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To study LV mass index and to evaluate the prevalence of LVH, and risk factors for its development, in type 2 DM patients with and without micro-albuminuria

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Abstract:

Diabetesmellitus is a heterogeneous group of diseases characterized by chronic elevation of glucose in the blood, the body is unable to produce enough insulin for its own needs, either because of impaired insulin secretion, impaired insulin action, or both. Diabetes affects around 300 million people world-wide and is increasing exponentially. Chronic exposure to high blood glucose is a leading cause of renal failure, visual loss and a range of other types of tissue damage. Diabetes also predisposes to arterial disease and is often accompanied by hypertension, lipid disorders and obesity. Many cases of diabetes and almost all of its unwanted long-term consequences are potentially avoidable diabetes is associated with cardiac death. LVH is an independent risk factor for cardiac events. Here we are presenting data from study done at Holy Family hospital Mumbai India

Keywords
DIABETES MELLITUS, ALBUMINURIA, LVH, LV MASS, CAD, CHF, MICRO-ALBUMINURIA, CVS

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INTRODUCTION

The prevalence of diabetes mellitus (DM) is increasing globally. It is projected that 366 million people will be diabetic in 2030, 290 million of whom will be living in developing countries.[1] Incidence of diabetes(2010) is 40 million in India alone. Poor glycemic control in these patients results in development of micro and macro vascular complications

which are the cause of death in 75–80% adult diabetics.[2].Cardiovascular complications account for the highest mortality in diabetic patients, mainly due to CAD and CHF. Diabetes is associated with a high prevalence of hypertension, dyslipidemia, and microalbuminuriaa. Even in populations with low cardiovascular risk, diabetes is associated with an increased incidence of cardiovascular death. Left ventricular hypertrophy (LVH), which is a prognostic sign and an independent risk factor for cardiac events, is often present in type 2 DM patients.[3].Left ventricular hypertrophy can itself contribute to increased rates of cardiovascular events, through its effects on ventricular function, coronary circulation and arrhythmogenesis. Available data provide substantial evidence of a consistent and strong relationship between the presence of LVH, either detected by an echocardiogram or an electrocardiogram (ECG), and subsequent cardiovascular morbidity, as well as all-cause mortality [4]. Microalbuminuria a marker of microangiopathy, is an early renal manifestation of diabetes. Persistent hyperglycemia causes hyperfilteration, advanced glycation products and activation of cytokines. All this causes glomerular damage and endothelial dysfunction leading to increased systemic vascular permeability.[5] It modulate the left ventricular mass and metabolism of cardiovascular risk factors like fibrinogen, and Lipoprotein(a).[6]. Therefore, the early identification of patients at risk, with investigation like 2-D echo and urine microalbumin and the subsequent initiation of renal and cardiovascular protective treatments, are of upmost importance. A annual screening of patients with type 2 diabetes mellitus for microalbuminuri and initiation of measures to retard the progression of renal and cardiovascular disease are now considered part of routine clinical practice.

AIMS AND OBJECTIVES: To study LV mass index and evaluate the prevalence of LVH, and risk factors for its development, in type 2 DM patients with and without micro-albuminuria.

1. To study LV mass index in type 2 diabetes mellitus patients.
2. To classify diabetic patients in two groups according to presence or absence of microalbumin in urine.
3. To compare LV mass index in type 2 diabetes mellitus patients with and without microalbuminuria.
4. To correlate LV mass index with duration of diabetes mellitus.
5. To correlate LV mass index with blood sugars [Fasting blood sugar, Post prandial blood Sugar and Glycosylated hemoglobin].
6. To correlate LV mass index with serum cholesterol and HDL level.
7. To correlate microalbuminuria with duration of diabetes mellitus.
8. To correlate microalbuminuria with Blood sugars[Fasting Blood Sugar, Postprandial Blood Sugar and Glycosylated hemoglobin]
9. To correlate microalbuminuria with serum cholesterol and HDL level.

HISTORY OF DIABETES: Diabetes was considered a disease of the wealthy in ancient India, and was known as Madhumeha (sweet urine disease); it was observed that ants were attracted to the urine. The ancient Greeks coined the term "diabetes", meaning excessive urination with dehydration, but neither they nor the Romans appreciated that the urine contained sugar; "diabetes" was considered a kidney disease until the 18th century.[7]. The sweet taste of the urine was known to Avicenna (~1000 AD) and to Thomas Willis in the 17th century. The sweet taste was known to bedue to glucose by the start of the 19th century and raised glucose in the blood was recognized. The modern era was heralded by the discovery of Oskar Minkowski that removal of the pancreas resulted in diabetes, followed by the discovery of insulin in 1921-22.[7]. The herbalists of the middle ages already knew the beneficial effects of the herb Galega officinalis, which ultimately led to the discovery of metformin. Likewise, Claude Bernard with his 'piqûre diabetique' already suspected that the brain was somehow involved in the causation of diabetes, a topic that continues to attract research attention till date. These examples show that many people have made the same observations and considered the same hypotheses at widely differing times and that valuable findings are sometimes obscured by the fogs of time.[7]

EPIDEMIOLOGY: Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million cases currently diagnosed with the disease.[8,9] In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million), United States (17.7 million) in second and third place respectively. According to Wild et al.[1] the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India.[1] It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million)and the United States (30.3 million) will also see significant increase in those affected by the disease.[1,10]. Although the Indian urban population has access to reliable screening methods and anti-diabetic medications, such health benefits are not often available to the rural patients. Food insecurity, illiteracy, poor sanitation, and dominance of communicable diseases may all contribute to this.[11] Such inadequacies contribute to an infrastructure that may result in poor diabetes screening and preventive services, non-adherence to diabetic management guidelines, lack of available counselling, and long distance travel to health services.Rural people suffer more from diabetic complications compared to their urban counterparts.[12]. Obesity is one of the major risk factors for diabetes [13]. Despite having lower overweight and obesity rates, India has a higher prevalence of diabetes compared to western countries suggesting that diabetes may occur at a much lower body mass index (BMI) in Indians compared to the Europeans.[13,14] Therefore, relatively lean Indian adults with a lower BMI may be at equal risk as compared to western counterparts.[15] FurthermoreIndians are genetically predisposed to the development of coronary artery disease due to dyslipidemia and low levels of high density lipoproteins; these determinants make Indians more prone to development of the complications of diabetes at an early age (20-40 years) compared with Caucasians (>50 years) and indicate that diabetes must be carefully screened, monitored and managed regardless of patient's age in Indian population.[16]

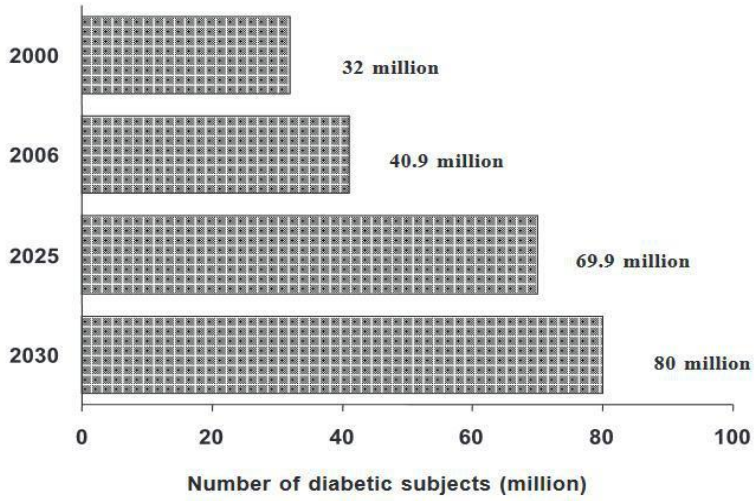

Figure1. Estimated number of diabetic subjects in India [1]

CLASSIFICATION OF DIABETES MELLITUS: Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to beta cell destruction, usually leading to absolute insulin deficiency)

2. Type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin resistance)

3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes)

4. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes

(Such as neonatal diabetes and maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as cystic fibrosis), and drug- or chemical-induced diabetes (such as in the treatment of HIV/AIDS or after organ transplantation). [17]

Table - 1: Criteria for the diagnosis of diabetes[18]:

FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.* or2-h PG ≥ 200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 grams anhydrous glucose dissolved in water [17].*or In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).Recently HbA1C >6.5 %) added as third option.[18].In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

CATEGORIES OF INCREASED RISK FOR DIABETES(PREDIABETES): In 1997 and 2003, the Expert Committee ondiagnosis and classification of diabetes mellitus.[19,20] recognized a group of individuals whose glucose levels did not meet the criteria for diabetes, but were too high to be considered normal. These persons were defined as having impaired fasting glucose (IFG) (FPG levels 100–125 mg/dL [5.6–6.9 mmol/L]) or impaired glucose tolerance (IGT) (2-h PG OGTT values of 140–199 mg/dL [7.8–11.0 mmol/L]). The World Health Organization (WHO) and a number of other diabetes organizations define the cut off for IFG at 110 mg/dL (6.1 mmol/L).“Prediabetes” is the term used for individuals with IFG and/or IGT, indicating the relatively high risk for the future development of diabetes. IFG and IGT should not be viewed as clinical entities in their own right but rather risk factors for diabetes and cardiovascular disease (CVD). IFG and IGT are associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol and hypertension.[19,20]. As with the glucose measures, several prospective studies that used HbA1C to predict the progression to diabetes demonstrated a strong association between HbA1C and subsequent diabetes. In a systematic review of 44,203 individuals from 16 cohort studies with a follow-up interval averaging 5.6 years (range 2.8–12 years), those with an A1C between 5.5 and 6.0% had a substantially increased risk of diabetes (5-year incidences from 9 to 25%). An HbA1C range of 6.0–6.5% had a 5-year risk of developing diabetes between 25–50% and a relative risk (RR) 20 times higher compared with an HbA1C of 5.0%. Hence, it is reasonable to consider an HbA1C range of 5.7–6.4% as identifying individuals with prediabetes. As with those with IFG and IGT, individuals with an HbA1C of 5.7–6.4% should be informed of their increased risk for diabetes and CVD and counseled about effective strategies to lower their risks.[21] Aggressive interventions and vigilant follow-up should be pursued for those considered at very high risk (e.g., those with HbA1Cs >6.0%).

