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Study of Lipid profile, Oxidative stress and Cardiopulmonary Parameters among Diabetes patients and its Management

Dr Syed Ateeq Ahmed Jafri[1], Dr Ahmed Abdul Bari Hazari[2], Dr. Rafia Jabeen Anwari[3]

[1]Assistant Professor, Department of Biochemistry, Ayaan Institute of Medical Sciences, Hyderabad.

[2] Associate Professor, Department Of Pharmacology, Ayaan Institute Of Medical Sciences, Hyderabad

[3]Associate Professor, Department of Physiology, Government Medical College; (GMC) Wanaparty, Government of Telangana

Corresponding Author: Dr. Rafia Jabeen Anwari

Abstract

Introduction: Diabetes mellitus (DM) is a syndrome characterized by abnormal insulin secretion, derangement in carbohydrate and lipid metabolism, and is diagnosed by the presence of hyperglycemia. Lipid abnormalities significantly contribute to the increased risk of cardiovascular disease and other morbidity in diabetics. There is a growing body of evidence showing that hyperglycaemia and dyslipidaemia are linked to increased cardiovascular risk. Oxidative stress induced by reactive oxygen species (ROS), which is generated by hyperglycaemia, is one of the major foci of recent research related to diabetes mellitus. Initial treatment of patients with type 2 diabetes mellitus includes Monotherapy with metformin is indicated for most patients.

Material and Methods: This is a prospective and observational study was conducted in the Tertiary Care Teaching Hospital over a period of 1 year. The patients were selected according to the American Diabetes Association (ADA) and include only those with type 2 diabetes, for a minimum of 3 months, and who met the following criteria for the study. These criteria were: type 2 diabetes mellitus without malnutrition or severe complications of the disease (cardiovascular, renal, visual and cerebral). Measurement of the variations of Physiological and Biochemical parameters was used to check. Spirometry is the most frequently used measure of lung function and is a measure of volume against time.

Results: In our study, FEV1 in Case Group was 2.42±0.44 and in Control Group 3.84±0.45. FVC of Case Group: 2.83±0.29 and Control Group: 3.79±0.45. There was statistical Significant between two groups. The differences in oxidative stress parameters across groups. Between controls and cases participants, there was a significant difference in TAOS ($p<0.000$) and MDA ($p<0.000$). In this study shows that mono and combination therapies for the treatment of type II DM. The present study revealed that most of the physicians initially prescribed mono therapy (25%) includes Metformin/Glibenclamide/Glimepiride/Gliclazide to control hyperglycaemia followed by dual therapy (35%) FDC of Metformin + Pioglitazone/Metformin + Glipizide/Metformin + Glimepiride/ Metformin + Saxagliptin/ Metformin +Voglibose and triple therapy (40%) includes Metformin + Glimepiride + Pioglitazone in Case group.

Conclusion: Patient-centered diabetes management can be accomplished with lifestyle modification and combination therapy. Metformin is an optimal first-line agent; newer GLP1 and SGLT2 agents have efficacy for glucose lowering coupled with weight loss and potential

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cardiovascular risk reduction; and insulin therapy is generally safe and effective for patients not controlled with noninsulin agents.

Keywords: Lipid profile, Cardiopulmonary fitness, Oxidative stress Diabetes, Management

Introduction

Diabetes mellitus (DM) is a syndrome characterized by abnormal insulin secretion, derangement in carbohydrate and lipid metabolism, and is diagnosed by the presence of hyperglycemia. [1] Diabetes is a major worldwide health problem predisposing to markedly increased cardiovascular mortality and serious morbidity and mortality related to development of nephropathy, neuropathy and retinopathy. [2] The prevalence of type 2 DM among adults varies from less than 5% to over 40% depending on the population in question. Due to increasing obesity, sedentariness and dietary habits in both Western and developing countries, the prevalence of type 2 DM is growing at an exponential rate. [3]

