NO	NO	NO	32	5	1	✓	-	-	✓	NO	76	89	110/70	106/66	1.56	76	31.27	4	-	-	-	✓	-	-	78	80	0.97	A	228	186	280	12.2	3	-	-	✓	P	-	-	✓	287	2	-	✓	222	3	-	-	✓	216	4	-	-	-	✓	26	1	✓	-	-
59	783268	58	3	-	-	✓	-	-	M	✓	NO	NO	✓	48	10	2	-	✓	-	NO	✓	78	88	154/84	146/80	1.63	73	27.6	3	-	-	✓	-	-	-	68	79	0.86	A	243	132	250	9.6	2	-	✓	-	A	✓	-	-	210	2	-	✓	176	2	-	✓	-	118	2	-	✓	-	-	56	2	-	✓	-
60	783289	38	1	✓	-	-	-	-	F	✓	✓	NO	✓	33	5	1	✓	-	-	✓	NO	82	86	136/86	110/70	1.62	62	23.9	2	-	✓	-	-	-	-	72	83	0.86	P	230	190	246	9.2	2	-	✓	-	P	-	-	✓	182	1	✓	-	164	2	-	✓	-	187	4	-	-	-	✓	62	3	-	-	✓
61	783304	55	3	-	-	✓	-	-	M	NO	NO	NO	NO	38	17	3	-	-	✓	✓	✓	76	86	136/86	130/80	1.68	80	28.4	3	-	-	✓	-	-	-	78	86	0.9	A	229	143	243	8.6	2	-	✓	-	A	✓	-	-	186	1	✓	-	156	2	-	✓	-	116	2	-	✓	-	-	38	1	✓	-	-
62	783367	50	3	-	-	✓	-	-	F	✓	✓	NO	NO	42	8	1	✓	-	-	✓	NO	86	89	136/86	110/70	1.68	102	36.2	5	-	-	-	-	✓	-	69	77	0.89	P	256	192	268	10.5	3	-	-	✓	A	✓	-	-	222	2	-	✓	186	2	-	✓	-	136	3	-	-	✓	-	48	2	-	✓	-
63	783385	46	2	-	✓	-	-	-	F	NO	NO	NO	NO	41	5	1	✓	-	-	NO	✓	76	89	110/70	100/66	1.6	78	30.46	4	-	-	-	✓	-	-	88	89	0.98	A	286	148	278	10.6	3	-	-	✓	P	-	-	✓	256	2	-	✓	188	2	-	✓	-	174	4	-	-	-	✓	44	2	-	✓	-
64	783409	68	4	-	-	-	✓	-	F	NO	NO	NO	NO	57	7	1	✓	-	-	✓	NO	75	88	110/70	100/70	1.73	67	22.4	2	-	✓	-	-	-	-	62	79	0.78	A	236	147	247	9.6	2	-	✓	-	A	✓	-	-	194	1	✓	-	156	2	-	✓	-	103	2	-	✓	-	-	59	2	-	✓	-
65	783457	65	4	-	-	-	✓	-	F	NO	✓	NO	✓	43	22	3	-	-	✓	✓	✓	86	89	166/88	128/68	1.56	88	36.21	5	-	-	-	-	✓	-	88	96	0.91	P	218	162	280	7.9	1	✓	-	-	P	-	-	✓	236	2	-	✓	210	3	-	-	✓	160	3	-	-	✓	-	34	1	✓	-	-
66	783461	63	4	-	-	-	✓	-	F	✓	NO	NO	✓	48	18	3	-	-	✓	NO	✓	62	73	148/88	140/80	1.61	103	40	6	-	-	-	-	-	✓	106	119	0.89	A	246	199	256	7.4	1	✓	-	-	A	✓	-	-	188	1	✓	-	178	2	-	✓	-	118	2	-	✓	-	-	34	1	✓	-	-
67	783492	53	3	-	-	✓	-	-	M	NO	✓	NO	✓	46	7	1	✓	-	-	✓	NO	89	96	156/86	150/90	1.63	68	25.6	3	-	-	✓	-	-	-	72	89	0.8	A	253	145	266	10.2	3	-	-	✓	A	✓	-	-	250	2	-	✓	238	3	-	-	✓	154	3	-	-	✓	-	48	2	-	✓	-
68	783524	51	3	-	-	✓	-	-	M	✓	✓	N	Y	36	15	2	-	✓	-	✓	NO	76	82	136/82	122/76	1.86	131	38	5	-	-	-	-	✓	-	112	118	0.94	P	248	152	287	9.7	2	-	✓	-	P	-	-	✓	228	2	-	✓	182	2	-	✓	-	151	3	-	-	✓	-	40	2	-	✓	-
69	783568	65	4	-	-	-	✓	-	F	✓	✓	NO	NO	52	13	2	-	✓	-	✓	✓	69	75	169/92	160/90	1.63	80	30.2	4	-	-	-	✓	-	-	82	90	0.91	A	224	146	246	9.8	2	-	✓	-	A	✓	-	-	210	2	-	✓	216	3	-	-	✓	118	2	-	✓	-	-	48	2	-	✓	-
70	783573	61	4	-	-	-	✓	-	F	NO	NO	NO	NO	46	15	2	-	✓	-	✓	✓	76	87	132/80	130/80	1.63	76	28.8	3	-	-	✓	-	-	-	82	89	0.92	A	212	142	233	9.3	2	-	✓	-	A	✓	-	-	188	1	✓	-	209	3	-	-	✓	86	1	✓	-	-	-	60	2	-	✓	-
71	783607	69	4	-	-	-	✓	-	M	NO	NO	NO	✓	52	17	3	-	-	✓	✓	NO	77	89	132/86	126/80	1.68	82	29.2	3	-	-	✓	-	-	-	78	89	0.87	A	233	154	236	8.4	2	-	✓	-	A	✓	-	-	188	1	✓	-	156	2	-	✓	-	112	2	-	✓	-	-	44	2	-	✓	-
72	783645	43	2	-	✓	-	-	-	M	NO	NO	NO	NO	35	8	1	✓	-	-	✓	NO	78	96	146/86	138/80	1.82	105	31.8	4	-	-	-	✓	-	-	92	97	0.94	A	280	164	254	9.2	2	-	✓	-	P	-	✓	-	216	2	-	✓	176	2	-	✓	-	136	3	-	-	✓	-	44	2	-	✓	-
