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Registry Study for Type 2 Diabetes Mellitus in a Diabetic Center in Saudi Arabia with Comparative Analysis for Controlled Versus Uncontrolled Cases

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Abstract

Background Aims: Comparative analysis of 109 controlled cases versus 120 uncontrolled cases to see the outcome for different treatment methods in type 2 Diabetes Mellitus.

Materials and Methods: The study was conducted in a Diabetic Center, included 229 Type 2 Diabetic Patients with mean age of 49.6 ± 12.6 years. 1.7% of patients were on diet only, 69% on oral hypoglycemic drugs, 4.8% on Insulin and 24.5% on combined insulin & oral hypoglycemic drugs.

Results: Vitamin D Level increased from 31.3 to 70.3ng/ml and 31.4 to 69.6ng/ml in controlled & uncontrolled patients between beginning & end of the study. Total cholesterol, HDL-C, LDL-C & TG improved by -11.2% & -4.8%, +19.8% & +3.1%, -11.1% & 0.8% and -30.4% & -3.4% in controlled & uncontrolled patients respectively.

Hba1c decreased by 15.4% in controlled patients, and by 6.0% in uncontrolled DM patients; (p=0.007). FBG also decreased by 24.9% and 8.1%, for controlled and uncontrolled DM patients. Vitamin D level was investigated in both groups; vitamin D increase (p-value 0.000) has an effect on diabetes mellitus type 2 control. A better lipid profile was seen with controlled patients than uncontrolled patients.

Conclusion: Controlled diabetic patients showed better clinical outcomes than uncontrolled patients regarding lipid profile, HbA1c, FBG and Vitamin D deficiency. Strict diabetes control regulates TG and HDL-C, which in turn decreases CV risk.

Keywords: Diabetes Mellitus type II; Control, Vitamin D; Lipid Profile;

Introduction

Type 2 Diabetes Mellitus [DM] incidence is increasing worldwide, and it can be due to many risk factors such as genetic, environmental or behavioral factors. [1] It is suggested through epidemiological data that 90% of type 2 diabetes cases are due to lifestyle and modifiable habits. [2] The main non-genetic risk factor is obesity. So, weight loss was shown to delay type 2 DM, however solely it is hard to maintain and depend on. [3-5]

Previous studies concluded that type 2 DM causes various microvascular [6-7] and macrovascular [8-9] complications, such as stroke [10], neuropathy [7], myocardial infarctions [6,11] and mortality [9,12]. The previous factors are due to the different glycaemia impairment thresholds. The risk of microvascular disorders is with extreme glycaemia concentrations, whereas it is believed that the risk of myocardial infarction increases with any increase in glycaemia. [13-14]

Prospective studies have shown that the majority of diabetic people become disabled or die due to vascular complications' consequences. [15] Glycated hemoglobin levels in addition to glycaemia levels are associated with major vascular complications. [16] Current guidelines recommendations for diabetic patients is to reach HbA1c of 7.0% or less. [17]

According to the International Diabetes Federation, Saudi Arabia is nationally considered one of the highest countries in the prevalence of diabetes around the world, as per the International Diabetes Federation [18]. Over the past few decades, Saudi Arabia has become a prompt developing country, where people's lifestyle has shifted to urbanization. It has been suggested by former studies that diabetes is present epidemically in Saudi Arabia, especially in urban areas. [19]

In this study we aim to compare between controlled and uncontrolled type 2 diabetic patients. The patient's FBG and HbA1c were assessed at the beginning and end of the study. Also, the patients' lipid profile was assessed and compared, since dyslipidemia [20] frequently accompanies diabetes type 2, increasing the risk of cardiovascular disease and hypertension.

Materials and Methods

An observational study was carried out on 229 Type 2 Diabetes Mellitus patients at a Diabetic Center in Riyadh, Saudi Arabia for four months enrollment between the 1st of January 2013 and 31st of March 2013. The statistical analysis will include:

Descriptive statistics included frequency tables (n, mean, median and standard deviation for continuous variables and n, frequency and percentage for categorical values). To test the differences between controlled and uncontrolled patients; paired t-test at 95% Confidence Interval was performed.

The patients were classified into two groups; 120 (52.4%) controlled and 109 (47.6%) uncontrolled, according to level of HbA1c and/or FBG, so patients with HbA1c of 7% or less are in the controlled group and if above 7% are in the uncontrolled group and FBG of 7 mmol/L or less are in the controlled group and above 7 mmol/L are in the uncontrolled group.

Out of the total 229 patients; 120 were controlled patients 63 (52.5%) were males and 57 (47.5%) were females. As for the remaining 109 uncontrolled DM patients; 63 (57.8%) of them were males, and 46 (42.2%) were females. The mean age for both groups was 49.2±12.7 and 50.1±12.6 years, for controlled and uncontrolled patients respectively.

