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Research Article

Correlation between Atherogenic Factors in Complicated and Uncomplicated Type 2 DM

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Abstract: Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The vascular complications of diabetes mellitus are further divided into micro vascular and macro vascular complications. There is an observed disparity between various vascular complications of diabetes and the atherogenic factors. The objectives were to study the atherogenic factors in type 2 diabetes patients in relation to complications and without complications. The work was carried out in the outpatient department and medical wards of Mamata General Hospital, Khammam. The study was done over a period of one year that included 100 type-2 diabetic patients. Pregnant and lactating women, patients with chronic alcoholism, hepatic, renal and thyroid disorders and Juvenile diabetes were excluded from the study. The investigations included Fasting blood sugar, Post lunch blood sugar, HbA1C, Lipid profile, Lipoprotein (a), Serum homocysteine, Urine albumin, sugar, ECG, Chest X-ray, Patient's height and weight, Serum creatinine, Fundoscopy. 93% of total patients with poor glycemic control, 18.27% had micro vascular complications and 13.97% had macro vascular complications. 51.61% of complicated diabetes had normal Lpa levels while 48.38% hadelevated levels. 75.36% of uncomplicated diabetes had normal Lp(a) levels and24.63% had elevated Lp(a) levels. Homocysteine was elevated in 58.06% of complicated diabetes and 40.5% ofuncomplicated diabetes while 59.42% of uncomplicated diabetes and 41.93% ofcomplicated diabetes showed normal homocysteine levels. In **c**onclusion, type 2 diabetes mellitus showed a strong correlation between glycemic status and incidence of diabetes complications. Hypercholesterolemia and homocysteine have added to the increased incidence of complications as additional factors in metabolic derangements as a consequence of poor glycemic control. The role of lipoprotein(a) in complications of diabetes need to be evaluated further. There is a strong case for routine addition of vitamin B6, B12, folate in addition to lipid lowering drugs on a routine basis.
Keywords: Hypercholesterolemia; Lipo protein (a); Serum Homocysteine.

INTRODUCTION

Diabetes mellitus [1] is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. It may be asymptomatic or may present clinically with characteristic symptoms like polyuria, polydipsia, polyphagia, nocturia or with one of its complications.

Diabetes has emerged as the chronic non-communicable disease of concern in developing countries as well [2]. With changing environment, urbanization and altered life styles, diabetes is also increasingly identified as a major cause of morbidity and mortality in India too, furthermore, Indians have high ethnic susceptibility for developing diabetes at a younger age group and develop vascular complications earlier and frequently during the natural progression of the disease [3]. At least 20 million people might be suffering from diabetes in India. The alarming rise in non-communicable disease warrants an immediate attention of experts to develop better diabetes health care facilities. Also it is essential not only to formulate effective treatment but also to give stress on preventive aspects of diabetes and vascular morbidity in the Indian context at the primary and secondary levels [3].

METHODOLOGY

Sample

100 type-2 diabetic patients, who had attended either as inpatients or outpatients to medicine department of Mamata General Hospital, Giriprasad Nagar, Khammam, Andhra Pradesh during the period from May 2012 to April 2013.

Inclusion criteria

Patients with type 2 DM

Exclusion criteria

- Pregnant and lactating women
- Patients with chronic alcoholism
- Patients with hepatic, renal and thyroid disorders
- Juvenile diabetes

Complete history was obtained from all these patients and a thorough physical examination was done. Their height, weight were measured. Fasting blood samples were taken after an overnight fasting of 10- 12hrs from every patient. FBS, PLBS, HbA1C, Lipid profile, Lipoprotein (a), serum homocysteine were analyzed. Other investigations like Hb, TC, ESR, and serum creatinine and urine analysis were done.

Diagnosis of Diabetes

Patients were diagnosed as diabetics if they meet the following Criteria: Symptoms of diabetes plus random blood glucose concentration > 11.1 mmol/1(200mg/l)
Or
Fasting plasma glucose ≥ 7.0mmol/l (126mg/dl)
Or
2 hr plasma glucose ≥ 11.1mmol/l (200mg/dl) during oral glucose tolerance test

In the absence of unequivocal hyperglycemia and acute metabolic decompensation, these criteria should be confirmed by repeat testing on different day. All patients with an episode of ketoacidosis and requiring insulin for survival or patients who required insulin within first year of diagnosis for control of hyperglycemia were considered as Type 1 and patients without an episode of ketoacidosis, controlled on oral hypoglycemic agents for more than a year after diagnosis were considered as Type 2.