73	783697	63	4	-	-	-	✓	-	F	NO	NO	NO	✓	56	7	1	✓	-	-	✓	NO	69	82	146/86	140/80	1.65	72	26.6	3	-	-	✓	-	-	-	73	89	0.82	A	249	156	240	6.9	1	✓	-	-	A	✓	-	-	192	1	✓	-	166	2	-	✓	-	122	2	-	✓	-	-	36	1	✓	-	-
74	783728	54	3	-	-	✓	-	-	F	✓	NO	NO	NO	42	12	2	-	✓	-	NO	✓	65	76	158/92	150/90	1.73	70	23.7	2	-	✓	-	-	-	-	73	86	0.84	A	249	134	246	8.6	2	-	✓	-	A	✓	-	-	188	1	✓	-	160	2	-	✓	-	108	2	-	✓	-	-	48	2	-	✓	-
75	783762	68	4	-	-	-	✓	-	M	✓	NO	NO	✓	50	18	3	-	-	✓	✓	✓	76	92	126/76	120/70	1.59	67	26.8	3	-	-	✓	-	-	-	69	79	0.82	A	223	159	239	8.9	2	-	✓	-	A	✓	-	-	216	2	-	✓	200	2	-	✓	-	130	3	-	-	✓	-	46	2	-	✓	-
76	783781	51	3	-	-	✓	-	-	F	✓	NO	NO	✓	39	12	2	-	✓	-	✓	NO	82	89	158/90	130/70	1.49	54	24.6	2	-	✓	-	-	-	-	76	89	0.85	P	280	196	268	9.2	2	-	✓	-	P	-	-	✓	182	1	✓	-	154	2	-	✓	-	103	2	-	✓	-	-	48	2	-	✓	-
77	783864	63	4	-	-	-	✓	-	M	NO	✓	NO	✓	53	10	2	-	✓	-	✓	NO	74	89	128/80	120/76	1.71	63	21.6	2	-	✓	-	-	-	-	61	79	0.77	A	234	149	245	9.3	2	-	✓	-	A	✓	-	-	188	1	✓	-	160	2	-	✓	-	118	2	-	✓	-	-	38	1	✓	-	-
78	783883	57	3	-	-	✓	-	-	F	NO	✓	NO	✓	38	19	3	-	-	✓	NO	✓	67	72	196/86	190/80	1.61	75	29.6	3	-	-	✓	-	-	-	84	96	0.87	A	267	166	279	8.6	2	-	✓	-	A	✓	-	-	176	1	✓	-	170	2	-	✓	-	106	2	-	✓	-	-	36	1	✓	-	-
79	783931	49	2	-	✓	-	-	-	F	NO	NO	NO	NO	36	13	2	-	✓	-	✓	✓	82	96	130/80	126/80	1.66	114	41.6	6	-	-	-	-	-	✓	104	109	0.95	A	218	130	266	9.2	2	-	✓	-	P	-	-	✓	228	2	-	✓	216	3	-	-	✓	152	3	-	-	✓	-	32	1	✓	-	-
80	783957	73	5	-	-	-	-	✓	F	✓	NO	NO	✓	54	19	3	-	-	✓	NO	✓	75	86	136/86	130/80	1.72	75	25.6	3	-	-	✓	-	-	-	68	82	0.8	A	269	169	271	8.6	2	-	✓	-	A	✓	-	-	224	2	-	✓	210	3	-	-	✓	140	3	-	-	✓	-	42	2	-	✓	-
81	783983	52	3	-	-	✓	-	-	M	✓	✓	✓	✓	46	6	1	✓	-	-	✓	NO	75	88	162/92	156/90	1.66	82	29.8	3	-	-	✓	-	-	-	75	84	0.89	A	239	144	228	7.6	1	✓	-	-	A	✓	-	-	198	1	✓	-	152	2	-	✓	-	134	3	-	-	✓	-	33	1	✓	-	-
82	784158	79	5	-	-	-	-	✓	M	NO	NO	NO	NO	72	7	1	✓	-	-	✓	NO	76	88	110/70	100/68	1.76	55	17.5	1	✓	-	-	-	-	-	76	86	0.88	A	218	210	236	7.8	1	✓	-	-	P	-	-	✓	182	1	✓	-	136	1	✓	-	-	92.8	1	✓	-	-	-	62	3	-	-	✓
83	784269	62	4	-	-	-	✓	-	F	NO	✓	NO	✓	51	11	2	-	✓	-	✓	NO	67	73	152/82	150/80	1.62	81	31.2	4	-	-	-	✓	-	-	86	91	0.94	A	226	145	258	11.2	3	-	-	✓	A	✓	-	-	188	1	✓	-	172	2	-	✓	-	106	2	-	✓	-	-	47	2	-	✓	-
84	784371	53	3	-	-	✓	-	-	M	✓	NO	NO	✓	44	9	1	✓	-	-	✓	NO	71	82	192/98	180/90	1.59	91	36	5	-	-	-	-	✓	-	101	113	0.89	A	286	159	292	9.6	2	-	✓	-	A	✓	-	-	230	2	-	✓	198	2	-	✓	-	142	3	-	-	✓	-	48	2	-	✓	-
85	784456	75	5	-	-	-	-	✓	F	✓	NO	NO	✓	53	22	3	-	-	✓	NO	✓	87	89	156/88	130/66	1.58	105	42.2	6	-	-	-	-	-	✓	96	99	0.96	P	312	222	326	13.5	3	-	-	✓	P	-	-	✓	228	2	-	✓	210	3	-	-	✓	140	3	-	-	✓	-	46	2	-	✓	-
86	784587	62	4	-	-	-	✓	-	M	✓	✓	NO	✓	53	9	1	✓	-	-	✓	NO	70	83	158/96	150/90	190	87	24.2	2	-	✓	-	-	-	-	88	99	0.88	A	251	154	242	7.8	1	✓	-	-	A	✓	-	-	188	1	✓	-	165	2	-	✓	-	121	2	-	✓	-	-	34	1	✓	-	-
87	784612	60	4	-	-	-	✓	-	F	✓	✓	NO	NO	44	16	3	-	-	✓	NO	✓	88	99	152/88	150/80	1.68	64	22.8	2	-	✓	-	-	-	-	64	76	0.84	A	216	157	256	11.4	3	-	-	✓	A	✓	-	-	224	2	-	✓	210	3	-	-	✓	136	3	-	-	✓	-	46	2	-	✓	-
88	784789	78	5	-	-	-	-	✓	F	NO	✓	NO	NO	45	33	3	-	-	✓	NO	✓	78	80	126/88	106/70	1.62	67	29	3	-	-	✓	-	-	-	92	94	0.97	P	190	146	198	7.8	1	✓	-	-	P	-	-	✓	204	2	-	✓	280	3	-	-	✓	120	2	-	✓	-	-	20	1	✓	-	-