Table2: Categories of increased risk for diabetes (prediabetes)

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL
(11.0mmol/L) (IGT)
OR
HbA1C 5.7–6.4%

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range

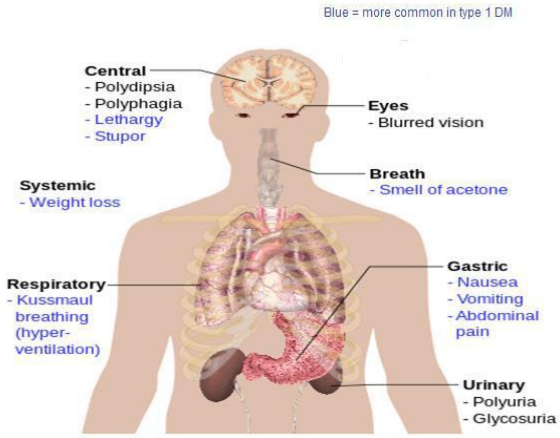

Figure2: Signs and symptoms of diabetes mellitus: The classic symptoms of diabetes are polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger), and weight loss.[22] Other symptoms that are commonly present at diagnosis include a history of blurred vision, itchiness, peripheral neuropathy, recurrent vaginal infections, and fatigue. Many people, however, have no symptoms during the first few years and are diagnosed on routine testing. People with type 2 diabetes mellitus may rarely present with hyperosmolarhyperglycemic state (a condition of very high blood sugar associated with a decreased level of consciousness and low blood pressure).[23]

Table 3 : Complications of diabetes mellitus

Microvascular Eye disease Retinopathy (Non-proliferative/ Proliferative) Macular edema Neuropathy Sensory and Motor (mono and Polyneuropathy) Autonomic Nephropathy (albuminuria and declining renal function) Macrovascular Coronary heart disease Peripheral arterial disease Cerebrovascular disease Other Gastrointestinal (gastroparesis, diarrhea) Genitourinary (uropathy/sexual dysfunction) Dermatologic Infections
Cataracts Glaucoma Cheiro-arthropathy * Periodontal disease Hearing loss Other comorbid conditions associated with diabetes (relationship to hyperglycemia is uncertain): depression, obstructive sleep apnea, fatty liver disease, hip fracture, osteoporosis (in type 1 diabetes), cognitive impairment or dementia, low testosterone in men * Thickened skin and reduced joint mobility.[24]

PREVENTION OR DELAY OF TYPE 2 DIABETES: Patients who are pre-diabetic should be referred to an intensive diet and physical activity behavioral counselling program adhering to the tenets of the Diabetes Prevention Program targeting loss of 7% of body weight and should increase their moderate physical activity (such as brisk

walking) to at least 150 min/week. Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially in those with a BMI >35 kg/m2, those aged <60 years, and women with prior GDM. At least annual screening for the development of diabetes in those with prediabetes is suggested. Screening and treatment of modifiable risk factors for CVD is suggested. [25] Intensive lifestyle modification programs have been shown to be very effective. In addition, pharmacological agents such as metformin, α-glucosidase inhibitors, orlistat and thiazolidinedione's have been shown to decrease incident diabetes to various degrees. Metformin has demonstrated long-term safety as pharmacological therapy for diabetes prevention. [25]

OBESITY MANAGEMENT FOR THE TREATMENT OF TYPE 2 DIABETES: There is strong and consistent evidence that obesity management can delay progression from prediabetes to type 2 diabetes and it also benefits type 2 diabetes treatment. In overweight and obese patients with type 2 diabetes, modest weight loss, defined as sustained reduction of 5% of initial body weight, has been shown to improve glycemic control and triglycerides and to reduce the need for glucose-lowering medication. Sustained weight loss of ≥7% is optimal.

At each patient visit, BMI should be calculated and documented in the medical record. In Asian Americans, the cutoff points to define overweight and obesity are lower: normal (<23 BMI kg/m2), overweight (BMI 23.0–27.4 kg/m2), obese (BMI 27.5–37.4 kg/m2) and extremely obese (BMI ≥37.5 kg/m2). Providers should counsel overweight and obese patients that higher BMI increases the risk of CVD. Providers should assess each patient's readiness to achieve weight loss and jointly determine weight loss goals and intervention strategies. Strategies include diet, physical activity, behavioral therapy, pharmacological therapy and bariatric surgery. The latter two strategies may be prescribed for carefully selected patients as adjuncts to other modalities. [26]

APPROACHES TO GLYCEMIC TREATMENT: Pharmacological Therapy for Type 1 Diabetes: People with type 1 diabetes should betreated with multiple-dose insulin injections (three to four injections per day of basal and prandial insulin) or continuous subcutaneous insulin infusion therapy. Educate individuals with type 1 diabetes on matching prandial insulin doses to carbohydrate intake, pre-meal blood glucose levels and anticipated physical activity.Most individuals with type 1 diabetes should use insulin analogs to reduce hypoglycemia risk. For patients with frequent nocturnal hypoglycemia and/or hypoglycemia unawareness, a sensor-augmented pump with a low glucose threshold feature may be considered. [27].

Pharmacological Therapy for Type 2 Diabetes: Metformin, if not contraindicated and if tolerated, is the preferred initial pharmacological agent for type 2 diabetes. Consider initiating insulin therapy (with or without additional agents) in patients with newly diagnosed type 2 diabetes who are symptomatic and/or have markedly elevated blood glucose levels or HbA1C.

If noninsulin monotherapy at the maximum tolerated dose does not achieve or maintain the HbA1C target over 3 months, then add a second oral agent, a glucagon-like peptide 1 receptor agonist, or basal insulin. A patient-centered approach should be used to guide the choice of pharmacological agents. Considerations include efficacy, cost, potential side effects, weight, comorbidities, and hypoglycemia risk and patient preferences. For patients with type 2 diabetes who are not achieving glycemic goals, insulin therapy should not be delayed.[27]

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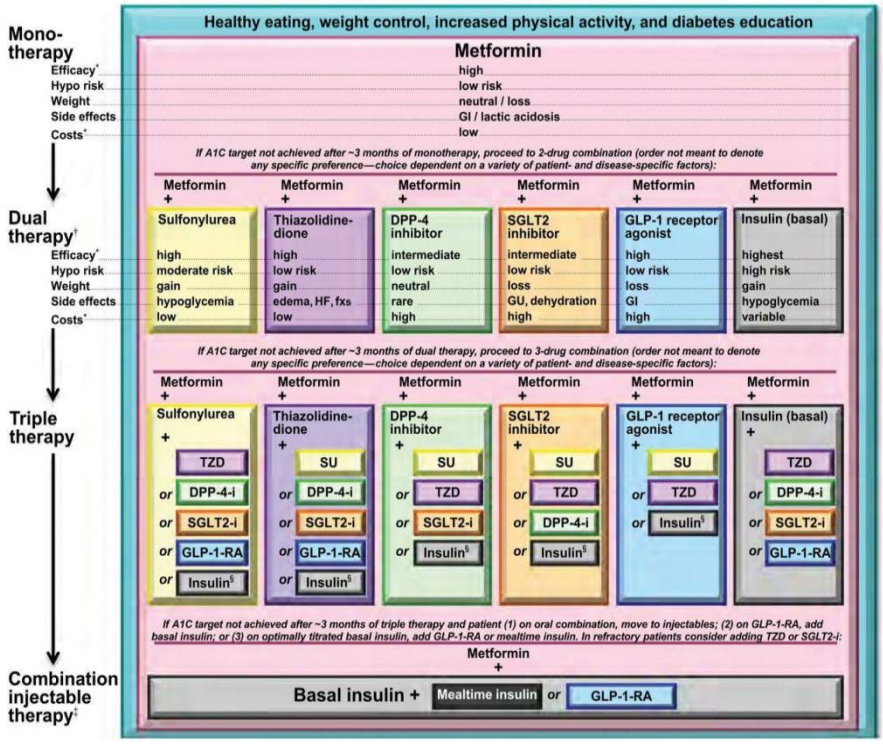
Figure – 3: Anti hyperglycemic therapy in type 2 diabetes



[DPP-4-i, DPP-4 inhibitor; fixes, fractures; GI, gastrointestinal; GLP-1-RA, GLP-1 receptor agonist; GU, genitourinary; HF, heart failure; Hypo, -hypoglycemia; SGLT2-i, SGLT2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione.]

†Consider starting at this stage when HbA1C is ≥9% (75 mmol/mol).

‡Consider starting at this stage when blood glucose is ≥300–350 mg/dL (16.7–19.4 mmol/L) and/or HbA1C is ≥10–12% (86–108 mmol/mol), especially if symptomatic or catabolic features are present, in which case basal insulin + mealtime insulin is the preferred initial regimen. Many patients with type 2 diabetes eventually require and benefit from insulin therapy. The progressive nature of type 2 diabetes and its therapies should be regularly and objectively explained to patients. Equipping patients with an algorithm for self-titration of insulin doses based on SMBG results improves glycemic control in patients with type 2 diabetes who are initiating insulin therapy. [27]

MICROALBUMINURIA & TYPE 2 DM: Diabetes has become the single most common cause of end stage renal disease. About 20-40% of patients with type 2 diabetes develop evidence of nephropathy. Diabetic nephropathy is first recognized as proteinuria. The main reason for performing the test for proteinuria is for the early detection of diabetic nephropathy in a patient who had diabetes for several years. Normally, protein is not present in the urine when measured by routine Dipstick Quantitative Test. This is because glomerulus generally prevents large molecules from entering renal filtrate. Normally less than 150 mg of proteins per day are excreted in urine. About 1/3RD of protein in urine is comprised of urine albumin, 1/3RD of small globulins, and 1/3RD of Tamm Horsfall Protein. Most of the proteins are normally reabsorbed by the proximal tubular epithelial cells. Proteinuria is referred to dipstick positive or Albumin Excretion Rate (AER) more than 200 µg/min or 300 mg/24 hrs.[28] Microalbuminuria is defined as the range in between urinary excretion of albumin of 20-200 µg/min or 30-300 mg/24 hrs. The Microalbuminuria is also defined as urinary albumin to creatinine ratio. Aratio of greater than 30-300 mg/gm of creatinine is considered as Microalbuminuria.[29] The central abnormality in Diabetic nephropathy is renal extracellular matrix accumulation in the mesengium. [30]

Table 4: Normal and abnormal urinary albumin excretion values[31]

First voided morning specimen				
Albumin Excretion	24 hr. collection (mg/24h)	Timed collection (µg/min)	Urine Albumin concentration* (mg/l)	Urine Albumin: Creatinine ratio** (mg/mmol)
Normoalbuminuria	<30	<20	<20	<3.5 women <2.5 men
Microalbu-minuria	30-300	20-200	20-200	3.5 to 35 women 2.5 to 25 men
Overt proteinuria	>300	>200	>200	>35 women >25 men

*urine albumin of 200mg/liter is equivalent to 300mg/litre of protein

** 3.5 as lower limit in females because of lower creatinine excretion.[31]

Methods of micro albumin estimation in urine: (A) Collection of sample: Albumin excretion varies with physiological factors like exercise posture, diuresis. Thus samples should not be collected after exercise, in the presence of urinary tract infection, during acute illness, immediately after surgery or after an acute fluid overload. The following are considered acceptable.[32]

- 24 hour collection
- Overnight (8 - 12 hour) urine sample collection
- Short term urine collection i.e. 1-2 hour collection (in laboratory or Clinic)
- Early morning sample voided is usually rather concentrated and using this sample has good correlation between the excretion rate and concentration of albumin.