Patients were categorized as to the quality of diabetes control using standard American Diabetes Association criteria (i.e. good control HbA1c <7 and poor control HbA1c >7).

Diagnostic criteria for dyslipidemia

The diagnostic criteria for dyslipidemia were taken as per NCEP, ATP III guidelines [4].

Dyslipidemia is said to be present in the presence of any of the following:

Total cholesterol ≥ 200mg/dl
Triglycerides ≥ 150 mg/dl
HDL-C < 40 mg/dl
LDL-C ≥ 130 mg/dl
Lp(a) > 30mg/dl

- Glycosylated Hb was estimated by ion exchange resin method.
- Total Cholesterol (TC), Triglycerides (TG), High density lipoprotein cholesterol (HDL C) were analyzed by enzymatic method using Hitachi 902 analyser.
- Low density lipoprotein cholesterol (LDL-C) was calculated by Friedewald formula
  i.e. LDL-C= TC – TG/5 – HDL.
- Very low density lipoproteins were calculated by the formula, VLDL= TG/5.
- Lp(a) was measured by Hitachi model 717(7160) automated analyzer.

Measurement of tHcy

- Measurement of tHcy in serum estimated by an enzyme conversion immunoassay (EIA). This assay is based on enzymatic conversion of tHcy (after reduction and release of endogenous homocysteine from proteins and/or disulfides) to S-adenosyl-L homocysteine (SAH) by the action of SAH hydrolase, followed by quantification of SAH in a competitive immunoassay with the use of a monoclonal antibody against SAH.
- Diabetic Retinopathy: the ocular fundi examined by direct ophthalmoscopy, after mydriasis.
- Retinopathy when present classified as non-proliferative diabetic retinopathy and proliferative diabetic retinopathy.
- NPDR was diagnosed when there is evidence of micro aneurysms, dot hemorrhages, exudates or cotton wool spots in the absence of any new vessels.
- PDR was diagnosed when any new vessels were present.
- NPDR and PDR were taken together as retinopathy for this study. Neuropathy was defined as failure to elicit knee and /or ankle reflexes after reinforcement with or without symptoms of neuropathy or gross sensory disturbance in both feet, in the absence of any other cause of neuropathy.
- Nephropathy was considered when proteinuria was present. Coronary artery disease was diagnosed if there are ECG changes suggestive of recent or past myocardial infarction or by previous hospital records.
- ABI of < 0.8 was considered as evidence of PVD.
- Cerebrovascular disease was diagnosed by imaging or evidence of any focal deficit.

RESULTS

Total number of patients studied: 100

Table 1: Age and gender distribution

Age	Male	Female	Percent (%)
30-40	8	10	18
41-50	13	11	24
51-60	21	18	39
61-70	7	9	16
71-80	3	0	3
Total	52	48	100

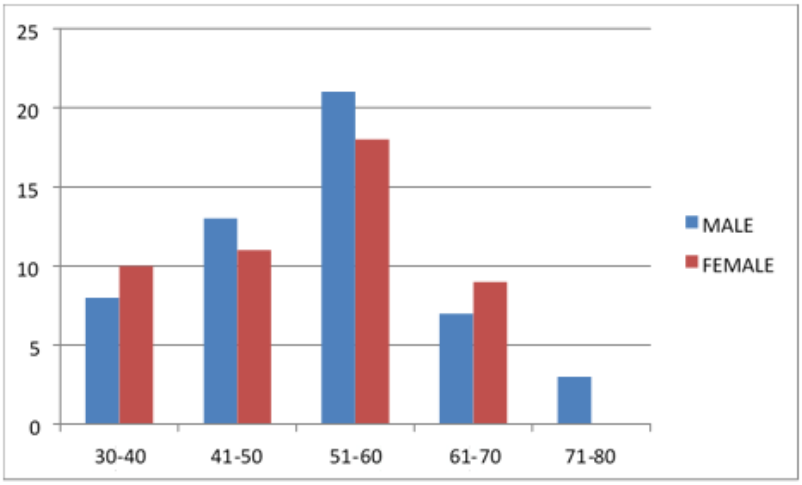

Fig. 1: Age and gender distribution

In this study consisting of 100 diabetic patients almost equal number of male and female patients are included. The majority of patients were in the age group 41-60years comprising almost 63% of total patients. None of the patients were below 30 years of age probably due to the fact that study was conducted in a tertiary centre were most of the patients had symptoms/ complications related to diabetes . 18% of patients were in the age group 30-40 yrs and 16% of patients were in the age group 61-70 yrs.