89	784825	63	4	-	-	-	✓	-	F	NO	✓	NO	NO	50	13	2	-	✓	-	✓	NO	76	89	158/86	150/90	1.73	73	24.5	2	-	✓	-	-	-	-	78	89	0.87	A	233	147	246	8.7	2	-	✓	-	A	✓	-	-	226	2	-	✓	192	2	-	✓	-	133	3	-	-	✓	-	54	2	-	✓	-
90	784938	58	3	-	-	✓	-	-	F	NO	NO	NO	NO	50	8	1	✓	-	-	✓	NO	92	94	150/90	132/82	1.61	70	26.8	3	-	-	✓	-	-	-	92	96	0.95	A	156	138	180	6.5	1	✓	-	-	P	-	-	✓	176	1	✓	-	162	2	-	✓	-	128	2	-	✓	-	-	48	2	-	✓	-
91	785158	56	3	-	-	✓	-	-	M	NO	✓	NO	NO	38	18	3	-	-	✓	✓	NO	74	84	156/92	150/90	1.69	67	23.6	2	-	✓	-	-	-	-	72	88	0.81	A	223	138	262	9.2	2	-	✓	-	A	✓	-	-	228	2	-	✓	178	2	-	✓	-	146	3	-	-	✓	-	46	2	-	✓	-
92	785375	59	3	-	-	✓	-	-	F	NO	NO	NO	NO	44	15	2	-	✓	-	NO	✓	96	98	150/90	146/86	1.72	66.8	22.6	2	-	✓	-	-	-	-	72	89	0.8	A	226	182	244	9.8	2	-	✓	-	A	✓	-	-	206	2	-	✓	202	3	-	-	✓	117	2	-	✓	-	-	48	2	-	✓	-
93	785568	47	2	-	✓	-	-	-	F	NO	✓	NO	NO	36	11	2	-	✓	-	✓	NO	68	88	136/86	130/80	1.59	101	40.2	6	-	-	-	-	-	✓	99	98	1.01	A	226	180	260	8.8	2	-	✓	-	P	-	-	✓	219	2	-	✓	176	2	-	✓	-	135	3	-	-	✓	-	48	2	-	✓	-
94	785794	59	3	-	-	✓	-	-	F	NO	✓	NO	✓	50	9	1	✓	-	-	NO	✓	65	75	148/96	140/90	1.61	85	32.8	4	-	-	-	✓	-	-	88	94	0.93	A	228	144	264	10.8	3	-	-	✓	A	✓	-	-	180	1	✓	-	198	2	-	✓	-	99	1	✓	-	-	-	41	2	-	✓	-
95	785924	52	3	-	-	✓	-	-	M	NO	NO	NO	NO	39	13	2	-	✓	-	NO	✓	76	88	166/100	160/90	1.7	86	29.8	3	-	-	✓	-	-	-	72	79	0.91	A	228	147	261	8.2	2	-	✓	-	A	✓	-	-	178	1	✓	-	210	3	-	-	✓	97	1	✓	-	-	-	39	1	✓	-	-
96	786258	52	3	-	-	✓	-	-	M	✓	✓	NO	NO	40	12	2	-	✓	-	✓	NO	96	98	140/90	120/70	1.72	83	28.2	3	-	-	✓	-	-	-	88	89	0.98	P	212	196	246	7.2	1	✓	-	-	P	-	-	✓	212	2	-	✓	173	2	-	✓	-	156	3	-	-	✓	-	21	1	✓	-	-
97	786589	62	4	-	-	-	✓	-	F	NO	NO	NO	✓	46	16	3	-	-	✓	✓	NO	68	80	160/90	156/86	1.63	71	26.8	3	-	-	✓	-	-	-	66	86	0.76	A	246	137	257	7.6	1	✓	-	-	A	✓	-	-	167	1	✓	-	132	1	✓	-	-	103	2	-	✓	-	-	37	1	✓	-	-
98	786864	48	2	-	✓	-	-	-	M	Y	Y	NO	Y	32	16	3	-	-	✓	✓	✓	88	92	140/90	120/80	1.79	108	33.8	4	-	-	-	✓	-	-	98	103	0.95	P	246	129	218	12.6	3	-	-	✓	P	-	-	✓	310	2	-	✓	258	3	-	-	✓	228	4	-	-	-	✓	30	1	✓	-	-
99	786934	60	4	-	-	-	✓	-	M	✓	NO	NO	✓	46	14	2	-	✓	-	NO	✓	92	96	136/80	110/68	1.59	93	36.8	5	-	-	-	-	✓	-	99	104	0.95	P	287	156	216	8.8	2	-	✓	-	P	-	-	✓	208	2	-	✓	190	2	-	✓	-	128	2	-	✓	-	-	42	2	-	✓	-
100	787258	58	3	-	-	✓	-	-	M	✓	✓	NO	✓	40	18	3	-	-	✓	✓	✓	66	69	156/88	110/70	1.52	51.7	22.4	2	-	✓	-	-	-	-	68	78	0.87	P	218	146	226	9.2	2	-	✓	-	A	✓	-	-	166	1	✓	-	180	2	-	✓	-	84	1	✓	-	-	-	46	2	-	✓	-
101	787648	56	3	-	-	✓	-	-	F	NO	✓	NO	✓	49	7	1	✓	-	-	✓	✓	73	82	136/86	130/80	1.69	73	25.9	3	-	-	✓	-	-	-	69	78	0.88	A	232	151	243	7.9	1	✓	-	-	A	✓	-	-	196	1	✓	-	170	2	-	✓	-	114	2	-	✓	-	-	48	2	-	✓	-
102	787982	53	3	-	-	✓	-	-	F	NO	✓	NO	✓	38	15	2	-	✓	-	NO	✓	64	71	136/86	136/80	1.59	93	36.8	5	-	-	-	-	✓	-	89	91	0.97	A	234	143	258	12.8	3	-	-	✓	A	✓	-	-	190	1	✓	-	182	2	-	✓	-	111	2	-	✓	-	-	42	2	-	✓	-
103	788357	57	3	-	-	✓	-	-	F	✓	✓	NO	NO	44	13	2	-	✓	-	✓	NO	76	84	136/80	110/70	1.58	92	37.2	5	-	-	-	-	✓	-	103	106	0.97	P	216	138	230	7.5	1	✓	-	-	P	-	-	✓	235	2	-	✓	188	2	-	✓	-	145	3	-	-	✓	-	52	2	-	✓	-