(B) Storage: Urine should be stored at 4°C after collection. Alternatively, 2ml of 50 g /L sodium azide can be added per 500ml of urine. Bacterial contamination and glucose have no effect. Specimens are stable for at least 2 weeks at 4 ° C and 5 months at -70 ° C. Freezing samples may decrease albumin but mixing immediately before assay eliminates this effect.[32]

C) Estimating microalbuminuria:

D) 1) Semi quantitative methods:

a) Micral microalbumin urine test strip (Roche Diagnostic) b) Climatic Microalbumin (Bayer Diagnostic)

2) Quantitative methods:

a) Immunoturbidimetry

b) Nephelometry

c) Radio immunoassay (RIA)

d) Chemiluminescent immunoassay (CLIA)

Chemiluminescence is a chemical reaction that emits energy in the form of light. When used with immunoassay technology, the light produced by the reaction indicates the amount of analytic in a sample.[32] This method was used in our study.

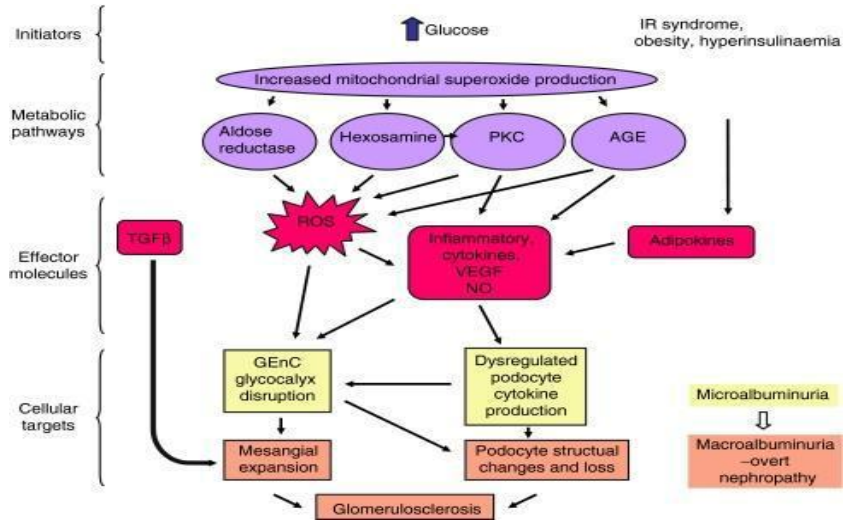


Figure 4: Pathways to microalbuminuria in diabetes mellitus [33]

Hyperglycemia, through increased mitochondrial superoxide production, dysregulates key intracellular metabolic pathways. These in turn lead to the production of effectors that directly cause glomerular endothelial cell (GEnC) dysfunction (particularly of the glycocalyx) and disturb podocyte–endothelial cell communication. This results in microalbuminuria. Progression of these lesions and development of other glomerular changes, including podocyte damage, lead to overt diabetic nephropathy.[33]

ALBUMINURIA AND CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES MELLITUS: A strong association has been reported between microalbuminuria and cardiovascular outcomes in patients with type 2 diabetes. Analysis of 3,498 patients with diabetes and 5,545 patients without diabetes in the Heart Outcomes Prevention Evaluation (HOPE)[34] study found that microalbuminuria increased the adjusted relative risk (RR) of major cardiovascular events (RR 1.83, 95% CI 1.64–2.05).[34] Participants with diabetes had a RR of 1.97 (95% CI 1.68–2.31) and those without diabetes had an RR of 1.61 (95% CI 1.36–1.90). Furthermore, Gimeno-Orna et al.[35] classified 436 type 2 diabetic patients into one of four groups based on if they had baseline cardiovascular disease or microalbuminuria. Patients with no baseline cardiovascular disease, but microalbuminuria had an increased RR for incident cardiovascular disease (RR 2.8, 95% CI 1.7–4.6) compared with patients with no baseline cardiovascular disease and normoalbuminuria. In addition, patients with no baseline cardiovascular disease and microalbuminuria had the same risk for a subsequent cardiovascular event as patients who had a previous cardiovascular event documented at baseline.[35] Microalbuminuria was a potent risk factor for cardiovascular events as a previous history of actual cardiovascular disease. Microalbuminuria may also be a risk factor for more severe or advanced cardiovascular disease as well. The 330 patients who underwent coronary angiography were divided into groups based on the presence or absence of diabetes and the presence or absence of microalbuminuria.[36] Diabeticcpatients with microalbuminuria had a higher prevalence of three vessel coronary artery disease compared with those without microalbuminuria (75 vs. 42%). This relationship was also seen in those patients studied without diabetes and with or without microalbuminuria (39 vs. 20%). Multiple lines of evidence demonstrate a strong association between the presence of microalbuminuria and the risk of adverse cardiovascular events. Evidence suggests that amount of urinary albumin excretion increases along the continuum from microalbuminuria to albuminuria and proteinuria, the risk of adverse cardiovascular events increases. Indeed some studies have suggested that the presence of microalbuminuria increases the relative risk of an adverse cardiovascular event similarly to the presence of hypercholesterolemia.[37]

TREATMENT OF ALBUMINURIA AND CARDIOVASCULAR OUTCOMES:

In patients who progress to overt nephropathy, microalbuminuria usually precedes macro albuminuria by an interval of 5 to 10 years. In patients with type 1 diabetes mellitus, blood pressure increases and renal function declines after the onset of macro albuminuria. However, in patients with type 2 diabetes mellitus, hypertension and a decline in renal function may occur when albumin excretion is still in the microalbuminuria range. Large clinical trials have demonstrated that achieving tight glycemic (i.e. glycosylated hemoglobin < 7.0%) and blood pressure (i.e. < 130/85mm Hg) control retards the progression of renal disease. There is accumulating evidence to suggest that the use of antihypertensive agents which target therenin-angiotensin system (RAS) can slow the progression of renal disease and provide cardio protection in patients with type 2 diabetes mellitus and microalbuminuria. Antihypertensive agents which target the RAS also appear to have advantages over and above reductions in systemic blood pressure. The annual screening of patients with type 2 diabetes mellitus for microalbuminuria, and the initiation of measures to retard the progression of renal and cardiovascular disease, are now considered part of routine clinical practice. In particular, the finding of microalbuminuria should provoke an intensified modification of the common risk factors for renal and cardiovascular disease that is hyperglycemia, hypertension, dyslipidemia and smoking. Antihypertensive therapy in patients with microalbuminuria and type 2 diabetes mellitus should be initiated with angiotensin converting enzyme (ACE) inhibitors or angiotensin-II type 1 receptor antagonists.[38] In the PREVEND Intervention Trial (PREVEND IT), patients with albuminuria treated with Fosinopril experienced a significant decrease in urinary albumin excretion(26%) and a trend toward a decrease in cardiovascular events (40%).[39]

Recommendations for patients with microalbuminuria [40]:

1) Reno protection with ACE inhibitors or angiotensin receptor blockers for patients with diabetes

2) BP control

<140/90 mmHg for the general population<130/80mmHg for patients with diabetes

3) Glycemic control: hemoglobin A1c <7%
4) Consider screening in patients with diabetes
5) LDL cholesterol control for diabetes in the general population

<100 mg/dl (<2.6 mmol/L) for patients with or without diabetes <70 mg/dl (<1.8 mmol/L) for patients with CVD

6) Correct disturbances in triglyceride and HDL level
7) Smoking cessation
8) Dietary limitation of salt (<3 g/d) and saturated fat
9) Regular exercise and weight control
10) Antiplatelet therapy

LV MASS INDEX AND TYPE 2 DM: Type 2 diabetic patients have raised morbidity and mortality from cardiovascular disease, compared with the non-diabetic background population.[41].The Framingham Heart Study revealed a marked increase in peripheral arterial disease (PAD), congestive heart failure (CHF), coronary artery disease (CAD), myocardial infarction (MI), and sudden death (risk increase from one- to fivefold) in DM. Risk factors for macrovascular disease in diabetic individuals include dyslipidemia, hypertension, obesity, reduced physical activity, and cigarette smoking. Additional risk factors more prevalent in the diabetic population include microalbuminuria, macro albuminuria, an elevation of serum creatinine, and abnormal platelet function. Cardiovascular complications account for the highest mortality in diabetic patients, mainly due to CAD and CHF. Diabetes is associated with a high prevalence of hypertension, dyslipidemia, and microalbuminuria, all known independent cardiovascular risk factors. Even in populations with low cardiovascular risk, diabetes is associated with an increased incidence of cardiovascular death.[3] Conversely a reduction in LVH predicts a lesserrisk for subsequent morbid events.[42]. Echocardiography provides a reliable noninvasive estimation of LVM and has been proven to be a more sensitive tool for the detection of LVH than other techniques.