Body Mass Index

Table 2: Prevalence of BMI

BMI	Male	Female	Percent (%)
Under Weight<18.5	1	2	3
Normal 18.5-24.9	15	15	30
Over Weight 25-29.9	22	11	33
Obese ≥ 30	14	20	34
Total	52	48	100

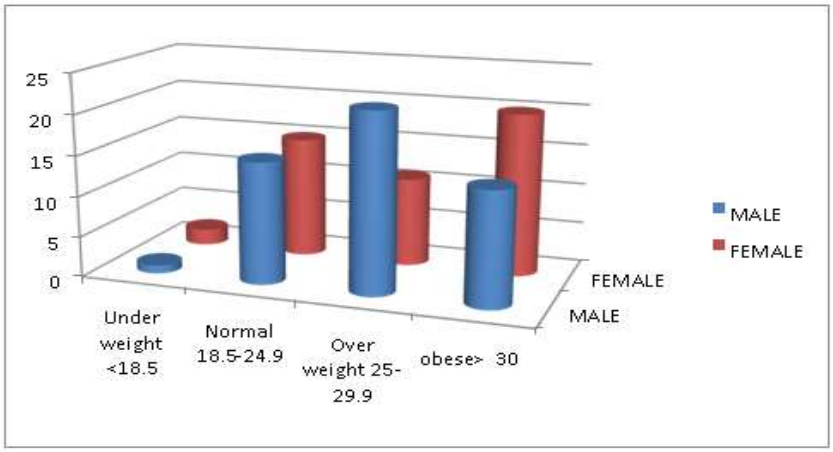

Fig. 2: Prevalence of BMI

30% of patients of both sexes had normal BMI. 33% of patients were overweight, out of which 66.66% were males and 33.33% were females. Obesity was found more in females (58.82%) as compared to males (41.17%) and accounts for 34% of total patients. Thus, 67% of total patients were either overweight or obese.

Table 3: Glycemic status and gender distribution

HbA1c	Male	Female	Percent (%)
<7% Good Control	2	5	7
>7% Poor Control	50	43	93
Total	52	48	100

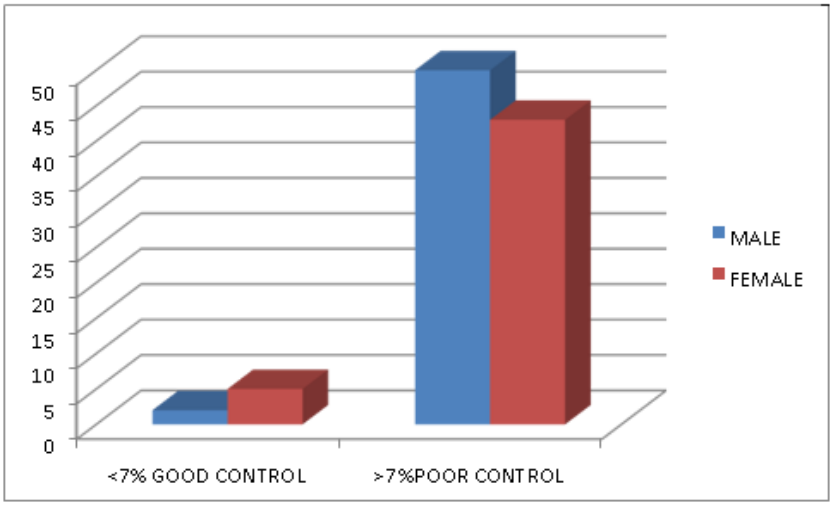

Fig. 3: Glycemic status and gender distribution

93% of all patients included in the study showed poor diabetic control with elevated HbA1c >7%. Males (53.76%) showed poor control as compared to females (46.23%). Good control was only in 7% of cases.