				Age groups						History												Examination																
																	Groups of duration of diabetes			Treatment history		Pulse (/min)		Blood Pressure (mmHg)						BMI Groups								
Case number	IP no.	Age (years)	Age groups	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	Sex	Giddiness	Tingling numbness in limbs	Pain abdomen	Excess/Absence of sweating	Age of onset of diabetes (Years)	Duration of diabetes (Years)	Duration Groups	5-9 years	10-15 years	>15 years	Oral drugs	Insulin	Supine	Standing	Supine	Standing	Height (m)	Weight (kg)	BMI (kg/m2)	BMI Groups	16-18.4 (kg/m2)	18.5-24.9 (kg/m2)	25-29.9 (kg/m2)	30-34.9 (kg/m2)	35-39.9 (kg/m2)	≥40 (kg/m2)	Waist circumference (cm)	Hip circumference (cm)	Waist to Hip Ratio
104	788675	56	3	-	-	✓	-	-	F	✓	NO	NO	NO	43	13	2	-	✓	-	✓	✓	64	75	146/86	140/80	1.69	62	21.8	2	-	✓	-	-	-	-	71	89	0.79
105	788835	51	3	-	-	✓	-	-	F	NO	✓	NO	✓	45	6	1	✓	-	-	✓	NO	87	98	136/86	130/80	1.69	63	22.4	2	-	✓	-	-	-	-	64	79	0.81
106	789456	47	2	-	✓	-	-	-	F	NO	NO	NO	NO	38	9	1	✓	-	-	✓	NO	92	98	132/82	126/76	1.76	84	27.4	3	-	-	✓	-	-	-	86	94	0.91
107	789682	51	3	-	-	✓	-	-	F	✓	✓	NO	✓	38	13	2	-	✓	-	✓	NO	71	84	110/70	100/76	1.71	80	27.4	3	-	-	✓	-	-	-	71	88	0.8
108	789739	59	3	-	-	✓	-	-	M	✓	✓	NO	✓	51	8	1	✓	-	-	✓	✓	86	89	140/90	116/76	1.69	60	21.3	2	-	✓	-	-	-	-	83	86	0.93
109	793459	57	3	-	-	✓	-	-	M	✓	NO	✓	NO	51	6	1	✓	-	-	NO	✓	74	88	148/86	140/90	1.68	82	29.2	3	-	-	✓	-	-	-	70	89	0.78
110	794569	48	2	-	✓	-	-	-	M	✓	NO	NO	✓	39	9	1	✓	-	-	✓	NO	70	82	110/70	100/70	1.67	81	29.4	3	-	-	✓	-	-	-	65	82	0.79
111	795864	50	3	-	-	✓	-	-	M	NO	NO	NO	NO	37	13	2	-	✓	-	NO	✓	76	88	136/86	128/80	1.59	81	32.2	4	-	-	-	✓	-	-	96	99	0.96
112	798634	60	4	-	-	-	✓	-	F	✓	NO	NO	✓	43	17	3	-	-	✓	NO	✓	64	75	156/86	150/80	1.67	88	31.6	4	-	-	-	✓	-	-	94	109	0.86
113	799658	53	3	-	-	✓	-	-	M	NO	NO	NO	NO	40	13	2	-	✓	-	NO	✓	72	80	130/70	126/72	1.79	89	27.8	3	-	-	✓	-	-	-	82	96	0.85
114	799965	66	4	-	-	-	✓	-	M	✓	✓	N	✓	43	23	3	-	-	✓	✓	✓	106	109	110/70	96/80	1.58	105	42.3	6	-	-	-	-	-	✓	118	106	1.11
115	800697	58	3	-	-	✓	-	-	F	✓	NO	NO	NO	49	9	1	✓	-	-	✓	NO	72	86	148/98	140/90	1.68	80	28.6	3	-	-	✓	-	-	-	69	81	0.85
116	803647	63	4	-	-	-	✓	-	M	✓	✓	NO	NO	45	18	3	-	-	✓	NO	✓	72	83	156/86	150/80	1.72	84	28.6	3	-	-	✓	-	-	-	82	99	0.82
117	806789	63	4	-	-	-	✓	-	F	✓	NO	NO	✓	40	23	3	-	-	✓	✓	NO	68	69	118/70	96/60	1.68	82	29.1	3	-	-	✓	-	-	-	96	100	0.96
118	807962	56	3	-	-	✓	-	-	F	NO	✓	NO	✓	39	17	3	-	-	✓	NO	✓	63	79	156/86	150/80	1.6	88	34.6	4	-	-	-	✓	-	-	89	93	0.95
119	808962	61	4	-	-	-	✓	-	M	NO	NO	NO	✓	52	9	1	✓	-	-	✓	✓	80	96	190/110	180/100	1.68	81	28.9	3	-	-	✓	-	-	-	68	76	0.89
120	809862	43	2	-	✓	-	-	-	F	✓	✓	NO	✓	37	6	1	✓	-	-	✓	NO	86	88	136/86	110/70	1.63	91	34.3	4	-	-	-	✓	-	-	75	86	0.87
121	815687	48	2	-	✓	-	-	-	F	✓	✓	NO	✓	43	5	1	✓	-	-	✓	NO	94	98	140/90	110/70	1.62	74	28.6	3	-	-	✓	-	-	-	88	92	0.95
122	823654	60	4	-	-	-	✓	-	M	✓	NO	✓	NO	45	15	2	-	✓	-	NO	✓	76	89	176/100	170/96	1.61	74	28.6	3	-	-	✓	-	-	-	68	79	0.86
123	836592	52	3	-	-	✓	-	-	F	NO	NO	NO	✓	37	15	2	-	✓	-	NO	✓	82	88	148/76	116/60	1.56	103	42.6	6	-	-	-	-	-	✓	98	92	1.06
124	846935	59	3	-	-	✓	-	-	M	✓	NO	NO	✓	45	14	2	-	✓	-	✓	NO	72	85	158/96	150/90	1.67	83	30.6	4	-	-	-	✓	-	-	82	94	0.88
125	863697	51	3	-	-	✓	-	-	F	✓	NO	NO	NO	43	8	1	✓	-	-	✓	✓	72	85	156/92	150/90	1.71	88	30.2	4	-	-	-	✓	-	-	79	86	0.91
126	863987	48	2	-	✓	-	-	-	M	NO	✓	NO	✓	41	7	1	✓	-	-	✓	NO	91	100	156/96	146/90	1.59	69	27.6	3	-	-	✓	-	-	-	106	110	0.96