Diabetic patients often suffer from vitamin D deficiency (142 patients), dyslipidemia (104 patients) and hypertension (75 patients). The highest was vitamin D deficiency, 79 (65.8%) and 63 (57.8%) for controlled and uncontrolled patients, respectively, as seen in table 1.

Hypertension (>140 /90 mmhg), Vitamin D Deficiency (< 30 mmol/L), Dyslipidemia (Total Cholesterol >6 mmol/L), Hypothyroid (TSH > 10)

As for type 2 DM treatments; different treatments were used oral hypoglycemic, insulin only, insulin & oral hypoglycemic and diet only, as seen in table 2.

Results

The hba1c and FBG were measured at the start and at the end of the study for all patients. Hba1c decreased 15.4% in controlled DM patients, while it decreased by 6.0% in uncontrolled DM patients. Showing highly statistical significant results (*p*-value 0.007) between the two groups. As for FBG, it decreased by 24.9% and 8.1% for controlled and uncontrolled respectively, with no significant statistical difference in either groups, as seen in table 3.

For the overall sample, there was a decrease in both hba1c and FBG by 10.7% and 15.9% respectively for patients taking oral hypoglycemic, both hba1c and FBG showed a very highly statistical significant result regarding diabetes management (*p*-value 0.000). As for patients taking both insulin & oral hypoglycemic; there was a decrease in hba1c & FBG between the start and end of the study, by -10.7% and -20.2% respectively, hba1c showing a very highly statistical significant results (*p*-value 0.000) and FBG showing a statistically significant results regarding diabetes control (*p*-value 0.020). There was also a decrease in hba1c and FBG for patients taking insulin only, by -7.4% and -12.7% respectively, hba1c showing statistical significance (*p*-value 0.065) and FBG showing no statistical significance. As for patients who were only regulating diet; there was a decrease in hba1c and an increase in FBG, by -6.3% and 3.1% respectively, with no statistical significant results for both hba1c and FBG. As seen in table 4.

The controlled DM group, total cholesterol, LDL-C, HDL-C, and triglycerides showed percent changes by -11.2%, -11.1%, 19.8%, -30.4%, respectively. And for the uncontrolled DM group, showed significant percent changes by -4.8%, -0.8%, 3.1% & -3.4% respectively between first and last visits, as seen in table 5.

Vitamin D results at base line and at the end of the study for both controlled and uncontrolled was very highly statistically

Table 1: Medical History

Medical History*	Controlled (n=120)		Uncontrolled (n=109)	
	No.	% of Pts.	No.	% of Pts.
Vitamin D Deficiency	79	65.80%	63	57.80%
Hypertension	34	28.30%	41	37.60%
Dyslipidemia	46	38.30%	58	53.20%
Hypothyroid	20	16.70%	8	7.30%
Others †	4	3.20%	7	6.30%

† Others: Obesity, Hyperthyroid, Thyroid nodule/Goiter, Papillary carcinoma, Anemia, Post Thyroidectomy, Hypocalcaemia & Renal failure.

Table 2: DM Treatment

	Total	Controlled	%	Uncontrolled	%
Oral	158	92	76.7%	66	60.6%
Insulin and Oral	56	20	16.70%	36	33.0%
Insulin	11	4	3.30%	7	6.4%
Diet only	4	4	3.3%	0	0.0%
Total	229	120	100.0%	109	100.0%

Table 3: HbA1c & FBG

	HbA1c % (base line)	HbA1c % (end of the study)	FBG mmol/L (base line)	FBG mmol/L (end of the study)
	Controlled			
N	115	115	77	77
Mean	7.7	6.5	8.4	6.3
SD	1.9	0.9	3	1.1
Mean Diff.	-1.2		-2.1	
% change	-15.4%		-24.9%	
p-value	**0.000**		**0.000**	
Uncontrolled				
N	103	103	55	55
Mean	9.7	9.1	11.7	10.8
SD	1.7	1.5	3.7	3.3
Mean Diff.	-0.6		-0.9	
% change	-6.0%		-8.1%	
p-value	0.000		0.119	
p-value between Controlled & Uncontrolled	**0.007**		**0.086**	

significant (*p*-value=0.000) when related to diabetes control, as seen in table 6.

Discussion

According to the UK Prospective Diabetes Study [UKPDS], controlled DM type 2 patients achieving median of 7.0% hba1c, have shown a significant reduction in micro-vascular risk of complications and a decrease in myocardial infarction incidence, compared with 7.9% median of hba1c, over a median of 10 years of follow up. [18] Patients with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of CVD. [22, 23]

In our study; we have measured various parameters to see the contrast between controlled and uncontrolled type 2 diabetic patients. The aim of diabetes control is to maintain normal blood glucose levels and to achieve hba1c of 7.0%. Hba1c and FBG decreased by the end of the study. Hba1c decreased by 15.4% in controlled patients, whereas decreased by 6.0% in uncontrolled DM patients; [*p*=0.007]. FBG also decreased by 24.9% and 8.1%, for controlled and uncontrolled DM patients.