Table 4: Complications and gender distribution

	Male	Female	Percent (%)
Uncomplicated Diabetes	36	33	69
Microvascular Complication	10	8	18
Macrovascular Complication	6	7	13
Total	52	48	100

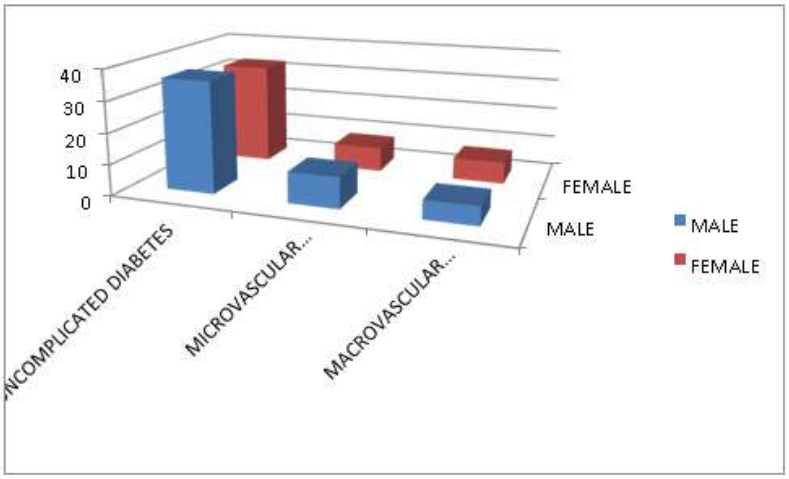

Fig. 4: Complications and gender distribution

69% of total patients included in the study showed no complications while 31% were found to have either microvascular or macrovascular complications.

Table 5: Complications in relation to duration of diabetes

Duration of Diabetes	Uncomplicated Diabetes	MicroVascular Complication	Macro Vascular Complication	Percent (%)
<5yr	29	6	4	39
6-10yr	28	5	5	38
11-15yr	12	6	2	20
>15yr	0	1	2	3
Total	69	18	13	100

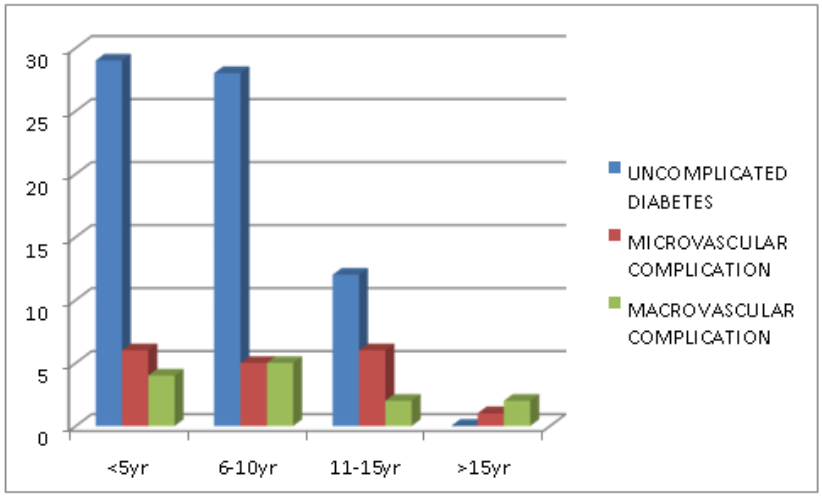

Fig. 5: Complications in relation to duration of diabetes

Diabetic patients of <5 yr duration, 25.64% of patients had complications, while 6- 10 yr duration were 26.31%, while 11- 15 yrs duration were 40% .while >15yr duration were 100% , this shows duration of diabetes is directly proportional to complications.

Hypercholesterolemia

Table 6: Prevalence of hypercholesterolemia

Lipid Profile	Male	Female	Percent (%)
Normal	14	7	21
Hypercholesterolemia	38	41	79
Total	52	48	100

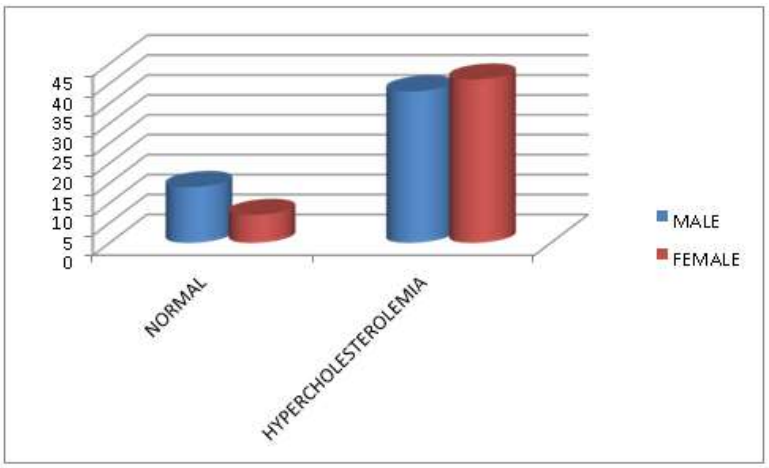

Fig. 6: Prevalence of hypercholesterolemia

79% of total patients showed hypercholesterolemia with almost equal proportion in males (48.10%) and females (51.89%).