127	864068	52	3	-	-	✓	-	-	M	✓	✓	✓	✓	39	13	2	-	✓	-	NO	✓	62	73	110/70	100/60	1.58	97	39.2	5	-	-	-	-	✓	-	90	93	0.96
128	864367	60	4	-	-	-	✓	-	F	✓	NO	NO	✓	50	10	2	-	✓	-	NO	✓	63	74	136/86	130/80	1.63	65	24.6	2	-	✓	-	-	-	-	62	88	0.7
129	864569	69	4	-	-	-	✓	-	M	✓	✓	NO	✓	55	14	2	-	✓	-	✓	✓	92	96	130/86	106/70	1.69	114	40.2	6	-	-	-	-	-	✓	119	109	1.09
130	864736	66	4	-	-	-	✓	-	M	✓	NO	NO	✓	53	13	2	-	✓	-	✓	NO	71	83	126/86	120/80	1.69	76	26.8	3	-	-	✓	-	-	-	67	79	0.82
131	864967	62	4	-	-	-	✓	-	M	✓	NO	NO	NO	40	22	3	-	-	✓	✓	✓	86	89	146/86	100/60	1.61	82	32	4	-	-	-	✓	-	-	79	88	0.89
132	865234	50	3	-	-	✓	-	-	M	NO	NO	NO	NO	42	8	1	✓	-	-	NO	✓	72	84	118/82	112/80	1.69	80	28.2	3	-	-	✓	-	-	-	74	89	0.83
133	865367	52	3	-	-	✓	-	-	M	✓	NO	NO	✓	40	12	2	-	✓	-	✓	✓	106	110	146/90	122/80	1.64	112	41.8	6	-	-	-	-	-	✓	119	107	1.11
134	865452	49	2	-	✓	-	-	-	F	✓	✓	NO	NO	42	7	1	✓	-	-	✓	✓	80	89	156/86	130/70	1.52	73	31.6	4	-	-	-	✓	-	-	80	96	0.83
135	865568	62	4	-	-	-	✓	-	M	✓	NO	NO	✓	40	22	3	-	-	✓	✓	NO	68	79	168/92	160/90	1.57	84	34.2	4	-	-	-	✓	-	-	98	112	0.87
136	865628	58	3	-	-	✓	-	-	M	✓	NO	NO	✓	38	20	3	-	-	✓	NO	✓	96	99	136/86	110/70	1.57	69	28	3	-	-	✓	-	-	-	68	79	0.86
137	865792	69	4	-	-	-	✓	-	F	✓	✓	NO	✓	55	14	2	-	✓	-	✓	✓	78	84	160/90	136/80	1.6	110	43.3	6	-	-	-	-	-	✓	108	102	1.05
138	865927	60	4	-	-	-	✓	-	M	✓	NO	NO	NO	47	13	2	-	✓	-	NO	✓	68	79	138/88	130/80	1.56	71	29.2	3	-	-	✓	-	-	-	73	92	0.79
139	866125	54	3	-	-	✓	-	-	F	NO	✓	NO	✓	42	12	2	-	✓	-	✓	NO	85	99	176/98	170/90	1.66	68	24.8	2	-	✓	-	-	-	-	69	78	0.88
140	866245	50	3	-	-	✓	-	-	M	NO	NO	NO	NO	44	6	1	✓	-	-	✓	NO	86	98	134/86	130/80	1.72	90	30.6	4	-	-	-	✓	-	-	88	94	0.93
141	866385	55	3	-	-	✓	-	-	F	NO	NO	NO	✓	39	16	3	-	-	✓	✓	✓	96	100	142/90	110/70	1.39	74	38.6	5	-	-	-	-	✓	-	87	93	0.93
142	866429	61	4	-	-	-	✓	-	F	✓	NO	NO	NO	44	17	3	-	-	✓	NO	✓	82	94	130/88	110/70	1.6	76.8	30	4	-	-	-	✓	-	-	90	102	0.88
143	866527	50	3	-	-	✓	-	-	M	✓	NO	NO	✓	43	7	1	✓	-	-	✓	NO	81	89	154/94	150/90	1.76	70	22.6	2	-	✓	-	-	-	-	69	76	0.84
144	866628	36	1	✓	-	-	-	-	F	✓	NO	NO	NO	31	5	1	✓	-	-	✓	NO	96	110	110/70	106/70	1.42	78	38.8	5	-	-	-	-	✓	-	102	106	0.96
145	866697	58	3	-	-	✓	-	-	F	✓	✓	NO	NO	43	15	2	-	✓	-	NO	✓	70	79	136/86	130/80	1.65	72	26.8	3	-	-	✓	-	-	-	71	86	0.82
146	866731	44	2	-	✓	-	-	-	F	NO	NO	NO	✓	38	6	1	✓	-	-	✓	NO	71	88	162/92	160/90	1.65	87	32	4	-	-	-	✓	-	-	82	90	0.92
147	866834	45	2	-	✓	-	-	-	M	✓	✓	NO	✓	35	10	2	-	✓	-	✓	NO	76	79	136/86	110/70	1.72	83	28.2	3	-	-	✓	-	-	-	88	89	0.988
148	866934	60	4	-	-	-	✓	-	M	✓	NO	NO	✓	52	8	1	✓	-	-	✓	NO	79	88	150/90	146/86	1.74	73	24.2	2	-	✓	-	-	-	-	65	78	0.83
149	867154	52	3	-	-	✓	-	-	F	NO	NO	NO	✓	41	11	2	-	✓	-	NO	✓	67	79	156/88	150/80	1.56	72	29.7	3	-	-	✓	-	-	-	65	83	0.78
150	867234	54	3	-	-	✓	-	-	M	✓	NO	NO	NO	45	9	1	✓	-	-	✓	NO	70	82	156/60	150/56	1.69	81	28.6	3	-	-	✓	-	-	-	72	89	0.8
151	867456	44	2	-	✓	-	-	-	F	NO	✓	NO	✓	32	12	2	-	✓	-	✓	NO	82	88	166/76	130/60	1.7	82	28.37	3	-	-	✓	-	-	-	92	99	0.92
152	867572	57	3	-	-	✓	-	-	M	NO	NO	NO	NO	46	11	2	-	✓	-	NO	✓	65	75	136/86	130/80	1.53	62	26.8	3	-	-	✓	-	-	-	64	81	0.79
153	867627	56	3	-	-	✓	-	-	F	NO	✓	NO	✓	43	13	2	-	✓	-	✓	NO	96	106	130/80	126/80	1.64	72	26.8	3	-	-	✓	-	-	-	79	89	0.88
154	867736	71	5	-	-	-	-	✓	F	✓	NO	NO	✓	48	23	3	-	-	✓	✓	✓	86	88	138/86	110/70	1.55	66	27.5	3	-	-	✓	-	-	-	70	89	0.78
155	867852	61	4	-	-	-	✓	-	M	✓	NO	NO	✓	47	14	2	-	✓	-	NO	✓	77	89	196/100	190/90	1.71	69	23.9	2	-	✓	-	-	-	-	82	96	0.85