Pathogenesis of cardiac remodeling: In diabetes mellitus chronic hyperglycemia leads to glucose toxicity, which contributes to cardiac injury through multiple mechanisms, including direct and indirect effects of glucose on cardiomyocytes, cardiac fibroblasts, and endothelial cells. Chronic hyperglycemia promotes the over-production of reactive oxygen species (ROS) through the electron transport chain which can induce apoptosis and activate poly (ADP-ribose) polymerase-1 (PARP). This enzyme mediates the direct ribo-sylation and inhibition of glyceraldehyde phosphate dehydrogenase (GAPDH), diverting glucose from the glycolytic pathway toward alternative biochemical cascades that participate in hyperglycemia induced cellular injury. These include increases in advanced glycation end products (AGEs) and the activation of the hexosamine pathway, the polyol pathway, and protein kinase C. Hyperglycemia induced apoptosis is stimulated by ROS, PARP, AGEs and aldose reductase. Hyperglycemia also contributes to altered cardiac structure and function through post-translational modification of extracellular matrix components (e.g. collagens) and altered expression and function of both the ryanodine receptor (RyR) and sarco (endo) plasmic reticulum Ca2+-ATPase (SERCA), which in aggregate contribute to decreased systolic and diastolic function.[43]

Echocardiography: Although LVM may be assessed using 2-dimensional (2D) or 3-dimensional (3D) echocardiography, M-mode was the first noninvasive imaging technique developed and remains the recommended method. Whether using M-mode, 2D, or 3D measurements, LVM estimation by echocardiography is based on subtraction of the left ventricular (LV) cavity volume from the volume enclosed by the correspondent epicardium to obtain the myocardial volume, then multiplying by the myocardial density (taken to be 1.05 g/ml).[44]. In patients without major cardiac geometry distortions, the American Society of Echocardiography (ASE) recommends a formula to estimate LVM from linear dimensions based on the assumption of the LV as a prolate ellipsoid of revolution

(Figure 5). Linear measurements of interventricular septum wall thickness (IVST), as well as left ventricular internal diameter (LVID) and posterior wall thickness (PWT), should be done from the parasternal acoustic window in end-diastole at the level of the LV minor axis (mitral valve leaflet tips) using 2D-targeted M-mode or directly from 2D images.[44]

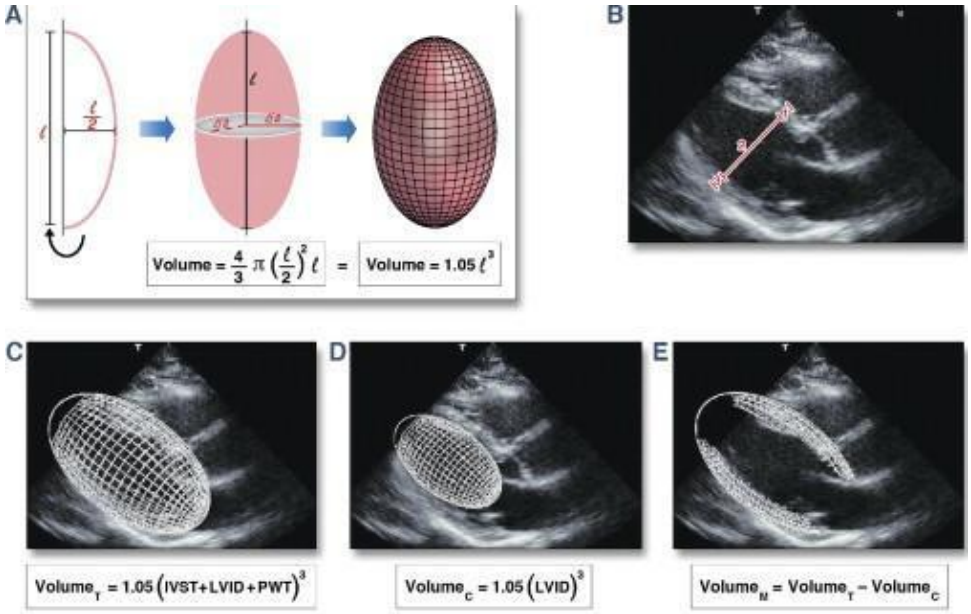


Figure 5: Principles for the Assessment of LVM by Echocardiography, asRecommended by the ASE

(A) A prolate ellipsoid of revolution, or prolate spheroid, is a 3-dimensional

Figure formed by revolving an ellipse about its major axes. The American Society of Echocardiography (ASE)-recommended formula assumes that the left ventricle has a prolate ellipsoid of revolution shape, with minor radii that are half the major radius.

(B) Schematic representation of the linear measurements for the assessment of LVM by echocardiography (parasternal view), according to the ASE

Recommendations.

1 = interventricular septum thickness (IVST); 2 = left ventricular internal dimension (LVID); 3 = posterior wall thickness (PWT).

(C to E) Images refer to a schematic representation of the steps for the estimation of left ventricular myocardial volume, as initially proposed by Devereux et al.[45] Left ventricular mass (LVM) is then calculated by multiplying the myocardial volume by the specific gravity of myocardium (1.05 g - approx.).

(C) Calculation for the total left ventricular volume (Volume T).

(D) Calculation for the left ventricular internal cavity volume (Volume C).

(E) Calculation for the left ventricular myocardial volume (Volume M).[44]

LV mass (ASE method) = 0.8 (1.04([LVID+PWT+IVST]3 – [LVID]3)) + 0.6 g where 1.04 is the specific gravity of the myocardium, and 0.8 is the correction factor. All measurements were made at end-diastole (at the onset of the R wave) in centimeters.[46]

Advantages of linear M mode method [47]

- Fast and widely used
- Wealth of published data
- Demonstrated prognostic value

- Fairly accurate in normally shaped ventricles (i.e., systemic hypertension, aortic stenosis)
- Simple for screening large populations

Indexing for Body Size: Both body size and body habitus are clearly associated with LV dimensions and mass. Diverse normalization and indexes were created and tested to adjust for three different sources of physiologic variation in LV mass: lean body mass, obesity, and gender. However, the interdependence of such associations should be carefully understood to allow an adequate correction of LV mass without distorting its association with cardiovascular disease.[48]. Several indexes for body size correction have been proposed, such as height, diverse algometric height adjustments, weight, body surface area, body mass index, and free-fat mass. The best way for normalization of LV mass is still controversial and another source of confusion. Different body-size adjustment criteria and their standard cut points result in different prevalence of patients with LVH. [48] The body surface area correction, using the Dubois formula.[49] reduces variability due to body size and gender.

Dubois formula: BSA (m2) = 0.007184 x Height(cm)0.725 x Weight(kg)0.425

LV mass index = LV mass (g)/BSA (m2).

Table-5: Normal ranges for LV mass indices[47]

	Women	Men
Linear method		
LV mass (g)	67–162	88–224
LV mass/BSA (g/m2)	43–95	49–115
Relative wall thickness (cm)	0.22–0.42	0.24–0.42
Septal thickness (cm)	0.6–0.9	0.6–1.0
Posterior wall thickness (cm)	0.6–0.9	0.6–1.0
2D method		
LV mass (g)	66–150	96–200
LV mass/BSA (g/m2)	44–88	50–102

MATERIAL AND METHODS:

We studied patient of type-2 diabetes mellitus in a span of 18 months after study approval from the hospital Ethics Committee. The study population included patients from diabetes OPD, medicine OPD, and medicine wards. A total of 62 patients included 31 cases who were type 2 diabetes patients with microalbuminuria and a similar number of type 2 diabetes patients without microalbuminuria:

Demographic and Physiological Parameters: Patient particulars such as age, sex, height, weight, body surface area (BSA), body mass index (BMI), and blood pressure were measured, and routine and relevant investigations like fasting blood sugar, postprandial blood sugar, HbA1c, serum creatinine, urine microalbumin, lipid profile, ECG, and echocardiography were also assessed.

Body mass index Estimation was done by taking weight in kilograms on a balance scale, the height was recorded in centimeters.

BMI = Weight (kg)/height (m2).

Body surface area (m2) BSA was measured using the following formula: (0.0001) × (71.84) × (Weight in kg) 0.425 × (Height in cm) 0.725

Fasting blood sugar: Venous blood samples were drawn in the morning following an overnight (minimum 8 h) fast and blood sample was sent tothe laboratory and was estimated with Dimension RXL Max. FBS Upto 120 mg/dl was considered as a normal and > 120 mg/dl was considered as a higher.

Serum creatinine was measured by Dimension RXL Max. upto 1.4 mg/dl was considered as a normal.

Postprandial blood sugar: venous blood sample collected after 2 hours of lunch. PPBS Up to 250 mg/dl was considered as a normal and > 250 mg/dl was considered as a higher.

Serum lipid levels were measured using Dimension RXL Max. Serum cholesterol level up to 224 mg/dl was considered as a normal and >224 mg/dl was considered as a higher. Serum **HDL level >** 35 mg/dl was considered as a normal and upto 35 mg/dl was considered as a lower.

HbA1c was measured using iron exchange high performance liquid chromatography by Biorad D-10. HbA1C upto 8% was considered as a controlled and > 8% was considered as a uncontrolled DM.

Micro-albuminuria estimation was done by Nycocard U-albumin test. Micro-albuminuria was defined as a urine albumin >200 mg/L.

Echocardiography: M-mode and pulsed Doppler echocardiography were performed according to the recommendations of the American Society of Echocardiography using Philips epic equipped with a 3.25-MHz transducer. Left ventricular dimensions LV dimensions were measured from 2D-guided M-mode echocardiograms of the LV at the level of mitral leaflet tips or the papillary muscle using the parasternal view. The thicknesses of the left ventricular posterior wall and the ventricular septum (from the leading edge to the trailing edge) were measured. These values were used to calculate the LV mass. The LV end-diastolic dimension was measured at the level of tips of the mitral leaflets as the largest LV dimension.

Left ventricular mass: The following equation provides a reasonable determination of LVM in grams:

LV mass (ASE method) = 0.8 (1.04 ([LVID+PWT+IVST]3 − [LVID]3)) + 0.6 g the LVM index (LVMI) was calculated by dividing the LVM with the surface area.

The upper limit of LVM was 162 g in females and 224 g in males. The upper limit of the LVMI was 95 g/m2 in females and 115 g/m2 in males.[47].Male and female patients with waist circumference values $\leq$ 102 and $\leq$ 88cm respectively, were considered to have a normal WC, whereas values >102 and >88 cm considered to have high WC.[50]

Statistical methods: Tests of significance Unpaired Student's t-test This is a statistical significance test for comparing one set of data with another, by comparing two means to see if they are significantly different, the data belonging to two different samples. SPSS software used to analyse data and perform a t-test. A P-value of <0.05 was considered significant.

Study Design: The study was a cross sectional study. The study was carried out for a period of 18 months at Holy Family Hospital, Bandra, Mumbai.

Study Sample: Assumptions: Level of significance =α: = 5%Power of analysis = ß = 90%. Mean difference among LV mass index in type II DM with and without microalbuminuria [55] = 43.39, SD = 24.46.Based on the above estimates, a sample size of 50 cases (25 in each group) would be sufficient to assess the objectives of study at 5% level of significance with 90% of Power. Considering 20% dropout, Total 62 (31 in each arm) cases will be enrolled to evaluate the objectives of study.

Formula used $n = 4\square 2$ where $\square$ = SD

And $\square$ = allowable error (here it is 10% as power of study is 90%)

Ref for Formula: Sample Size Calculations in Clinical Research

By: Shein - Chung Chow, Jun Shao and Hnasheng Wang

Inclusion Criteria: Patients on oral or injectable antidiabetic therapy among already diagnosed diabetic patients. Patients not on antidiabetic therapy but fulfilling the American Diabetic Association definition for DM.

Exclusion Criteria: Patients with ischemic heart disease and cardiomyopathyrenal dysfunction Hypertension

Data Collection: Confidentiality was maintained throughout the study phase, access to data was given only to personnel involved in the study that includes the study investigators, supervisors, biostatistician, study nurses and research committee. Monitoring of data and analysis of study was done after successful enrollment of 62 patients. All the study related files and documents were stored in a safe locker at research office of Holy Family Hospital.