Table 7: Duration of DM and hypercholesterolemia

Duration of DM	Normal Lipid Profile	Hypercholesterolemia	Percent (%)
<5yr	7	32	39
6-10yr	10	28	38
11-15yr	3	17	20
>15yr	1	2	3
Total	21	79	100

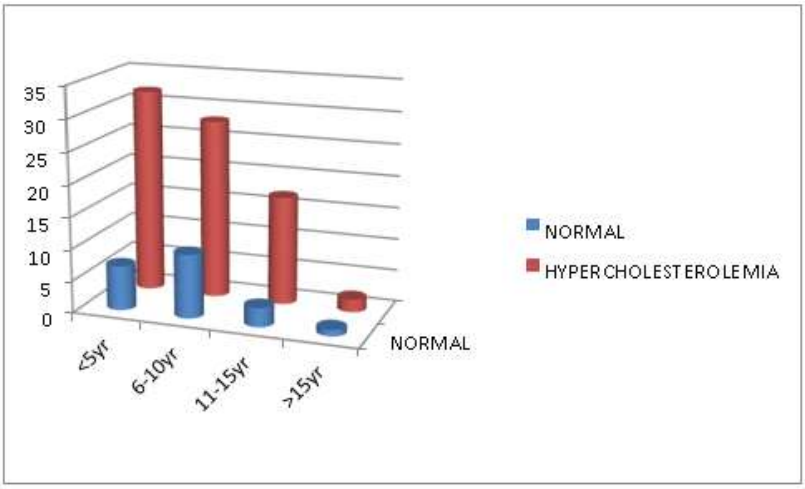

Fig. 7: Duration of DM and hypercholesterolemia

82.05 % of diabetic patients showed hypercholesterolemia with <5yr duration, 73.68% with 6-10yr duration and 85 % with 11- 15 yr duration , this shows hypercholesterolemia is directly proportional to duration of diabetes.

Table 8: Hypercholesterolemia and glycemic status

HbA1c	Normal Lipid Profile	Hypercholesterolemia	Percent (%)
<7% Good Control	2	5	7
>7% Poor Control	19	74	93
Total	21	79	100

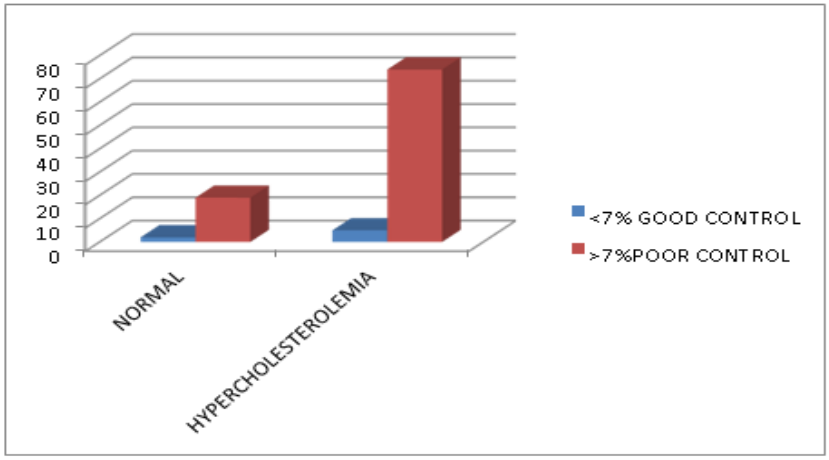

Fig. 8: Hypercholesterolemia and glycemic status

79.56% with poor glycemic control had hypercholesterolemia while only 28.57% showed normal cholesterol with good glycemic control. Poor glycemic control is directly proportional to hypercholesterolemia.