	Examination	Investigations																															
							HbA1c Groups			Gallstones		Present				Cholesterol groups				Triglycerides groups					LDL groups						HDL groups		
Case number	Diabetic Autonomic Neuropathy	Random Blood Sugar (mg/dl)	Fasting blood sugar (mg/dl)	Post-prandial Blood Sugar (mg/dl)	HbA1c (%)	HbA1c Groups	6.5-7.9 (%)	08 to 9.9 (%)	≥10 (%)		Absent	Solitary	Multiple	Total Cholesterol (mg/dl)	Total Cholesterol Group	<200 mg/dl	≥200 mg/dl	Triglycerides (mg/dl)	Triglycerides Groups	<150 mg/dl	150-200 mg/dl	>200 mg/dl	LDL (mg/dl)	LDL Groups	<100 mg/dl	100-129 mg/dl	130-160 mg/dl	>160 mg/dl	HDL (mg/dl)	HDL Groups	<40 mg/dl	40-60 mg/dl	>60 mg/dl
104	A	250	133	246	7.6	1	✓	-	-	A	✓	-	-	187	1	✓	-	152	2	-	✓	-	109	2	-	✓	-	-	47	2	-	✓	-
105	A	216	155	239	9.8	2	-	✓	-	A	✓	-	-	266	2	-	✓	184	2	-	✓	-	107	2	-	✓	-	-	40	2	-	✓	-
106	A	248	183	290	10.6	3	-	-	✓	A	✓	-	-	168	1	✓	-	186	2	-	✓	-	82	1	✓	-	-	-	48	2	-	✓	-
107	A	253	152	244	7.6	1	✓	-	-	A	✓	-	-	210	2	-	✓	168	2	-	✓	-	138	3	-	-	✓	-	38	1	✓	-	-
108	P	206	130	218	6.8	1	✓	-	-	P	-	-	✓	146	1	✓	-	140	1	✓	-	-	52	1	✓	-	-	-	66	3	-	-	✓
109	A	259	177	263	9.2	2	-	✓	-	A	✓	-	-	216	2	-	✓	187	2	-	✓	-	126	2	-	✓	-	-	52	2	-	✓	-
110	A	244	139	237	7.3	1	✓	-	-	A	✓	-	-	188	1	✓	-	235	3	-	-	✓	102	2	-	✓	-	-	39	1	✓	-	-
111	A	258	186	246	12.2	3	-	-	✓	P	-	-	✓	260	2	-	✓	248	3	-	-	✓	172	4	-	-	-	✓	38	1	✓	-	-
112	A	266	179	274	8.2	2	-	✓	-	A	✓	-	-	196	1	✓	-	210	3	-	-	✓	112	2	-	✓	-	-	42	2	-	✓	-
113	A	232	186	269	10.2	3	-	-	✓	A	✓	-	-	188	1	✓	-	150	2	-	✓	-	100	2	-	✓	-	-	58	2	-	✓	-
114	P	356	222	380	14.6	3	-	-	✓	P	-	-	✓	312	2	-	✓	260	3	-	-	✓	226	4	-	-	-	✓	34	1	✓	-	-
115	A	259	133	286	6.9	1	✓	-	-	A	✓	-	-	250	2	-	✓	190	2	-	✓	-	164	4	-	-	-	✓	48	2	-	✓	-
116	A	283	177	298	9.4	2	-	✓	-	A	✓	-	-	192	1	✓	-	210	3	-	-	✓	106	2	-	✓	-	-	44	2	-	✓	-
117	P	222	136	280	6.6	1	✓	-	-	P	-	-	✓	276	2	-	✓	215	3	-	-	✓	201	4	-	-	-	✓	32	1	✓	-	-
118	A	236	142	248	11.6	3	-	-	✓	A	✓	-	-	170	1	✓	-	192	2	-	✓	-	96	1	✓	-	-	-	35	1	✓	-	-
119	A	245	137	270	7.8	1	✓	-	-	A	✓	-	-	199	1	✓	-	187	2	-	✓	-	122	2	-	✓	-	-	39	1	✓	-	-
120	P	228	142	238	8.9	2	-	✓	-	A	✓	-	-	140	1	✓	-	132	1	✓	-	-	61	1	✓	-	-	-	52	2	-	✓	-
121	P	198	148	210	7.9	1	✓	-	-	P	-	-	✓	106	1	✓	-	147	1	✓	-	-	65	1	✓	-	-	-	62	3	-	-	✓
122	A	238	145	226	7.9	1	✓	-	-	A	✓	-	-	200	2	-	✓	162	2	-	✓	-	131	3	-	-	✓	-	36	1	✓	-	-
123	P	286	210	292	12.6	3	-	-	✓	P	-	-	✓	280	2	-	✓	256	3	-	-	✓	176	4	-	-	-	✓	52	2	-	✓	-
124	A	230	153	241	10.2	3	-	-	✓	A	✓	-	-	206	2	-	✓	154	2	-	✓	-	119	2	-	✓	-	-	56	2	-	✓	-
125	A	289	149	256	9.4	2	-	✓	-	A	✓	-	-	188	1	✓	-	149	1	✓	-	-	109	2	-	✓	-	-	49	2	-	✓	-
126	A	218	146	229	10.2	3	-	-	✓	A	✓	-	-	196	1	✓	-	176	2	-	✓	-	118	2	-	✓	-	-	42	2	-	✓	-
127	A	238	141	268	12.3	3	-	-	✓	A	✓	-	-	175	1	✓	-	168	2	-	✓	-	103	2	-	✓	-	-	38	1	✓	-	-
128	A	251	132	253	6.8	1	✓	-	-	A	✓	-	-	186	1	✓	-	140	1	✓	-	-	112	2	-	✓	-	-	46	2	-	✓	-
129	P	312	218	326	7.9	1	✓	-	-	P	-	-	✓	152	1	✓	-	178	2	-	✓	-	64	1	✓	-	-	-	52	2	-	✓	-
130	A	243	140	238	9.3	2	-	✓	-	A	✓	-	-	192	1	✓	-	216	3	-	-	✓	113	2	-	✓	-	-	35	1	✓	-	-
131	P	210	130	222	7.4	1	✓	-	-	A	✓	-	-	206	2	-	✓	178	2	-	✓	-	128	2	-	✓	-	-	36	1	✓	-	-
132	A	255	148	246	9.2	2	-	✓	-	A	✓	-	-	216	2	-	✓	156	2	-	✓	-	142	3	-	-	✓	-	42	2	-	✓	-
133	P	216	168	238	9.6	2	-	✓	-	P	-	-	✓	280	2	-	✓	210	3	-	-	✓	196	4	-	-	-	✓	42	2	-	✓	-
134	P	242	198	268	11.2	3	-	-	✓	A	✓	-	-	136	1	✓	-	140	1	✓	-	-	60	1	✓	-	-	-	48	2	-	✓	-
135	A	276	169	284	9.2	2	-	✓	-	A	✓	-	-	188	1	✓	-	190	2	-	✓	-	104	2	-	✓	-	-	46	2	-	✓	-
136	P	210	140	236	7.2	1	✓	-	-	A	✓	-	-	201	2	-	✓	180	2	-	✓	-	133	3	-	-	✓	-	32	1	✓	-	-
137	P	238	160	300	7.8	1	✓	-	-	P	-	-	✓	242	2	-	✓	212	3	-	-	✓	177	4	-	-	-	✓	22	1	✓	-	-
138	A	249	200	269	7.9	1	✓	-	-	A	✓	-	-	176	1	✓	-	150	2	-	✓	-	92	1	✓	-	-	-	54	2	-	✓	-
139	A	247	186	257	7.9	1	✓	-	-	A	✓	-	-	236	2	-	✓	216	3	-	-	✓	150	3	-	-	✓	-	42	2	-	✓	-
140	A	242	154	256	6.9	1	✓	-	-	A	✓	-	-	178	1	✓	-	196	2	-	✓	-	96	1	✓	-	-	-	42	2	-	✓	-
141	P	260	186	278	11.6	3	-	-	✓	P	-	-	✓	218	2	-	✓	226	3	-	-	✓	124	2	-	✓	-	-	48	2	-	✓	-
142	P	252	142	272	11.2	3	-	-	✓	A	✓	-	-	178	1	✓	-	166	2	-	✓	-	92	1	✓	-	-	-	52	2	-	✓	-
143	A	213	159	246	7.2	1	✓	-	-	A	✓	-	-	178	1	✓	-	156	2	-	✓	-	108	2	-	✓	-	-	38	1	✓	-	-
144	A	245	162	266	11.6	3	-	-	✓	P	-	-	✓	278	2	-	✓	250	3	-	-	✓	202	4	-	-	-	✓	26	1	✓	-	-
145	A	222	148	268	9.6	2	-	✓	-	A	✓	-	-	199	1	✓	-	180	2	-	✓	-	130	3	-	-	✓	-	33	1	✓	-	-
146	A	228	155	233	10.4	3	-	-	✓	A	✓	-	-	224	2	-	✓	176	2	-	✓	-	134	3	-	-	✓	-	54	2	-	✓	-
147	P	238	160	240	10.2	3	-	-	✓	P	-	✓	-	238	2	-	✓	228	3	-	-	✓	134	3	-	-	✓	-	58	2	-	✓	-
148	A	217	157	232	9.5	2	-	✓	-	A	✓	-	-	252	2	-	✓	162	2	-	✓	-	183	4	-	-	-	✓	36	1	✓	-	-
149	A	247	136	256	10.6	3	-	-	✓	A	✓	-	-	156	1	✓	-	186	2	-	✓	-	68	1	✓	-	-	-	50	2	-	✓	-
150	A	239	134	242	10.2	3	-	-	✓	A	✓	-	-	190	1	✓	-	170	2	-	✓	-	116	2	-	✓	-	-	40	2	-	✓	-
151	P	222	133	266	9.2	2	-	✓	-	P	-	-	✓	168	1	✓	-	154	2	-	✓	-	95	1	✓	-	-	-	42	2	-	✓	-
152	A	222	161	231	8.8	2	-	✓	-	A	✓	-	-	194	1	✓	-	176	2	-	✓	-	106	2	-	✓	-	-	52	2	-	✓	-
153	A	218	148	237	9.8	2	-	✓	-	A	✓	-	-	216	2	-	✓	176	2	-	✓	-	108	2	-	✓	-	-	48	2	-	✓	-
154	P	218	148	259	11.6	3	-	-	✓	A	✓	-	-	178	1	✓	-	158	2	-	✓	-	106	2	-	✓	-	-	46	2	-	✓	-
155	A	225	154	239	7.9	1	✓	-	-	A	✓	-	-	192	1	✓	-	162	2	-	✓	-	128	2	-	✓	-	-	30	1	✓	-	-