Lipid abnormalities significantly contribute to the increased risk of cardiovascular disease and other morbidity in diabetics. There is a growing body of evidence showing that hyperglycaemia and dyslipidaemia are linked to increased cardiovascular risk. [4] It has been demonstrated that high levels of serum TC, triglycerides, LDL, VLDL, glycated haemoglobin (HbA_{1c}), microalbuminuria, hypertension, low concentration of HDL and increased body mass index (BMI) are significantly associated with coronary heart disease. [5]

Oxidative stress induced by reactive oxygen species (ROS), which is generated by hyperglycaemia, is one of the major foci of recent research related to diabetes mellitus. Diabetes mellitus is characterized by hyperglycaemia together with biochemical alterations of glucose and lipid peroxidation. [6] There are several studies that have evaluated free radical induced lipid peroxidation and the antioxidants in diabetic patients. [7] Some complications of diabetes mellitus are associated with increased activity of free radical-induced lipid peroxidation and accumulation of lipid peroxidation products. [8] Mechanisms that contribute to increased lipid peroxide formation in diabetic patients include: hyperglycaemic-induced glucose auto-oxidation, non-enzymatic glycation of proteins and lipids, increased sorbitol pathway activity, oxidation of advanced glycation end-products (AGEs) and cyclooxygenase dependent formation of prostaglandin H2 (PGH_2). [9]

Initial treatment of patients with type 2 diabetes mellitus includes lifestyle changes focusing on diet, increased physical activity and exercise, and weight reduction, reinforced by consultation with a registered dietitian and diabetes self-management education, when possible. [10] Monotherapy with metformin is indicated for most patients, and insulin may be indicated as initial treatment for those who present with catabolic features (polyuria, polydipsia, weight loss in the setting of very high glucose levels, eg, glycated hemoglobin [A1C] >9 percent). [11]

For most patients, we add a second medication when the individualized glycemic treatment goal is not achieved within three months with metformin plus lifestyle intervention. This is consistent with guidelines from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) consensus guideline for medical management of hyperglycemia and underscores the importance of avoiding delay in treatment intensification.

Material and Methods:

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This is a prospective and observational study was conducted in the Tertiary Care Teaching Hospital over a period of 1 year.

Inclusion Criteria: The patients were selected according to the American Diabetes Association (ADA) and include only those with type 2 diabetes, for a minimum of 3 months, and who met the following criteria for the study. These criteria were: type 2 diabetes mellitus without malnutrition or severe complications of the disease (cardiovascular, renal, visual and cerebral).

Exclusion Criteria: Morbid obese, chronic alcoholism, Chronic Smoking, pregnant, lactating women, kyphosis, scoliosis.

Measurement of the variations of Physiological and Biochemical parameters was used to check. Spirometry is the most frequently used measure of lung function and is a measure of volume against time. It is a simple and quick procedure to perform: patients are asked to take a maximal inspiration and then to forcefully expel air for as long and as quickly as possible (a forced vital capacity manoeuvre). Measurements that are made include:

- Forced expiratory volume in one second (FEV1)
- Forced vital capacity (FVC)
- The ratio of the two volumes (FEV1/FVC)

All of the above measurements were carried out under standard environmental conditions, by continuously measuring the temperature, humidity, and atmospheric pressure which enabled comfort temperature. Body mass (kg) and body height (m) was measured using standardized anthropometric techniques. Body mass index was calculated for all participants as the ratio of body mass (kg) divided by the body height (m) squared.

On the baseline visit, medical history was reviewed, demographic data were recorded, and blood samples taken for biochemical investigations. Blood was drawn from an antecubital vein. The blood was drawn between 7:30 am and 9:00am, without stasis, and the serum was separated within an hour of collection. The biochemical investigations that were determined included lipid profile – serum TC, Triglyceride, HDL, LDL and VLDL. Fasting blood glucose was measured. Oxidative stress indicators included: Concentration of Malonaldehyde (MDA), Total antioxidants (TAOS). The fasting blood glucose concentration was determined by glucose-oxidase method. Total cholesterol, triglyceride and HDL were determined by enzymatic methods. High density lipoprotein was measured after precipitating VLDL and LDL cholesterol in the presence of magnesium ions. The LDL fraction was calculated by the Friedwald formula. Malondialdehyde concentration in the serum was measured spectrophotometrically according to Yagi Method.