Assessment of Patients: Clinical examination: Clinical profile of all the patients were taken including detail clinical history Pulse and Blood pressure Height, Weight Waist circumference Cardiovascular, Respiratory and per abdomen examination

Investigations: Blood sugar (fasting and post prandial), HbA1C, Urine micro albumin, Lipid profile, Creatinine, 2D – Echo, ECG.

OBSERVATION AND RESULTS: DEMOGRAPHICAL DATA

Table 6: Sex distributions of study cases:

Sex	Number of patients (N= 62)	Percentage (%)
Male	22	35.5
Female	40	64.5

- Above data shows that in our study, 64.5 % of the cases were female and 35.5% of the cases were male.

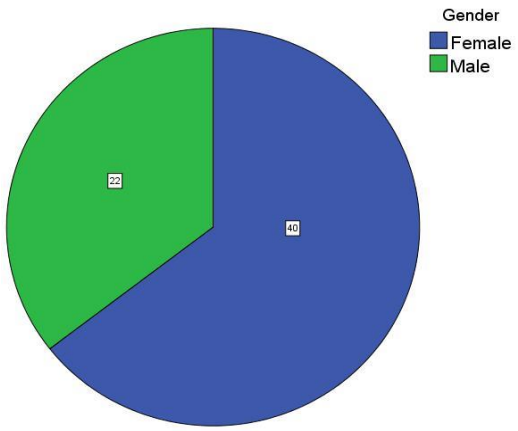


Figure 6: Sex distributions of study case:

Table 7: Age distribution of study cases:

	No.	Minimum age	Maximum age	Mean	Std. Deviation
age	62	36	79	57.19	11.790

The age range was 36–80 years with a mean age of 57.19 ± 11.79 years.

Table 8: Comparison of LV mass index in patients with & without microalbuminuria:

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
LV Mass index groups	Normal	22	71.0%	4	12.9%
	High	9	29.0%	27	87.1%
Mean ± SD		94.45 ± 22.44		116.32 ± 17.50	

By Student T Test P < 0.05 Significant

Above data reveals that 87.1% of cases in patients with MAU had high LV mass index while 29.0% of patients without MAU had high LV mass index. Mean LV mass index in patients with MAU was 116.32g/m2 which was significantly higher than mean LV mass index which was 94.45g/m2 in patients without MAU.

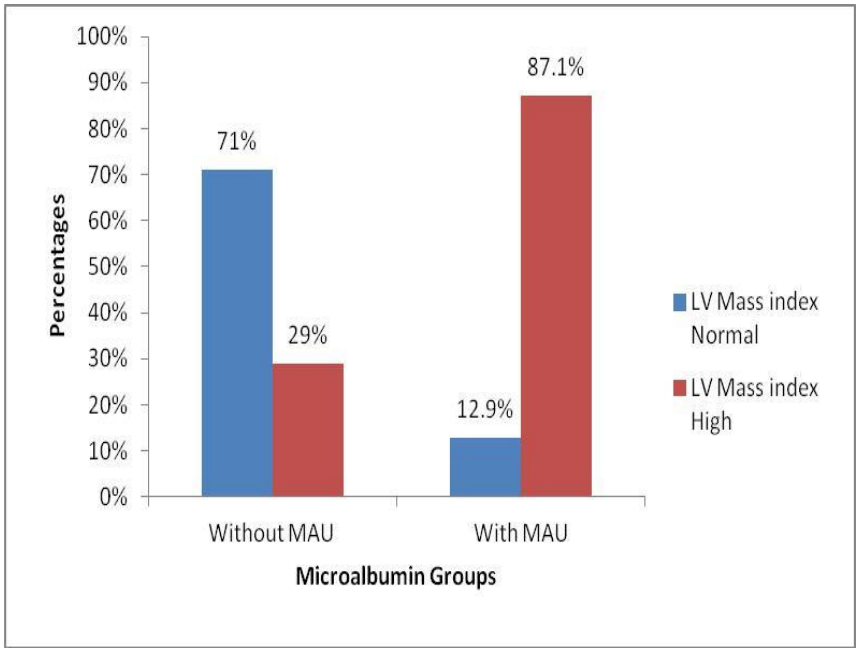


Figure7: Comparison of LV mass index in patients with & without microalbuminuria

Table 9: Comparison of LV mass in patients with & without microalbuminuria

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
LV Mass Groups	Normal	23	74.2%	6	19.4%
	High	8	25.8%	25	80.6%
Mean ± SD		167.55 ±	48.41	194.68	± 41.71

By Student T Test P = 0.021 Significant

Above data reveals that 80.6% of cases in patients with MAU had high LV mass while 25.8% of patients without MAU had high LV mass. Mean LV mass in patients with MAU was 194.68 g which was significantly higher than mean LV mass which was 167.55 g in patients without MAU.

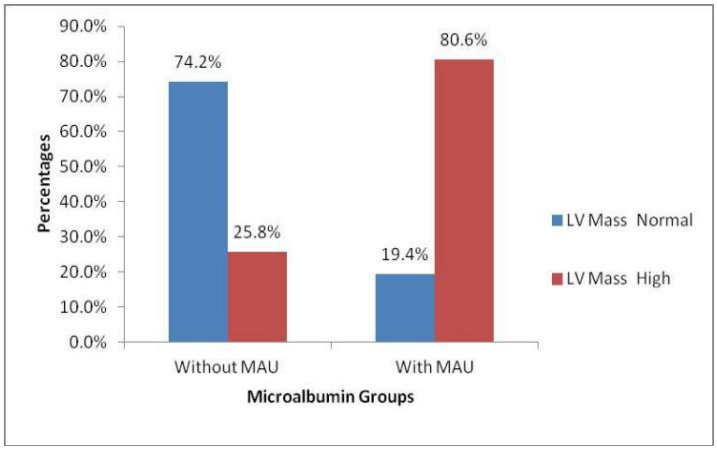


Figure 8: Comparison of LV mass in patients with & without microalbuminuriaa:

Table10: Comparison of duration of DM in patients with & without microalbuminuria:

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
Duration of DM Groups	up to 10 years	25	80.6%	13	41.9%
	>10 years	6	19.4%	18	58.1%
Mean ± SD		6.45 ±	5.29	13.45	± 7.07

By Student T Test P < 0.05 Significant

Above data reveals that 58.1% of cases in patients with MAU had duration of DM more than 10 years while 19.4% of patients without MAU had duration of DM more than 10 years. Mean duration of DM in patients with MAU was 13.45 years which was significantly higher than mean duration of DM which was 6.45 years in patients without MAU

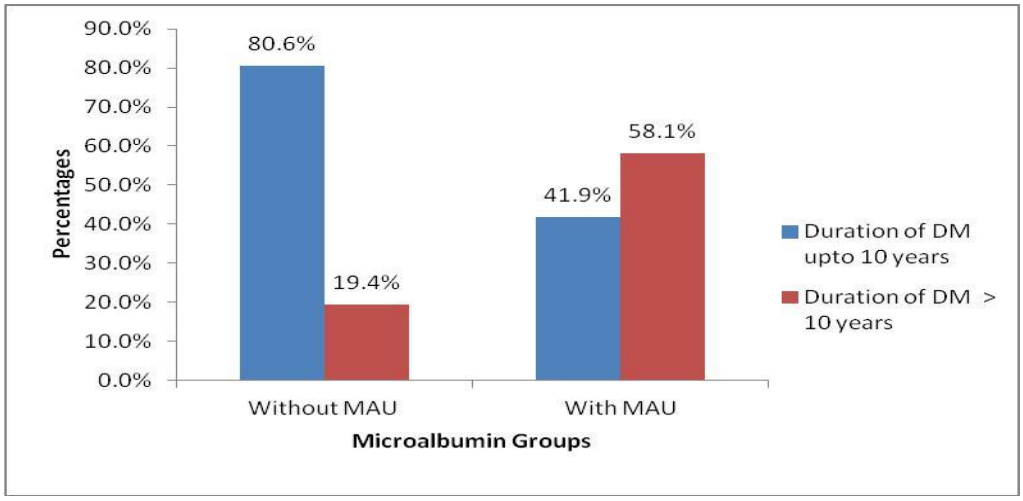


Figure – 9: Comparison of duration of DM in patients with & without microalbuminuria

Table – 11: Comparison of FBS in patients with & without microalbuminuria

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
FBS Groups	upto 120 mg/dl	4	12.9%	5	16.1%
	>120 mg/dl	27	87.1%	26	83.9%
Mean ± SD		166.55 ±	53.20	188.39	± 62.02

By Student T Test P = 0.142 Not Significant

Above data reveals that 83.9% of cases in patients with MAU had FBS >120 -mg/dl while 87.1% of patients without MAU had FBS >120 mg/dl. Mean FBS in patients with MAU was 188.39 mg/dl which was insignificantly higher than mean FBS which was 166.55 mg/dl in patients without MA

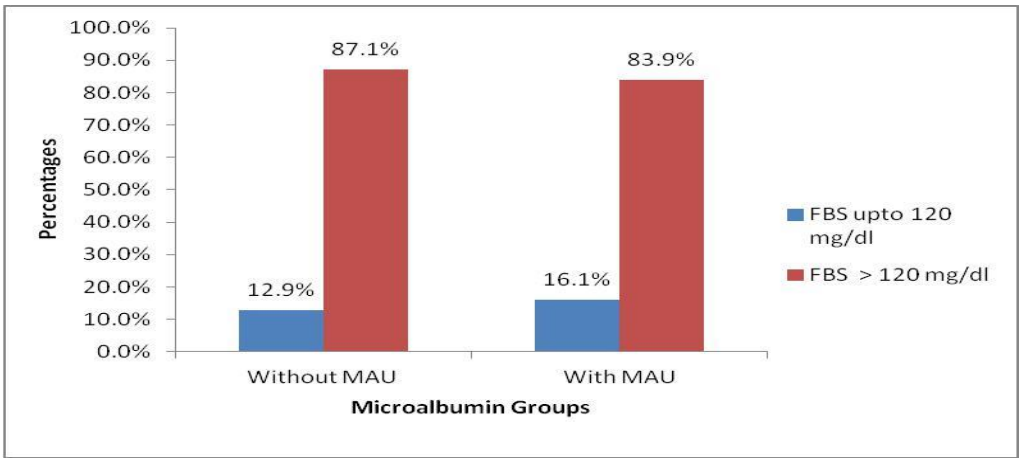


Figure10 : Comparison of FBS in patients with & without microalbuminuria

Table – 12: Comparison of PPBS in patients with & without microalbuminuria

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
PPBS Groups	up to 250 mg/dl	23	74.2%	17	54.8%
	>250 mg/dl	8	25.8%	14	45.2%
Mean ± SD		209.55 ±	74.83	245.39	± 74.78

By Student T Test P = 0.064 Not Significant

Above data reveals that 45.2% of cases in patients with MAU had PPBS >250 mg/dl while 25.8% of patients without MAU had PPBS > 250 mg/dl. Mean PPBS in patients with MAU was 245.39 mg/dl which was insignificantly higher than mean PPBS which was 209.55 mg/dl in patients without MAU.