Case number	IP no.	Age (years)	Age groups	Age groups: 30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	Sex	History: Giddiness	Tingling numbness in limbs	Pain abdomen	Excess/Absence of sweating	Age of onset of diabetes (Years)	Duration of diabetes (Years)	Duration Groups	Groups of duration of diabetes: 5-9 years	10-15 years	>15 years	Treatment history: Oral drugs	Insulin	Examination: Pulse (/min) Supine	Pulse (/min) Standing	Blood Pressure (mmHg) Supine	Blood Pressure (mmHg) Standing	Height (m)	Weight (kg)	BMI (kg/m2)	BMI Groups	BMI Groups: 16-18.4 (kg/m2)	18.5-24.9 (kg/m2)	25-29.9 (kg/m2)	30-34.9 (kg/m2)	35-39.9 (kg/m2)	≥40 (kg/m2)	Waist circumference (cm)	Hip circumference (cm)	Waist to Hip Ratio	Diabetic Autonomic Neuropathy	Investigations: Random Blood Sugar (mg/dl)	Fasting blood sugar (mg/dl)	Post-prandial Blood Sugar (mg/dl)	HbA1c (%)	HbA1c Groups	HbA1c Groups: 6.5-7.9 (%)	08 to 9.9 (%)	≥10 (%)	Gallstones	Gallstones: Absent	Present: Solitary	Present: Multiple	Total Cholesterol (mg/dl)	Total Cholesterol Group	Cholesterol groups: <200 mg/dl	≥200 mg/dl	Triglycerides (mg/dl)	Triglycerides Groups	Triglycerides groups: <150 mg/dl	150-200 mg/dl	>200 mg/dl	LDL (mg/dl)	LDL Groups	LDL groups: <100 mg/dl	100-129 mg/dl	130-160 mg/dl	>160 mg/dl	HDL (mg/dl)	HDL Groups	HDL groups: <40 mg/dl	40-60 mg/dl	>60 mg/dl
156	867935	47	2	-	✓	-	-	-	M	✓	NO	NO	✓	32	15	2	-	✓	-	NO	✓	82	88	160/100	136/70	1.79	131	41.1	6	-	-	-	-	-	✓	116	111	1.04	P	252	160	286	9.8	2	-	✓	-	**P**	-	-	✓	276	2	-	✓	256	3	-	-	✓	188	4	-	-	-	✓	36	1	✓	-	-
157	868034	68	4	-	-	-	✓	-	F	✓	NO	NO	NO	51	17	3	-	-	✓	NO	✓	64	75	136/86	130/80	1.72	80	27.2	3	-	-	✓	-	-	-	76	88	0.86	A	239	186	246	7.6	1	✓	-	-	**A**	✓	-	-	188	1	✓	-	162	2	-	✓	-	103	2	-	✓	-	-	52	2	-	✓	-
158	868245	55	3	-	-	✓	-	-	M	NO	NO	NO	NO	43	12	2	-	✓	-	✓	NO	72	88	130/80	124/76	1.66	95	34.6	4	-	-	-	✓	-	-	88	97	0.9	A	236	178	248	7.8	1	✓	-	-	**A**	✓	-	-	176	1	✓	-	196	2	-	✓	-	90	1	✓	-	-	-	46	2	-	✓	-
159	868368	50	3	-	-	✓	-	-	F	✓	NO	NO	✓	38	12	2	-	✓	-	NO	✓	92	99	132/86	110/70	1.62	77.6	29.6	3	-	-	✓	-	-	-	67	92	0.72	P	282	196	296	11.2	3	-	-	✓	**A**	✓	-	-	206	2	-	✓	146	1	✓	-	-	141	3	-	-	✓	-	29	1	✓	-	-
160	868452	38	1	✓	-	-	-	-	F	NO	NO	NO	NO	33	5	1	✓	-	-	NO	✓	86	98	110/70	116/76	1.48	94	43	6	-	-	-	-	-	✓	99	97	1.02	A	262	188	286	10.8	3	-	-	✓	**P**	-	-	✓	280	2	-	✓	268	3	-	-	✓	196	4	-	-	-	✓	30	1	✓	-	-
161	868503	66	4	-	-	-	✓	-	F	NO	✓	NO	✓	46	20	3	-	-	✓	NO	✓	77	89	142/86	140/80	1.76	92	30.6	4	-	-	-	✓	-	-	74	82	0.9	A	256	165	249	9.6	2	-	✓	-	**A**	✓	-	-	216	2	-	✓	210	3	-	-	✓	118	2	-	✓	-	-	56	2	-	✓	-
162	868607	68	4	-	-	-	✓	-	F	NO	✓	NO	✓	54	14	2	-	✓	-	✓	NO	78	86	186/100	140/70	1.48	87	39.8	5	-	-	-	-	✓	-	82	86	0.95	P	280	196	292	11.8	3	-	-	✓	**P**	-	-	✓	228	2	-	✓	214	3	-	-	✓	157	3	-	-	✓	-	28	1	✓	-	-
163	868695	47	2	-	✓	-	-	-	M	✓	✓	NO	NO	39	8	1	✓	-	-	✓	NO	70	79	166/96	160/90	1.71	90	31	4	-	-	-	✓	-	-	82	89	0.93	A	226	157	237	9.8	2	-	✓	-	**A**	✓	-	-	226	2	-	✓	190	2	-	✓	-	150	3	-	-	✓	-	38	1	✓	-	-
164	868786	48	2	-	✓	-	-	-	F	NO	NO	NO	NO	41	7	1	✓	-	-	✓	NO	76	88	134/82	126/80	1.59	81	32.4	4	-	-	-	✓	-	-	79	86	0.91	A	276	201	288	8.9	2	-	✓	-	**A**	✓	-	-	196	1	✓	-	178	2	-	✓	-	108	2	-	✓	-	-	52	2	-	✓	-
165	868834	60	4	-	-	-	✓	-	F	NO	NO	NO	NO	40	20	3	-	-	✓	NO	✓	73	86	162/90	156/86	1.58	65	26.4	3	-	-	✓	-	-	-	62	79	0.78	A	257	148	248	8.8	2	-	✓	-	**A**	✓	-	-	199	1	✓	-	160	2	-	✓	-	121	2	-	✓	-	-	46	2	-	✓	-
166	868920	56	3	-	-	✓	-	-	F	✓	✓	NO	✓	39	17	3	-	-	✓	✓	NO	76	80	136/80	110/68	1.76	80	26	3	-	-	✓	-	-	-	86	89	0.96	P	216	138	240	6.8	1	✓	-	-	**P**	-	-	✓	156	1	✓	-	152	2	-	✓	-	59	1	✓	-	-	-	66	3	-	-	✓
167	869034	51	3	-	-	✓	-	-	M	✓	✓	NO	NO	42	9	1	✓	-	-	✓	NO	82	94	144/90	140/90	1.62	77	29.4	3	-	-	✓	-	-	-	69	76	0.9	A	293	167	299	8.6	2	-	✓	-	**A**	✓	-	-	186	1	✓	-	176	2	-	✓	-	102	2	-	✓	-	-	48	2	-	✓	-
168	869198	62	4	-	-	-	✓	-	M	✓	NO	NO	✓	51	11	2	-	✓	-	✓	NO	72	84	146/96	140/90	1.7	81	28.3	3	-	-	✓	-	-	-	69	76	0.9	A	242	141	250	10.3	3	-	-	✓	**A**	✓	-	-	210	2	-	✓	222	3	-	-	✓	133	3	-	-	✓	-	32	1	✓	-	-
169	869257	53	3	-	-	✓	-	-	M	✓	✓	NO	✓	37	16	3	-	-	✓	NO	✓	92	94	146/86	122/70	1.8	128	39.6	5	-	-	-	-	✓	-	109	116	0.93	P	248	180	256	10.6	3	-	-	✓	**P**	-	-	✓	258	2	-	✓	268	3	-	-	✓	170	4	-	-	-	✓	34	1	✓	-	-
170	869365	62	4	-	-	-	✓	-	M	✓	✓	NO	NO	53	9	1	✓	-	-	✓	NO	67	77	156/88	150/80	1.69	84	29.6	3	-	-	✓	-	-	-	72	89	0.8	A	224	159	235	9.6	2	-	✓	-	**A**	✓	-	-	210	2	-	✓	176	2	-	✓	-	126	2	-	✓	-	-	48	2	-	✓	-
171	869452	58	3	-	-	✓	-	-	M	✓	NO	NO	✓	40	18	3	-	-	✓	✓	NO	86	89	140/90	118/80	1.68	75.5	26.8	3	-	-	✓	-	-	-	92	95	0.96	P	287	200	296	12.2	3	-	-	✓	**P**	-	-	✓	158	1	✓	-	196	2	-	✓	-	54	1	✓	-	-	-	64	3	-	-	✓
172	869528	54	3	-	-	✓	-	-	M	✓	NO	NO	✓	45	9	1	✓	-	-	✓	NO	80	92	148/94	140/90	1.75	71	23.5	2	-	✓	-	-	-	-	64	79	0.81	A	215	158	228	9.4	2	-	✓	-	**A**	✓	-	-	186	1	✓	-	156	2	-	✓	-	112	2	-	✓	-	-	42	2	-	✓	-
173	869610	45	2	-	✓	-	-	-	F	✓	NO	NO	✓	38	7	1	✓	-	-	✓	NO	88	96	138/86	110/70	1.7	92	32	4	-	-	-	✓	-	-	88	96	0.91	P	233	166	256	9.8	2	-	✓	-	**A**	✓	-	-	166	1	✓	-	150	2	-	✓	-	73	1	✓	-	-	-	63	3	-	-	✓
174	869783	60	4	-	-	-	✓	-	M	✓	✓	NO	NO	47	13	2	-	✓	-	✓	NO	68	79	168/100	160/90	1.68	80	28.6	3	-	-	✓	-	-	-	71	89	0.79	A	229	135	234	9.7	2	-	✓	-	**A**	✓	-	-	188	1	✓	-	156	2	-	✓	-	104	2	-	✓	-	-	52	2	-	✓	-
175	869824	52	3	-	-	✓	-	-	F	✓	✓	NO	NO	39	13	2	-	✓	-	✓	NO	76	79	136/80	112/70	1.64	69.6	25.9	3	-	-	✓	-	-	-	72	89	0.8	P	232	176	246	7.8	1	✓	-	-	**A**	✓	-	-	156	1	✓	-	126	1	✓	-	-	100	2	-	✓	-	-	30	1	✓	-	-
176	869913	52	3	-	-	✓	-	-	F	✓	✓	NO	NO	43	9	1	✓	-	-	✓	NO	82	89	136/86	110/70	1.8	72	22.5	2	-	✓	-	-	-	-	86	99	0.86	P	218	170	256	9.8	2	-	✓	-	**A**	✓	-	-	170	1	✓	-	136	1	✓	-	-	96	1	✓	-	-	-	46	2	-	✓	-
177	870003	60	4	-	-	-	✓	-	M	✓	NO	NO	✓	50	10	2	-	✓	-	✓	NO	76	85	182/86	180/80	1.72	64	21.8	2	-	✓	-	-	-	-	68	86	0.79	A	223	155	250	8.2	2	-	✓	-	**A**	✓	-	-	203	2	-	✓	180	2	-	✓	-	132	3	-	-	✓	-	32	1	✓	-	-
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199	871782	63	4	-	-	-	✓	-	M	✓	✓	NO	✓	42	21	3	-	-	✓	✓	✓	82	86	126/80	100/60	1.92	150	40.8	6	-	-	-	-	-	✓	129	119	1.08	P	310	186	282	13.2	3	-	-	✓	**P**	-	-	✓	297	2	-	✓	238	3	-	-	✓	223	4	-	-	-	✓	26	1	✓	-	-
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ANNEXURE-IV