Results:

Table 1: Distribution of Anthropometric parameters of cases and control Group

Parameter	Case Mean ± SD	Control Mean ± SD	p value
Age (years)	48.35 ±4.34	46.34 ± 4.62	0.446

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Height (cms)	167.34 ± 14.32	165.34 ± 14.53	0.089
Weight (kg)	67.54 ± 6.45	63.64 ± 6.53	0.001
BMI (kg/m^2)	25.65 ± 2.42	21.34 ± 2.63	0.001
WHR	0.81 ± 0.07	0.81 ± 0.02	0.005

There was no significant difference in age, height of the study subjects, as indicated in Table 1. Between case and control group, there was a significant difference in weight ($p< 0.001$), BMI ($p <0.001$), and WHR ($p <0.005$) in table 1.

Table 2: Distribution of cardiovascular parameters of cases and control Group

Parameter	Case Mean ± SD	Control Mean ± SD	p value
HR (bpm)	87.26 ± 3.40	76.72± 3.24	0.001
SBP (mmHg)	131.32 ± 11.54	122.48 ± 11.53	0.001
DBP (mmHg)	93.14 ± 8.45	81.53 ± 7.21	0.001
MAP(mmHg)	99.34 ± 9.24	86.43 ± 7.34	0.001

Individuals are shown and Heart rate ($p <0.001$), blood pressure (SBP $p< 0.001$, DBP $p <0.001$, MAP $p <0.001$) all showed statistically significant differences in table 2.

Table 3: Comparison of FEV1 and FVC in cases and control Group

	Case Mean ± SD	Control Mean ± SD	p-value*
FEV1	2.42±0.44	3.84±0.45	<0.05
FVC	2.83±0.29	3.79±0.45	<0.05
FEV1/FVC (%)	86.21±7.39	70.42±7.42	<0.05
MVV	96.24±8.32	119.52±11.42	<0.05

FEV1: Forced expiratory volume in 1st second, FVC: Forced Vital Capacity,

FEV1 in Case Group was 2.42±0.44 and in Control Group 3.84±0.45. FVC of Case Group: 2.83±0.29 and Control Group: 3.79±0.45. There was statistical Significant between two groups in table 3.

Table 4: Distribution of Blood Glucose Level between cases and control Group

Parameter	Case Mean ± SD	Control Mean ± SD	p value
Fasting Blood glucose (mg/dl)	148.53□13.64	71.83□8.72	0.001
Post prandial Blood glucose (mg/dl)	215.64□22.75	117.25□21.43	0.001
HbA1c (%)	8.12□0.73	5.35□0.69	0.001

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Table 5: Distribution of Lipid profile between cases and control Group

Parameter	Case Mean ± SD	Control Mean ± SD	p value
Total cholesterol	182.84□17.64	160.67□18.4	0.001
Triglycerides	168.34□16.76	117.25□11.86	0.001
HDL	39.61□3.54	41.69□3.24	0.001
LDL	109.56 ± 7.34	96.34 ± 9.24	0.001
VLDL	21.91± 2.32	23.45± 2.16	0.001

Table 6: Distribution differences in oxidative stress between Case and control group

Parameter	Case Mean ± SD	Control Mean ± SD	p value
TAOS (mM)	0.49± 0.41	1.89 ± 0.52	0.001
MDA (mM)	12.48 ±3.42	7.24 ± 0.84	0.001

The differences in oxidative stress parameters across groups. Between controls and cases participants, there was a significant difference in TAOS ($p<0.000$) and MDA ($p<0.000$) in table 5.

Table 6: Distribution of drug therapy.

Therapy	Case (% of Population)
Monotherapy	25 %
Dual therapy	35 %
Triple therapy	40 %

In table 6, shows that mono and combination therapies for the treatment of type II DM. The present study revealed that most of the physicians initially prescribed mono therapy (25%) includes Metformin/Glibenclamide/Glimepiride/Gliclazide to control hyperglycaemia followed by dual therapy (35%) FDC of Metformin + Pioglitazone/Metformin + Glipizide/Metformin + Glimepiride/ Metformin + Saxagliptin/ Metformin +Voglibose and triple therapy (40%) includes Metformin + Glimepiride + Pioglitazone in Case Group

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Table 7: Management of oral Antidiabetic drug therapy.