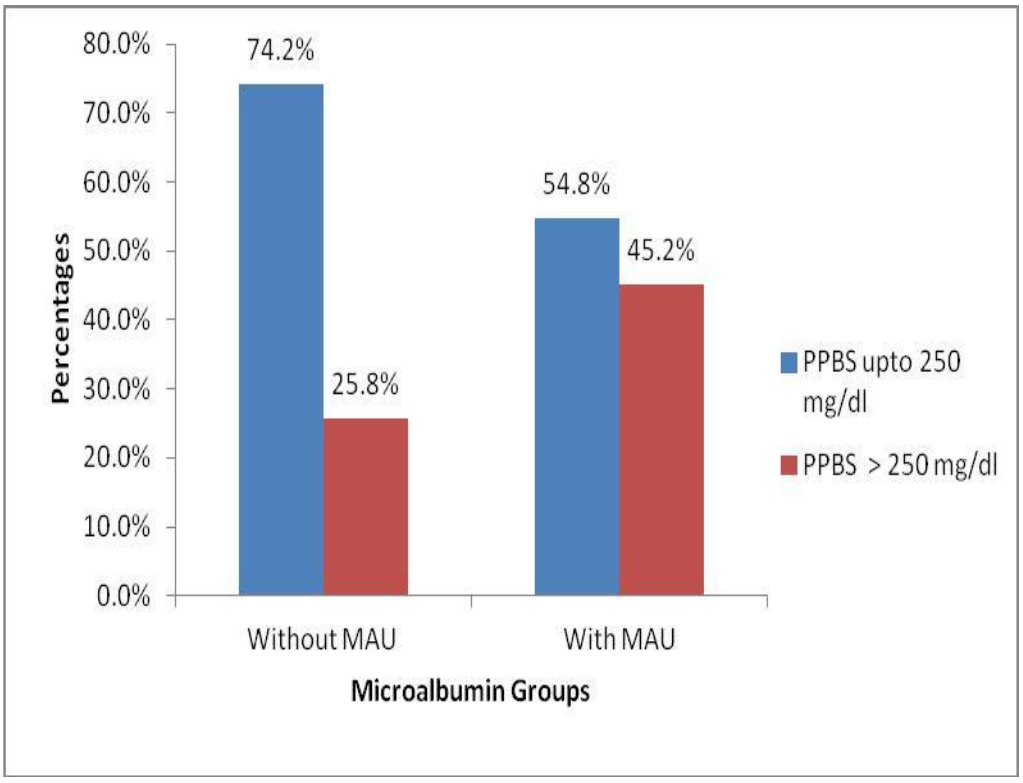


Figure 11: Comparison of PPBS in patients with & without microalbuminuria

Table 13: Comparison of HbA1c in patients with & without microalbuminuria

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No	%
HbA1c	up to 8 %	19	61.3%	10	32.3%
Groups	>8 %	12	38.7%	21	67.7%
Mean ± SD		8.17 ±	1.77	9.34	± 2.17

By Student T Test P = 0.024 Significant

Above data reveals that 67.7% of cases in patients with MAU had HbA1C

> 8 % while 38.7% of patients without MAU had HbA1C > 8%. Mean HbA1C in patients with MAU was 9.34 % which was significantly higher than mean HbA1C which was 8.17 % in patients without MAU.

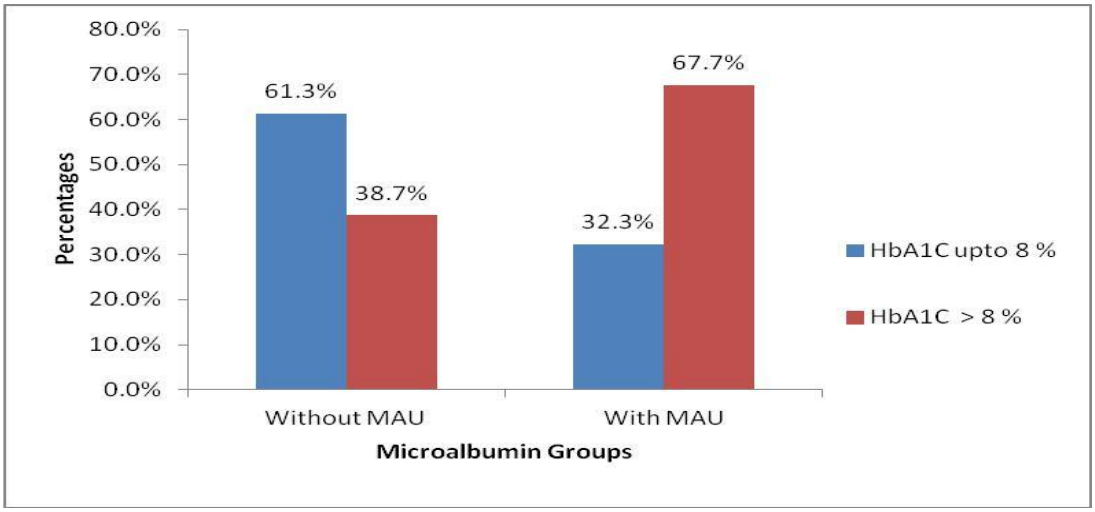


Figure12: Comparison of HbA1c in patients with & without microalbuminuria:

Table14: Comparison of WC (waist circumference) in patients with & without microalbuminuria

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
WC	Normal	20	64.5%	11	35.5%
Groups	High	11	35.5%	20	64.5%
Mean ± SD		91.87 ±	11.72	95.32	± 13.87

By Student T Test P = 0.294 Not Significant

Above data reveals that 64.5% of cases in patients with MAU had high WC while 35.5% of patients without MAU had high WC. Mean WC in patients with MAU was 95.32 cm which was insignificantly higher than mean WC which was 91.87 cm in patients without MAU.

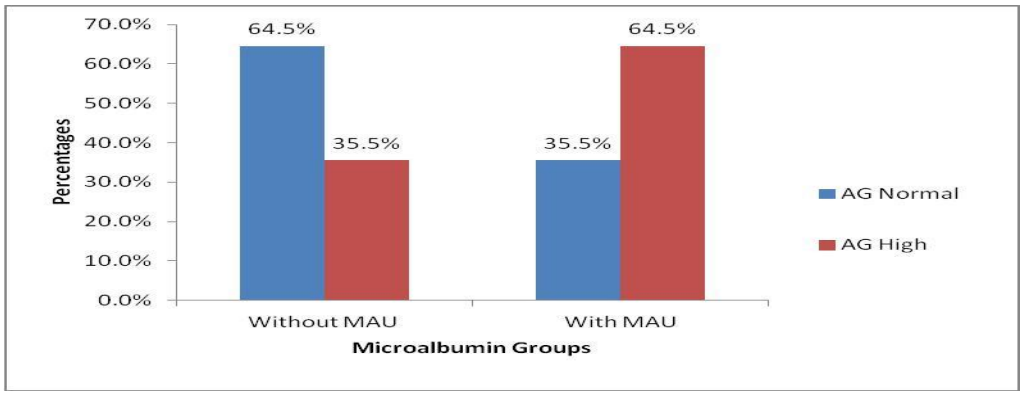


Figure13: Comparison of WC (waist circumference) in patients with & without microalbuminuria

Table 15: Comparison of cholesterol level in patients with & without microalbuminuria

		Microalbumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
Cholesterol groups	Normal	29	93.5%	20	64.5%
	High	2	6.5%	11	35.5%
Mean ±	SD	154.65 ±	39.65	190.16	± 50.67

By Student T Test P = 0.003 Significant

Above data reveals that 35.5% of cases in patients with MAU had high cholesterol level while 6.5% of patients without MAU had high cholesterol level. Mean cholesterol in patients with MAU was 190.16 mg/dl which was significantly higher than mean cholesterol which was 154.65 mg/dl in patients without MAU.

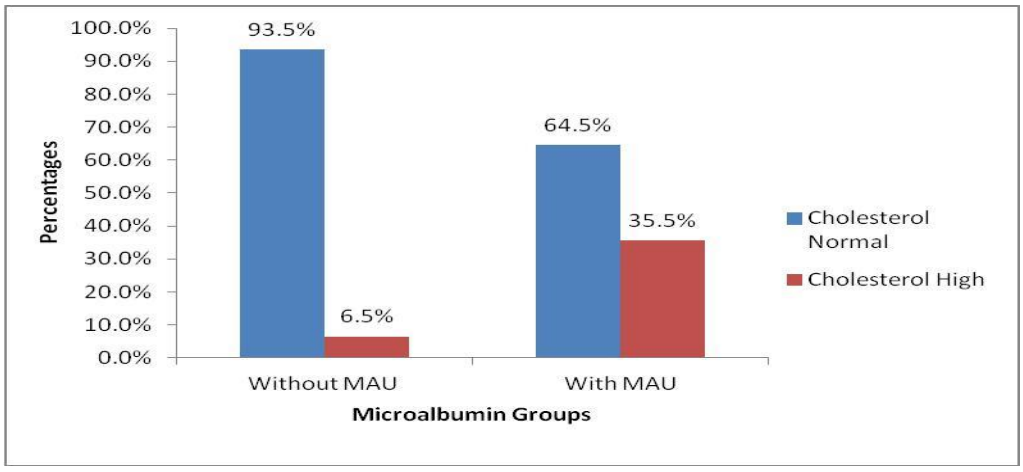


Figure 14: Comparison of cholesterol level in patients with & without microalbuminuria

Table16: Comparison of HDL in patients with & without microalbuminuria:

		Micro albumin Groups			
		Without MAU		With MAU	
		No.	%	No.	%
HDL groups	Normal	16	51.6%	10	32.3%
	Low	15	48.4%	21	67.7%
Mean ± SD		36.00 ±	11.00	33.81	± 10.22

By Student T Test P = 0.419 Not Significant

Above data reveals that 67.7% of cases in patients with MAU had low HDL level while 48.4% of patients without MAU had low HDL level. Mean HDL in patients with MAU was 33.81 mg/dl which was insignificantly lower than mean HDL which was 36.00 mg/dl in patients without MAU.