KEY TO MASTER CHART

Age groups:

1---- 30 – 39 years

2 ---- 40 – 49 years

3 ----50 – 59 years

4 ---- 60 – 69 years

5 ---- 70 – 79 years

Duration of Diabetes groups:

1---- 05 – 09 years

2 ----10 – 15 years

3 ---- > 15 years

BMI groups:

1 ---- 16 - 18.4 kg/m^2

2 ---- 18.5-24.9 kg/m^2

3 ---- 25-29.9 kg/m^2

4 ---- 30-34.9 kg/m^2

5 ----- 35-39.9 kg/m^2

6 ---- ≥40 kg/m^2

HbA1c Groups:

1---- 6.5-7.9 %

2 ---- 08 to 9.9 %

3 ---- ≥10 %

Total Cholesterol groups:

1---- < 200 mg/dl

2---- ≥ 200 mg/dl

Triglycerides groups:

1 ---- < 150 mg/dl

2 ---- 150-200 mg/dl

3 ---- > 200 mg/dl

LDL groups:

1 ---- <100 mg/dl

2 ---- 100-129 mg/dl

3 ---- 130-160 mg/dl

4 ---- >160 mg/dl

HDL groups:

1 ---- <40 mg/dl

2 ---- 40-60 mg/dl

3 ---- >60 mg/dl

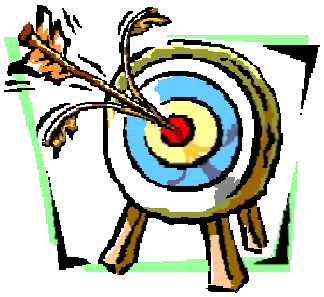
M ---- Male

F ---- Female

A ---- Absent

P ---- Present

Introduction



Objectives

Review of Literature

Methodology

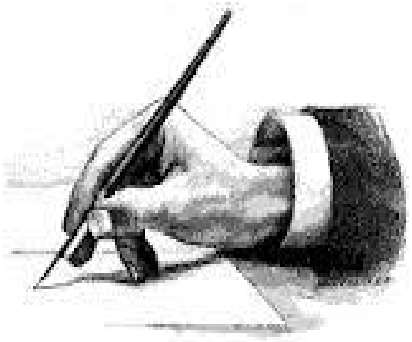
Results

Discussion

Conclusion

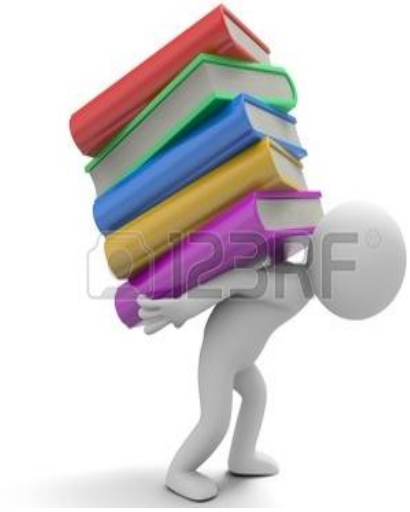
Summary

Bibliography



Annexure-I

Annexure-II



Annexure-III

Annexure-IV