Table 9: Complications in relation to glycemic status

	< 7% Good Control	>7% Poor Control	Percent (%)
Uncomplicated Diabetes	6	63	69
Microvascular Complication	1	17	18
Macrovascular Complication	0	13	13
Total	7	93	100

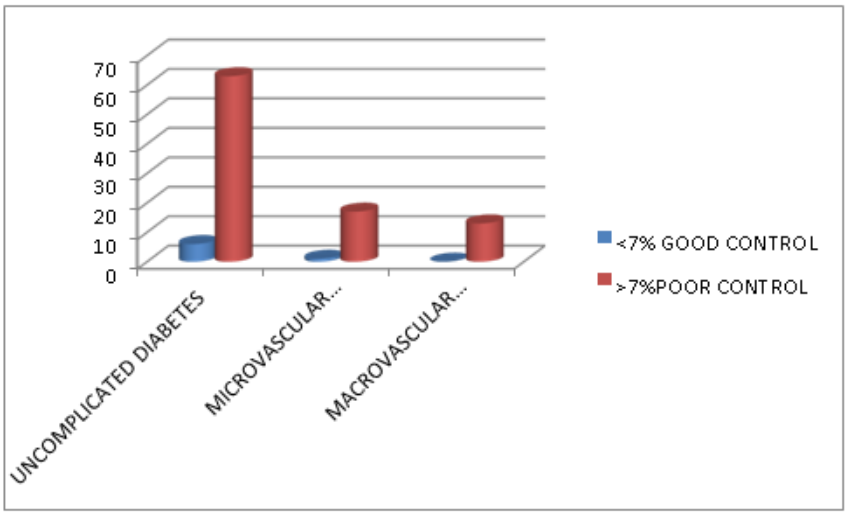

Fig. 9: Complications in relation to glycemic status

93% of total patients with poor glycemic control, 18.27% had micro vascular complications and 13.97% had macro vascular complications.

Table 10: Lipoprotein (a) levels and gender distribution

Lipoprotein (A)	Male	Female	Percent (%)
Normal	39	29	68
Abnormal	13	19	32
Total	52	48	100

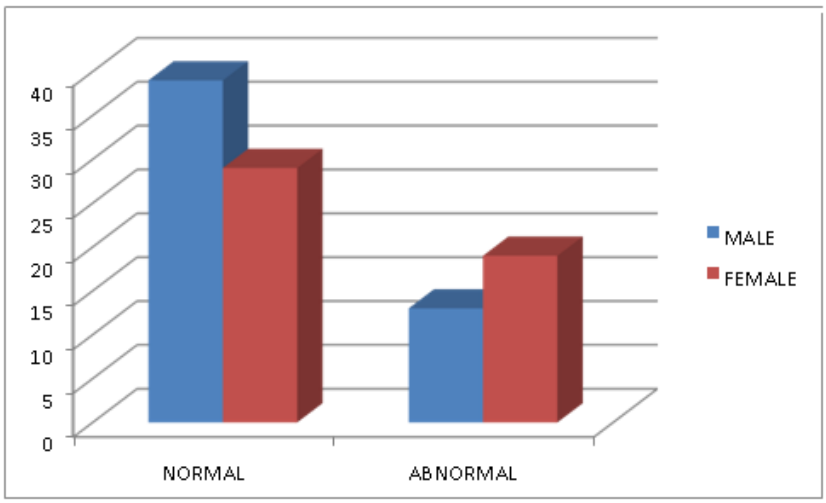

Fig. 10: Lipo protein (a) levels and gender distribution

68% of total patients showed normal Lp (a) levels while 32% showed elevated Lp(a) levels, the elevated were more in females(59.37%) compared to males(40.62%).

Table 11: Lipoprotein (a) levels in relation to complications

Lp (a) Level	Uncomplicated Diabetes	Microvascular Complication	Macrovascular Complication	Percent (%)
Normal	52	10	6	68
Abnormal	17	8	7	32
Total	69	18	13	100