Previous studies have compared the intensive treatment with conventional treatment. The intensive treatment showed the following results: 12% reduction [*p*=0.029] to any diabetes related end point; 10% reduction [*p*= 0.34] in death related to diabetes; 16% reduction [*p*=0.052] in myocardial infarction; 11% increase [*p*=0.52] in stroke incidence; and 25% reduction [*p*=0.0099] in microvascular diseases. [24]

Another study performed in Kumamoto, Japan compared 100 randomized type 2 diabetic patients with intensive and conventional insulin therapy, and were followed up for 6 years. The intensively treated group had less retinopathy [13% vs 38%, *p*=0.007], nephropathy [10% vs 30%, *p*=0.005], and neuropathy [12.8% vs 64.6% increase in lower extremity vibration threshold, *p*< 0.05] than the conventionally treated group. The hba1c levels at the end of the study were 7.1% vs 9.4% in the two groups, respectively. [25]

It was also seen that the treatment with metformin showed a significant advantage over the conventional treatment in obese patients [n=1704]: a 32% reduction of diabetes-related end points [*p*=0.002], a 42% reduction of diabetes-related deaths [*p*=0.017], and a 36% reduction of all-cause mortality [*p*=0.011]. Patients taking metformin also had less weight gain and fewer hypoglycemic attacks than those taking insulin or sulfonylureas. The above results show that the complications in type 2 diabetes are reduced through the reduction of blood glucose. [24] In our study, for patients taking oral hypoglycemic there was a decrease in both hba1c and FBG by 10.7% and 15.9% respectively [*p*-value 0.000]. Also in patients taking both insulin & oral hypoglycemic; there was a decrease in hba1c & FBG between the start and end of the study, by -10.7% [*p* value 0.000] and -20.2% [*p*-value 0.020] respectively. As for patients taking insulin only, by -7.4% and -12.7% for hba1c and FBG respectively, and patients only regulating diet; there was a decrease in hba1c and an increase in FBG, by -6.3% and 3.1% respectively. This conveys how controlling diabetes shows significant difference in regulating both hba1c and FBG.

Table 4: HbA1c & FBG per Treatment Regimen

		HbA1c % (base line)	HbA1c % (end of the study)	FBG mmol/L	FBG mmol/L
Oral	N	149	149	98	98
	Mean	8.4	7.5	9.4	7.9
	SD	2.0	1.7	3.5	2.9
	Mean Diff.	-0.9		-1.5	
	% change	-10.7%		-15.9%	
	p-value	**0.000**		**0.000**	
Insulin and Oral	N	54	54	27	27
	Mean	9.4	8.4	11.8	9.4
	SD	2.0	1.7	4.0	4.2
	Mean Diff.	-1.0		-2.4	
	% change	-10.7%		-20.2%	
	p-value	**0.000**		**0.020**	
Insulin	N	11	11	3	3
	Mean	9.2	8.5	9.1	8.0
	SD	2.2	2.1228	3.6	1.6
	Mean Diff.	-0.7		-1.2	
	% change	-7.4%		-12.7%	
	p-value	**0.065**		**0.458**	
Diet only	N	4	4	4	4
	Mean	6.7	6.3	7.0	7.3
	SD	0.9	0.4	1.5	1.2
	Mean Diff.	-0.4		0.2	
	% change	6.3%		3.1%	
	p-value	**0.383**		**0.525**	

Another similar trial randomized 153 men with type 2 diabetes to intensive control or standard therapy. At the end of 27 months of follow-up, the mean hba1c values were significantly lower in the intensive group [7.3% vs 9.4%; *p* <0.001]. [26] In a previous study, it was illustrated that the median for hba1c was 8.4% for conventional therapy and 6.9% for intensive therapy. [27] Also, it was seen that the risk for micro-vascular problems decreases by 37% and the risk of mortality decreases by 21% for each 1% reduction in hba1c. [28-30] The incidence of micro-vascular risk was lower than that of myocardial infarction in patients with the lowest category of mean hba1c.[11] This illustrates how hyperglycemia may be a contributing factor for cardiovascular risk for diabetic patients, rather than only the conventional risks, such as smoking, hypertension and dyslipidemia. [31]

Numerous studies, which were conducted to observe the correlation between Vitamin D insufficiency and type 2 DM, is recently being investigated to see the links and correlation between them.[32-33] Vitamin D insufficiency is common in type 2 DM patients, resulting in lowering insulin secretion from the pancreas, however with no alterations in glucagon secretion. [34] Evidence show that supplementation of vitamin D in type 2 DM patients improves impaired glucose tolerance and insulin resistance through increasing the release of pancreatic insulin by