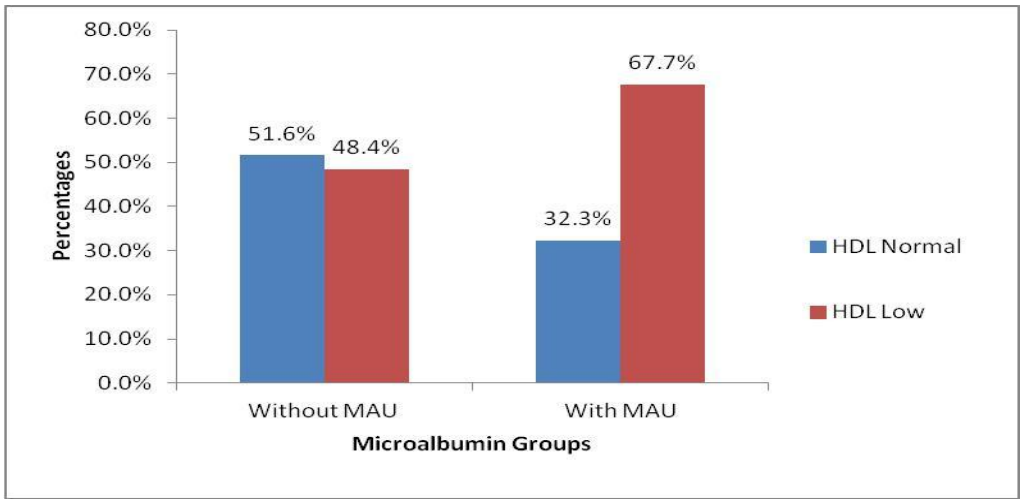


Figure 15: Comparison of HDL in patients with & without microalbuminuria

Table 17: Comparison of LV mass index and duration of DM:

		LV Mass index groups			
		Normal		High	
		No.	%	No.	%
Duration of DM Groups	up to 10 years	19	73.1%	19	52.8%
	>10 years	7	26.9%	17	47.2%
Mean ± SD		7.73	± 6.04	11.56	± 7.50

By Student T Test P =0.036 Significant

Above data reveals that patients with normal LV mass index 73.1 % had duration of DM up to 10 years and 26.9% had it for > 10 years. In patients with high LV mass index 52.8% had DM up to 10 years and 47.2% had it for > 10

years. Mean duration of DM was 7.73 years in patients with normal LV mass index and 11.56 years in patients with high LV mass index and difference was significant.

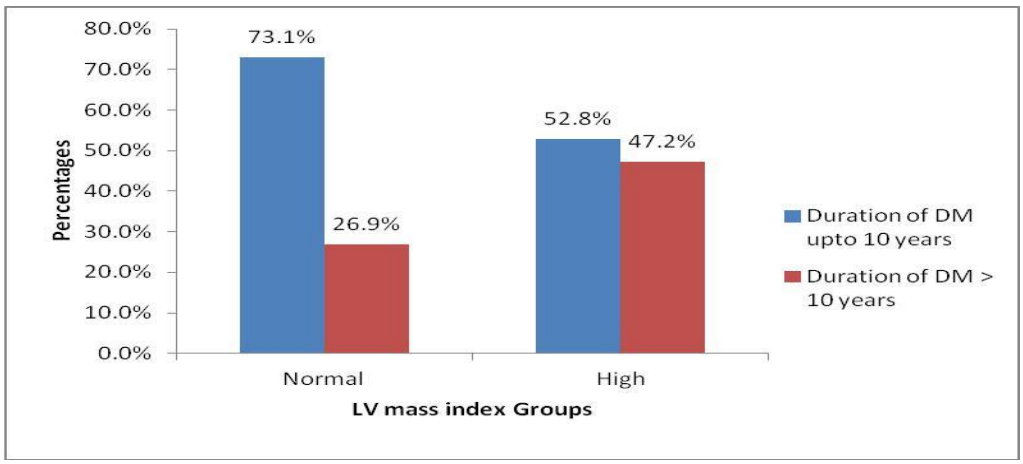


Figure 16: Comparison of LV mass index and duration of DM

Table 18: Comparison of LV mass index and FBS:

		LV Mass index groups			
		Normal		High	
		No.	%	No.	%
FBS Groups	upto 120 mg/dl	6	23.1%	3	8.3%
	>120 mg/dl	20	76.9%	33	91.7%
Mean ± SD		159.35 ± 53.26		190.56	± 59.06

By Student T Test P =0.037 Significant

Above data reveals that patients with normal LV mass index 23.1 % had FBS upto 120 mg/dl and 76.9% had it > 120 mg/dl. In patients with high LV mass index 8.3% had FBS upto 120 mg/dl and 91.7% had it > 120 mg/dl. Mean FBS was 159.35 mg/dl in patients with normal LV mass index and 190.56 mg/dl in patients with high LV mass index and difference was significant

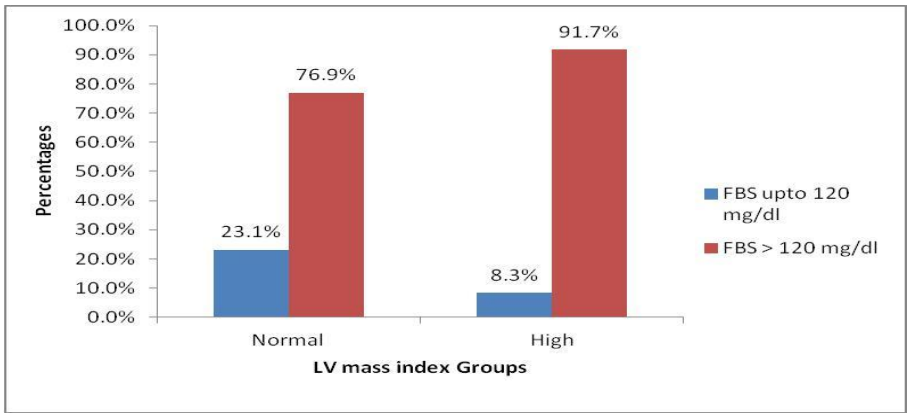


Figure17: Comparison of LV mass index and FBS

Table19: Comparison of LV mass index and PPBS

		LV Mass index groups			
		Normal		Higher	
		No.	%	No.	%
PPBS Groups	upto 250 mg/dl	21	80.8%	19	52.8%
	>250 mg/dl	5	19.2%	17	47.2%
Mean ± SD		201.65 ± 69.21		246.11	± 76.73

By Student T Test P =0.022 Significant

Above data reveals that patients with normal LV mass index 80.8 % had PPBS up to 250 mg/dl and 19.2% had it > 250 mg/dl. In patients with high LV mass index 52.8% had PPBS up to 250 mg/dl and 47.2% had it > 250 mg/dl. Mean PPBS was 201.65 mg/dl in patients with normal LV mass index and 246.11 mg/dl in patients with high LV mass index and difference was significant.

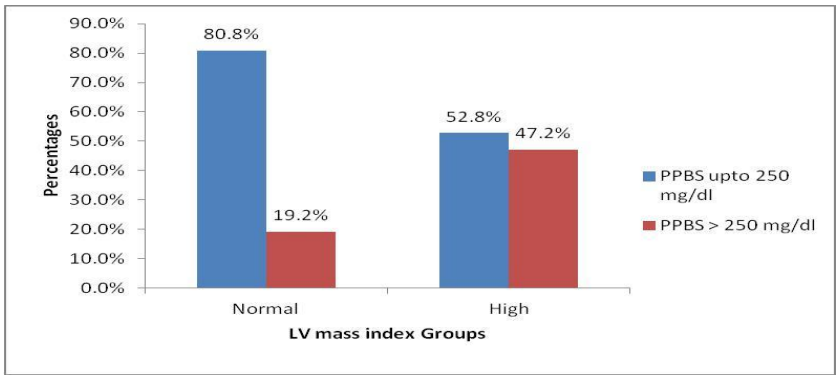


Figure18: Comparison of LV mass index and PPBS

Table 20: Comparison of LV mass index and HbA1C

		LV Mass index groups			
		Normal		High	
		No.	%	No.	%
HbA1c Groups	upto 8 %	16	61.5%	13	36.1%
	>8 %	10	38.5%	23	63.9%
Mean ± SD		8.10 ±	1.90	9.22	± 2.05

By Student T Test P =0.033 Significant

Above data reveals that patients with normal LV mass index 61.5% had HbA1C up to 8 % and 38.5% had it > 8%. In patients with high LV mass index 36.1% had HbA1C up to 8 % and 63.9% had it > 8%. Mean HbA1C was 8.10% in patients with normal LV mass index and 9.22 % in patients with high LV mass index and difference was significant.

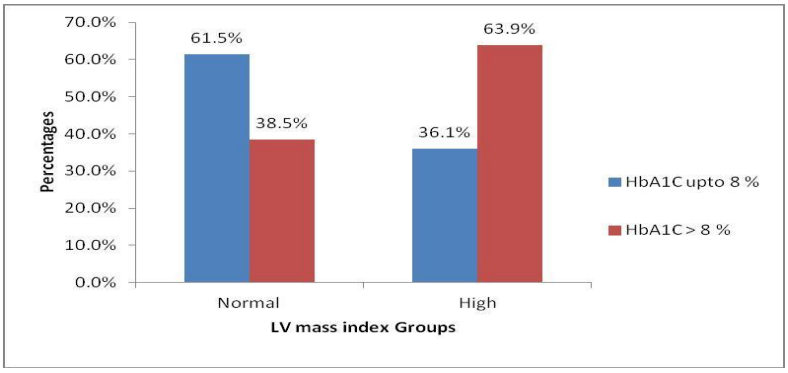


Figure 19: Comparison of LV mass index and HbA1

Table 21: Comparison of LV mass index and cholesterol level;

		LV Mass index groups			
		Normal		High	
		No.	%	No.	%
Cholesterol groups	Normal	24	92.3%	25	69.4%
	High	2	7.7%	11	30.6%
Mean ± SD		152.19 ± 42.48		187.00	± 47.91

By Student T Test P =0.004 Significant

Above data reveals that patients with normal LV mass index 92.3% had normal cholesterol level and 7.7% had high cholesterol level. In patients with high LV mass index 69.4% had normal cholesterol level and 30.6% had high cholesterol level. Mean cholesterol was 152.19 mg/dl in patients with normal LV mass index and 187.00 mg/dl in patients with high LV mass index and difference was significant.