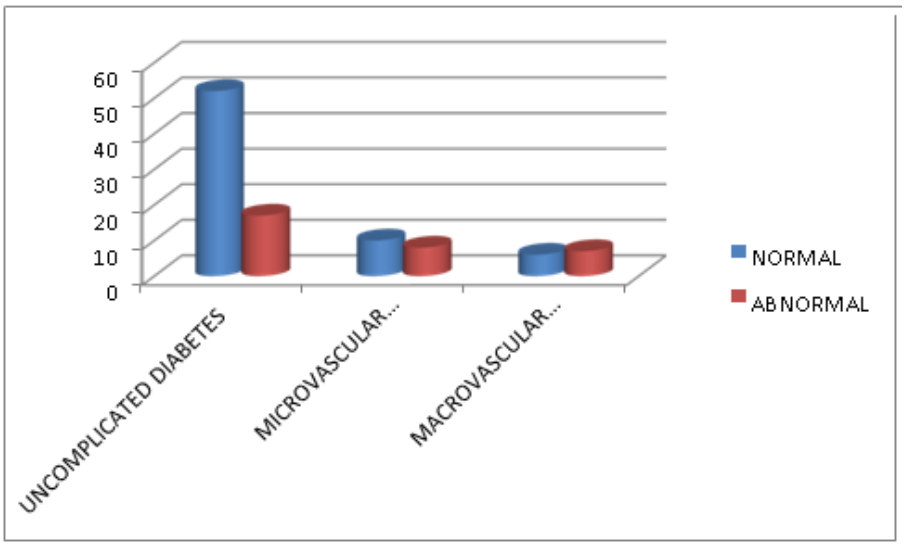

Fig. 11: Lipoprotein (a) levels n relation to complications

51.61% of complicated diabetes had normal Lp (a) levels while 48.38% had elevated levels. 75.36% of uncomplicated diabetes had normal Lp (a) levels and 24.63% had elevated Lp (a) levels.

Table 12: Homocysteine levels and gender distribution

Homocysteine	Male	Female	Percent (%)
Normal	27	27	54
Abnormal	25	21	46
Total	52	48	100

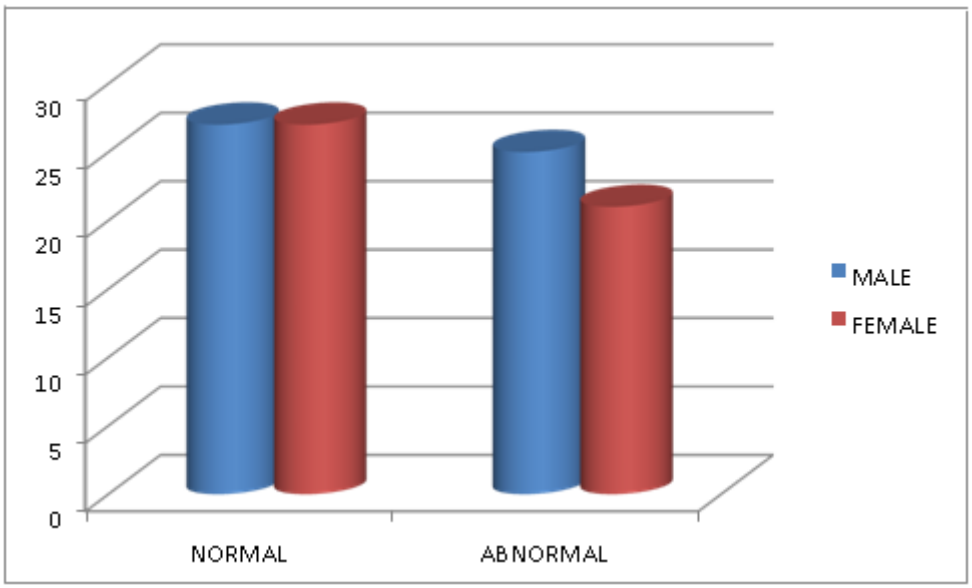

Fig. 12: Homocysteine levels and gender distribution

46% of diabetic patients had elevated homocysteine levels with almost equal distribution in both sexes.

Table 13: Homocysteine levels in relation to complications

Homocysteine Levels	Uncomplicated Diabetes	Microvascular Complication	Macrovascular Complication	Percent (%)
Normal	41	8	5	54
Abnormal	28	10	8	46
Total	69	18	13	100