Table 5: Lipid Profile								
	Cholesterolmmol/L (base line)	**Cholesterol mmol/L (end of the study)**	**LDL-C mmol/L (base line)**	**LDL-C mmol/L (end of the study)**	**HDL-C mmol/L (base line)**	**HDL-C mmol/L (end of the study)**	**Triglyceride mmol/L (base line)**	**Triglyceride mmol/L (end of the study)**
controlled								
N	81	81	78	78	75	75	80	80
Mean	4.9	4.3	2.9	2.6	1.1	1.3	2.2	1.5
SD	1.3	1	0.9	0.8	0.3	1.1	3.7	0.8
Mean Diff	-0.5		-0.3		0.2		-0.7	
% change	-11.2%		-11.1%		19.8%		-30.4%	
p-value	**0.002**		**0.005**		**0.080**		**0.091**	
Uncontrolled								
N	51	51	50	50	50	50	52	52
Mean	5.1	4.8	3.2	3.1	1.1	1.1	2.2	2.1
SD	1.2	1.1	0.9	1.7	0.2	0.3	1.7	1.9
Mean Diff	-0.2		0.0		0.0		-0.1	
% change	-4.8%		-0.8%		3.1%		-3.4%	
p-value	**0.134**		**0.908**		**0.112**		**0.746**	

Table 6: Vitamin D & S. Calcium				
	Vitamin D ng/ml (base line)	**Vitamin D ng/ml (end of the study)**	**Serum Calcium mmol/L (base line)**	**Serum Calcium mmol/L (end of the study)**
Controlled				
N	62	62	71	71
Mean	31.3	70.3	2.2	2.2
SD	13.6	27.5	0.1	0.3
Mean Diff	39.0		0.0	
% change	124.3%		-0.3%	
p-value	**0.000**		**0.832**	
Uncontrolled				
N	39	39	50	50
Mean	31.4	69.6	2.3	2.3
SD	9.5	32.5	0.1	0.1
Mean Diff	38.2		0.0	
% change	121.4%		0.9%	
p-value	**0.000**		**0.109**	

stimulating its synthesis in pancreatic islets. [34-35] There are data that also link and suggest that low vitamin D level might be causally linked to impaired insulin sensitivity.[36-38] It was also found that endothelial function, which is a powerful marker for cardiovascular risk is improved with vitamin D supplementation. [34] In our study vitamin D was investigated in both uncontrolled and controlled groups, it was shown to increase Vitamin D level by; 121.4% and 124.3% respectively, both showing very highly significant results in our study [*p*-value 0.000], that vitamin D status has an effect on diabetes mellitus type 2 control. Vitamin D enhances calcium reabsorption by the kidney and increases the ingested calcium uptake by the gut, leading to the increase of both minerals in the plasma. [39] So, previous studies were made to see the effect of Vitamin D on insulin and its resistance, however in our study we investigate the effect of diabetes control on vitamin D levels and by subsequence the effect on Calcium levels.

Numerous studies have also been made on the correlation between calcium status and diabetes. It has been found that calcium levels are lower in diabetic patients compared to control non-diabetic patients. [40] It was also seen in some prospective studies that low calcium intake is inversely correlated with type 2 DM incidence. [41-44] However, in our study serum calcium showed non-significant results when related to diabetes in either groups p=0.109 and p=0.832 for the uncontrolled group and controlled group, respectively.

Dyslipidemia is one of the main diseases that accompany Diabetes Mellitus, so lipid concentration is a marker of the condition. A prior study illustrated that improved glycemic control has been shown to lower LDL_C levels, [45-48] which theoretically should lower the risk of developing CHD for patients with diabetes. [49-52] In this study, it was seen that controlled patients showed a better lipid profile than uncontrolled patients, since total cholesterol, LDL-C and Triglyceride [TG] levels declined more in controlled patients and HDL-C increased more in controlled patients. The cholesterol level decreased from base line to the end of the study by 4.8% and 11.2%, for uncontrolled [*p*-value 0.134] and controlled [*p*-value 0.002] patients

respectively. LDL-C decreased markedly in controlled patients than in uncontrolled patients, by 11.1% and 0.8%, respectively. Also, TG decreased by 3.4% on uncontrolled patients, while was decreased by 30.4% in controlled patients. As for HDL-C, it increased by 19.8% in controlled patients but only by 3.1% in uncontrolled patients.

Conclusion

Controlled diabetic patients showed better clinical outcomes than uncontrolled patients regarding lipid profile, hba1c, FBG and Vitamin D deficiency. Strict diabetes control regulates TG, LDL-C and HDL-C, which in turn decreases CV risk.

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