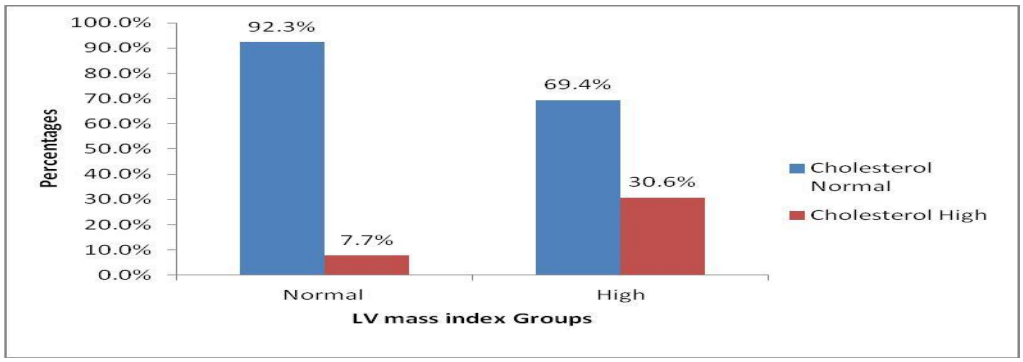


Figure 20: Comparison of LV mass index and cholesterol level

Table 22: Comparison of LV mass index and HDL level

		LV Mass index groups			
		Normal		High	
		No.	%	No.	%
HDL groups	Normal	11	42.3%	15	41.7%
	Low	15	57.7%	21	58.3%
Mean ± SD		35.58 ± 11.35		34.42	± 10.14

By Student T Test P =0.674 Not Significant

Above data reveals that patients with normal LV mass index 42.3% had normal HDL level and 57.7% had low HDL level. In patients with high LV mass index 41.7% had normal HDL level and 58.3% had low HDL level. Mean HDL

was 35.58 mg/dl in patients with normal LV mass index and 34.42 mg/dl in patients with high LV mass index and difference was not significant.

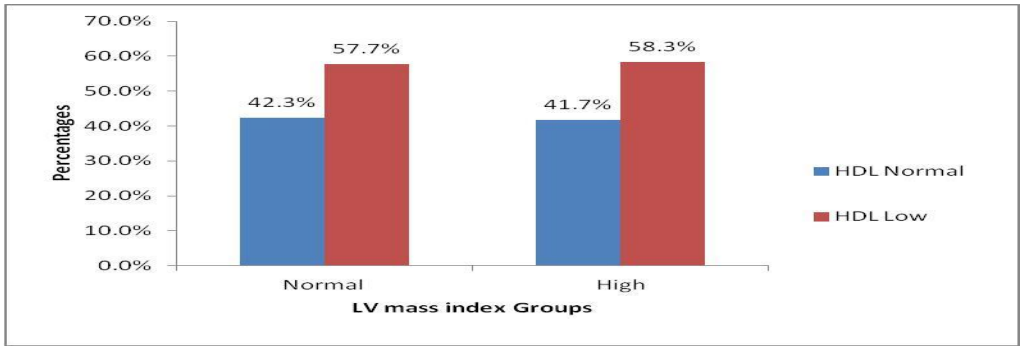


Figure – 21: Comparison of LV mass index and HDL level

DISCUSSION:

Heart disease occurs eventually in a majority of patients with DM and continues to be a notable factor in overall diabetes associated morbidity and mortality. Increased LVM may contribute to the increased cardiovascular risk because LVH is an ominous prognostic sign and an independent risk factor for sudden death, ventricular dysrhythmia, myocardial ischemia, coronary h heartdiseaseand heartfailure. Chronichyperglycemia in DMexpresses its toxicity by forming non-enzymatic glycation of tissue macromolecules such as, proteins, lipids and deoxyribonucleic acid (DNA) to form irreversibly bound advanced glycated end products.[52] Such products have been found to accumulate in tissues such as the heart.[53].Microalbuminuria, a marker of microangiopathy, is an early renal manifestation of diabetes. Persistent hyperglycemia causes hyperfilteration, advanced glycation products and activation of cytokines. All this causes glomerular damage and endothelial dysfunction leading to increased systemic vascular permeability.[54] LVH is associated with MAU in diabetes. Angiotensin-converting enzymes inhibitors are effective both in controlling blood pressure and reversing LVH.[51]. Cardiovascular risk factors were studied in type II diabetic patients in presence of MAU and the results were compared with patients without MAU. Diabetic patients with MAU showed significantly raised LVMI as compared to patients without MAU. In our study mean LV mass index was significantly higher in patients with MAU as compared to patients without MAU (116.32 vs 94.45, P <0.005). Study done by Kaur S et al.[55] al had similar results, they reported that mean LV mass index was significantly higher in patients with MAU as compared to patients without MAU. Association of LVMI and MAU have been reported by even Salmasi etal.[56]. In our study, mean LV mass, duration of DM, HbA1C level and cholesterol level were significantly higher in patients with MAU as compared to patients without MAU. Study done by Mbanya JCN et al.[57] found that mean LV mass and duration of DM were higher in patients with MAU as compared to patients without MAU. Study done by Liu et al.[58] found that mean duration of DM, HbA1C level, LV mass, and LV mass index were significantly higher in diabetic patients with MAU as compared to patients without MAU. Study done by Maity A et al.[59] showed that patients with poor glycemic control with documented high level of HbA1c (particularly HbA1c>8%) had higher micro albumin excretion in urine. They also found significant positive correlation between duration of diabetes and microalbuminuria. Study done by Pasko et al.[60] found that Mean HbA1C, cholesterol level and duration of DM were higher in patients with MAU as compared to without MAU.In our study 67.7% of cases in patients with MAU had low HDL level while 48.4% of patients without MAU had low HDL level. However the difference was not significant. Similarly in study done by liu et al.[58] there was no significant difference in HDL level among both groups. In our study, mean FBS in patients with MAU was higher than mean FBS in patients without MAU (188.39 vs 166.55, P = 0.142) and mean PPBS in patients with MAU was higher than mean PPBS in patients without MAU (245.39 vs 209.55, P = 0.064). But difference was not significant. In contrast, study done by Rao PP et al.[61] mean FBS and PPBS was significantly higher in MAU group as compared to without MAU group. (164.82 vs 118.36, P<0.01) (226.52 vs 161.7 P<0.001).In our study, Mean WC in patients with MAU was 95.32 cm which was insignificantly higher than mean AG which was 91.87cm in patients without MAU. (95.32 vs 91.87, p = 0.294). Similar to our study, Pasko et al.[60] reported that mean WC was insignificantly higher in MAU group as compared to without MAU group. In contrast, Nelag E et al.[62] found a significant positive association between WC

and microalbuminuria (P = 0.009). So, abdominal obesity is a predictor for development of microalbuminuria. This underlines the importance of measuring waist circumference when assessing cardiovascular risk factors in diabetic patients.In diabetes, non-enzymatic glycation of proteins and formation of advanced glycation end products have the potential to quench nitric oxide and then diminish the vasodilatory capacity of the peripheral musculararteries. Reduced nitric oxide availability may cause vasoconstriction and alter growth of vascular muscle, as well as producing cellular injury in prolonged hyperglycemia.[63] Thus prolonged hyperglycemia can modify the timing and magnitude of the pulse wave reflection to augment systolic load of the left ventricle. The impaired systolic loading condition of the left ventricle may cause the heart to adapt to muscular hypertrophy and may increase the ratio of left ventricular weight to body weight, an indicator of cardiac hypertrophy. [63] Accordingly, regression analysis of risk factors for the development of LVMI revealed that HbA1c was the major determinant of LVMI, indicating the importance of serum glucose control. All of these findings suggest that glucose homeostasis plays pivotal roles in the evolution of ventricular mass. In the diabetic population, HbA1c level is a valid and reliable marker for glycemic control and for predicting morbidity and mortality. [64]. In our study mean duration of DM was significantly more in patients with high LV mass index as compared to patients with normal LV mass index. (11.56 vs 7.73, P = 0.036).Mean FBS (190.56 vs 159.35, P = 0.037), PPBS (246.11 vs 201.65, P = 0.022), HbA1C (9.22 vs 8.10, p = 0.033) and cholesterol (187.00 vs 152.19, P= 0.004) level were significantly high in patients with high LV mass index as compared to patients with normal LV mass index. Similar to our findings, Santra S et al.[65] found that mean duration of DM (8.53 VS 6.61, P <0.0001) , and HbA1C (9.30 vs 7.88, P < 0.001) were significantlyyhigher in patients with high LV mass index as compared to patients with normal LV mass index. However in his study contrary to our study, mean FBS (150.55 vs 118.44, P =0.098) and PPBS (219.22 vs 214.40, P = 0.740) even though higher in patients with high LV mass index as compared to patients with normal LV mass index, was not significant. Sato et al.[66] also reported a significant positive correlation between glycemic control, duration of DM, and severity of nephropathy and LVMI.In our study there was no significant correlation between LVMI and HDL level. (34.42 vs 35.58, P = 0.674). In contrast, study done by ChienKL et al.[67] LV mass values were found to be negatively associated with HDL values at statistically significant level.Risk factors like high HbA1C, uncontrolled FBS and PPBS, high cholesterol and low HDL level, high waist circumference and duration in type 2 DM patients were associated with increase in LV mass which is indirect marker for adverse cardiac outcome. These risk factors are also associated with microalbuminuria which is again a marker for impending adverse renal outcome.

SUMMARY

1. LV mass and LV mass index was significantly higher in diabetic patients with MAU as compared to patient without MAU.
2. Duration of DM, HbA1C level and total cholesterol level are significantly higher in patients with MAU as compared to patients without MAU. So patients with above risk factors have more chances of having nephropathy.
3. There was no significant co- relation between FBS, PPBS, HDL level, and waist circumference with microalbuminuria in diabetic patients.
4. LV mass index in diabetic patients increases with the duration of diabetes. So patients with a longer duration of diabetes have more chances of having LVH.
5. LV mass index in diabetic patients also increases with the FBS, PPBS and HbA1c level. So a poor glycemic control is also associated with more chances of having LVH.
6. LV mass index in diabetic patients also increases with total cholesterol level.
7. There was no significant co-relation between HDL level and LV mass index.

CONCLUSIONS:

1. Microalbuminuria has a positive correlation with LV mass and LV mass index.
2. Duration of DM and poor glycemic control suggested by high HbA1C are risk factors for development of microalbuminuria.

3. Total cholesterol is an independent risk factor for microalbuminuria.
4. In DM patients, LVMI increases as the duration of DM increases.
5. Parameters like blood sugars, HbA1C and total cholesterol have positive correlation with LVMI.
6. Early screening of Type 2 DM patients with 2-D echo and urine micro albumin level is required to identify patients who are at risk for future cardiovascular and renal complications. Modifiable risk factors can be controlled with lifestyle modification and pharmacological intervention which can help to reduce adverse outcome.

LIMITATIONS OF THE STUDY

The study used the M-mode formula for calculation of LV mass while its calculation by 3-dimensional echocardiography was not performed. Our study evaluated the cardiac parameters at the time of presentation and no follow up was done. The effect of intervention was not studied and requires a large study over a long duration of time.

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