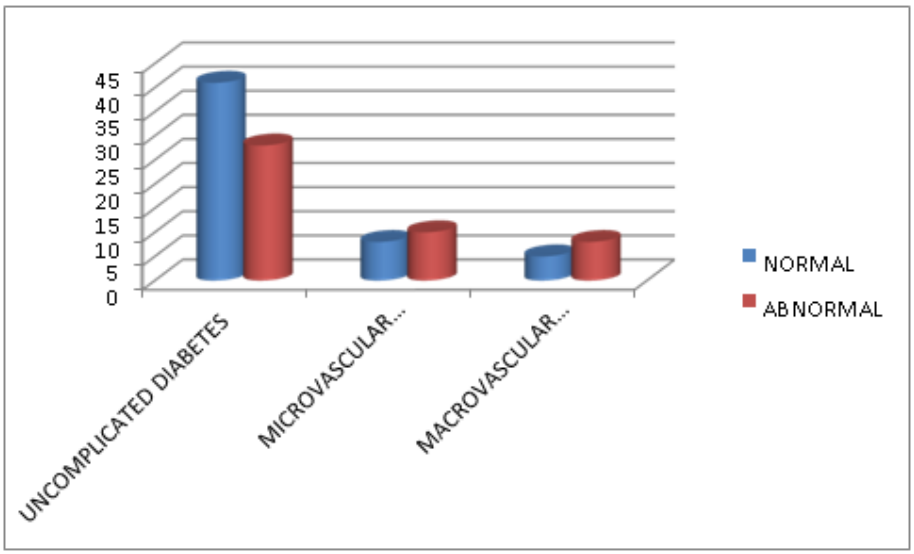

Fig. 13: Homocysteine levels in relation to complications

Homocysteine was elevated in 58.06% of complicated diabetes and 40.5% of uncomplicated diabetes while 59.42% of uncomplicated diabetes and 41.93% of complicated diabetes showed normal homocysteine levels.

DISCUSSION

100 type 2 diabetic patients were included in the study and following categorization into complicated and uncomplicated subsets were correlated with duration of diabetes, body mass index, glycemic status as assessed by HbA1C levels, serum cholesterol levels.

There is a positive correlation between complications and duration of diabetes mellitus, body mass index, glycemic status and elevated cholesterol levels as reported in many studies.

In my study, 67% of patients had a BMI of ≥25 with a mean of 26.84±4.31 is supported with H.E. Bays *et al*. [5] with a mean of 27.9±2.9 and Gabriela Vazquez *et al*. [6] study with a mean of 25.8±4.3.

In my study 93% of total patients with poor glycemic control, 18.27% had microvascular complications and 13.97% had macro vascular complications Diabetic patients of <5 yr duration, 25.64% of patients had complications, while 6- 10 yr duration were 26.31%, while 11- 15 yrs duration were 40% .while >15yr duration were 100%, this shows duration of diabetes is directly proportional to complications.

Hypercholesterolemia was more prevalent in over weight and obese patients with type 2 DM than non-obese patients, which is statistically significant ($p<0.01$) and the findings are supported by Arora [7], Arora *et al*. [8], H. E. Bays *et al*. [5] and Ali Chehrej MD *et al*. [9].

Present study shows that obese patients had significantly elevated TC, TG, and LDL-C and reduced HDL-C than non-obese. In a study by Sunil Gupta *et al*. [10] higher BMI was associated with ↑TC, ↑ TG, and ↑LDL-C. These studies also suggest that ↑BMI was associated with increasing hypercholesterolemia.

The present study suggests that hypercholesterolemia was more prevalent in diabetics and was associated with poor glycemic status. According to A. Al-Adsani *et al*. [11] TC, TG, LDL-C levels were strongly associated with glycemic control. In Ismail *et al*. [12] study glycemic status was an important determinant of TC, TG and LDL-C.

This study also correlated well in support of other studies and established the fact of importance of euglycemic status with lifestyle modifications and appropriate anti diabetic therapy and lipid lowering medication.

In this particular study, the role of lipoprotein (a) and serum homocysteine were additionally estimated to asses either singly or both together as additional factors affecting the diabetes complication.

A significant number of patients showed elevated homocysteine levels might have contributed to the increased type 2 diabetes complications. Our study was supported by study conducted by Martin Buysschaert and Anne-Sophie Dramais. They found that 31% of the cohort (group 1) had raised total homocysteine (mean ± 1 SD) values, whereas group 2 had normal values. The prevalence of macroangiopathy was higher in group 1 than in group 2 subjects [13].

In patients with increased cholesterol levels but with normal homocysteine levels showed lesser number of complications, suggesting that homocysteine is probably an important contributor to the complications of diabetes.

There is a strong case for vitamin B6, B12, folate addition along with lipid lowering medication which is cost effective and contributes to the low incidence of diabetes complications rate.

Lipoprotein (a) levels were elevated in equal proportions in complicated and uncomplicated diabetes, but did not show any correlation with glycemic status, cholesterol and homocysteine levels.

It is probable that lipoprotein (a) [14] may exert any additional effect in promoting atherogenesis as an individual risk factor, but in the study they did not show any positive correlation.

CONCLUSION

Type 2 diabetes mellitus showed a strong correlation between glycemic status and incidence of diabetes complications. Hypercholesterolemia and homocysteine have added to the increased incidence of complications as additional factors in metabolic derangements as a consequence of poor glycemic control.

The role of lipoprotein (a) in complications of diabetes is needed to be evaluated further.

There is a strong case for routine addition of vitamin B6, B12, folate in addition to lipid lowering drugs on a routine basis.

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