Drugs	Case
Metformin, Glibenclamide, Glipizide, Gliclazide, Glimepiride	78%
Dapagliflozin and Teneligliptin	22%

i. Sulfonylureas: Tolbutamide, Glibenclamide, Glipizide, Gliclazide, Glimepiride etc. ii. Meglitinide analogues: Repaglinide, Nateglinide

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iii. Biguanides: Metformin
iv. A Glucosidase inhibitors: Acarbose, Miglitol, Voglibose
v. Thiazolidinediones: Pioglitazone

Discussion

T2DM is mainly characterized by the development of increased morbidity and mortality for cardiovascular disease (CVD), so that it has been suggested that diabetes may be considered a cardiovascular disease. [12] However, CVD risk is elevated long before the development of diabetes. One of the most important of these possible antecedents is considered insulin resistance. In genetically predisposed subjects, the combination of excess caloric intake and relatively scarce physical activity, with the likely consequence of obesity, can induce a state of resistance to the action of insulin. [13]

Many studies have suggested that β-cell dysfunction results from prolonged exposure to high glucose, elevated FFA levels, or a combination of both. [14] β Cells are particularly sensitive to ROS because they are low in free-radical quenching (antioxidant) enzymes such as catalase, glutathione peroxidase, and superoxide dismutase. Therefore, the ability of oxidative stress to damage mitochondria and markedly blunt insulin secretion is not surprising; for example, it has been demonstrated that oxidative stress generated by short exposure of β-cell preparations to H_2O_2 increases production of p21 and decreases insulin mRNA, cytosolic ATP, and calcium flux in cytosol and mitochondria. [15]

The key role of increased glucose metabolism in producing impaired β-cell function through oxidative stress has recently been confirmed. Intracellular ROS increased 15 minutes after exposure to high glucose, and this effect was blunted by inhibitors of the mitochondrial function. [16] Glucose-induced insulin secretion was also suppressed by H_2O_2, a chemical substitute for ROS. Impaired insulin secretion has been associated with an FFA-induced increase in ROS, both in vitro and in vivo. [17] Interestingly, it has been reported that both FFA and glucose may impair insulin secretion in β cells by activating uncoupling of protein. [18] In the case of hyperglycemia, it has been shown that such activation is accomplished by hyperglycemia-induced superoxide formation in mitochondria. [19]

In this study, we found a positive correlation between TG and a negative correlation between LDL-c, HDL-c. It is widely recognized that insulin resistance (IR) plays a critical role in the pathogenesis of dyslipidemia. However, in contrast, one study suggested that lipid buildup also causes IR. [20] Studies have shown that IR impacts the metabolism of triglycerides, HDLc, and low-density lipoprotein cholesterol (LDL-c) through several mechanisms. [21] Increased levels of hepatic triglyceride lipase (HTGL) have also been associated with IR, which may result in faster HDL-c clearance and lower HDL-c levels, ultimately causing hypertriglyceridemia and reduced HDL-c values. It should be noted that dyslipidemia are risk factors for CVDs and DM. [22]

Conclusion

Patient-centered diabetes management can be accomplished with lifestyle modification and combination therapy. Metformin is an optimal first-line agent; newer GLP1 and SGLT2 agents have efficacy for glucose lowering coupled with weight loss and potential cardiovascular risk reduction; and insulin therapy is generally safe and effective for patients not controlled with

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noninsulin agents. In younger, healthy, newly diagnosed patients, a hemoglobin A_{1c} level less than 7% should be the goal; in older individuals with comorbidities, less stringent goals with a focus on safety and avoidance of hypoglycemia are critical. Antihyperglycemic therapy should be combined with evidence-based treatment of cholesterol and blood pressure for cardiovascular risk reduction. Although the cardiovascular benefits of SGLT2 and GLP1 agents merit consideration, these medications are not replacements for statin therapy or blood pressure management for reducing the risk of cardiovascular disease.

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