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Original Research Article

Evaluation of Diabetes with Obesity as a Risk Factor

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Abstract

Introduction: Obesity is a condition marked by pathological excess of body fat. Accumulation of harmful lipid species takes place in ectopic tissues. This results in local inflammation, thereby leading to endothelial dysfunction, insulin resistance, and non-alcoholic fatty liver disease. Hyperglycemia causes a series of dysregulated metabolic changes.

Aims and Objective: To find out the effect of obesity in patients with type-2 diabetes mellitus.

Methods: This is an observational study that was conducted on 100 patients with type II diabetes mellitus. The patients were divided into two groups, namely, the obesity group with 55 patients and the control group with 45 patients. The baseline characteristics of the patients were analyzed as other clinical and laboratory features related to diabetes and obesity. The parameters were analyzed and compared statistically between the two mentioned groups.

Results: The study found that there are significant differences between the two groups in Fasting Blood Glucose, Total Cholesterol, LDL, SBP, and cardiopulmonary complications like Atrial Fibrillation, Frequent Pulmonary Infection, and Hypertension ($p<0.05$). It was found that there is a significant difference in BMI and Waist Hip Ratio (WHR) between the 2 groups ($p<0.05$). The fasting blood glucose is seen as high in the obesity group (154.23±4.65), and HbA1c % is slightly high in the obesity group. HDL levels are high in the control group (59.23±3.67) and LDL is seen high in the obesity group (229.35±6.5).

Conclusion: The study has concluded that obesity can be considered a risk factor for diabetes which specifically impacts long-term cardio-pulmonary complications.

Keywords: hypertension, obesity, diabetes, hypertension, BMI.

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Introduction

Obesity is a condition marked by pathological excess of body fat [1]. This results after persistent and positive energy balance. This is a problematic condition and an obese person is vulnerable to numerous comorbidities such as Type-2 Diabetes Mellitus, hypertension, certain cancer, coronary artery disease as well as cardiovascular disease, and so on [2,3,4]. The severity of the condition may result in sleep apnea, gallstones, asthma, glomerulosclerosis, endothelial dysfunction, and dyslipidemia [5]. Moreover, systemic processes like metabolic inflammation and mitochondrial dysfunction are caused by obesity. In obesity, the capacity of adipocytes to store lipids, increases. This results in the leakage of cytokinins and fatty acids derived from circulation [6]. Accumulation of harmful

lipid species takes place in ectopic tissues. This results in local inflammation, thereby leading to endothelial dysfunction, insulin resistance, and non-alcoholic fatty liver disease [7]. In the current scenario, a significant number of more than half of the USA population will become obese. Similar circumstances will happen in other developed countries [8]. Moreover, its severity is increasing day by day and contributing to morbidity and mortality all over the world [9]. The most devastating and dangerous consequence of obesity is Type 2 Diabetes Mellitus. T2DM is marked by a constant declination of insulin resistance by constant insulin secretion at an increasingly alarming rate [10]. Insulin resistance caused by obesity accelerates the exhaustion of pancreatic islets thereby causing complex and multifactorial Type 2 Diabetes Mellitus [11, 12]. Genetic and environmental factors lead to obesity. Consumption of calorie-rich food and an inactive physical lifestyle creates an obesogenic environment [13, 14]. Moreover, innate genetic composition makes a person vulnerable to obesity. In obese patients diagnosed with diabetes, a large number of carbohydrates and fatty acids get exposed to the heart. This increases the physiological function of the heart, thereby altering the ratio of metabolites [15]. Change in the lipid composition of the membrane adversely affects endocytosis, exocytosis, and transport of substances causing organ dysfunction [16].

The diabetic population is prone to acute chronic infections when compared to non-diabetic patients. The need for providing mechanical ventilation and mortality is 3.1 times greater in diabetic patients than non-diabetic subjects [17]. They have a greater inflammatory storm. They are prone to low-grade chronic inflammation which makes the condition critical by causing cytokine storms, ultimately leading to death making the condition severe and then eventually death [18, 19]. Hyperglycemia causes a series of dysregulated metabolic changes [20,21]. Moreover, obesity increases superoxide production causing inflammation in pathways and immune dysfunction [22].

Materials and Methods

Research Design

This is an observational study that was conducted during the period of one year on 100 patients who visited our department of endocrinology, diagnosed with type II diabetes mellitus. The patients were divided into two groups, namely, the obesity group with 55 patients and the control group with 45 patients. The selection to each group was done by the random selection method. The baseline characteristics of the patients were analyzed as other clinical and laboratory features related to diabetes and obesity. The parameters were analyzed and compared statistically between the two mentioned groups.

Inclusion and Exclusion Criteria

Patients who came to the outpatient department of our hospital who follow the study protocol and give informed consent for the study are included. Patients who provide informed consent for the study are included in the study. Patients above 20 years of age diagnosed with cancer and undergoing chemotherapy are included in the study. Patients with more than 53% of LV injection fraction are also included.

Patients who did not follow the study protocol did not finish it, or did not provide consent were not included in the study. Patients with less than 53% of LV injection fraction, patients with diabetes, coronary artery disease, and non-ischemic cardio-myopathies are excluded from the study.

Statistical Analysis

The study used SPSS 25 for effective analysis. The continuous data were expressed as mean±sd while discrete data were expressed as frequency and its respective percentage. The data

arrangement has been done in MS Excel. The study employed ANOVA for conducting an analysis between the two groups. The level of significance was considered to be $p<0.05$.

Ethical Approval

The patients were given a thorough explanation of the study by the authors. Written consent has been obtained from each patient. The study process has been approved by the Ethical Committee of the concerned hospital.

Results

Table 1 shows the baseline characteristics of patients, they are divided into two groups obesity and control groups. BMI is seen as high in the obesity group (34.2±1.67), waist to hip ratio is seen as high obesity group (41.35±1.12). The mean age of the patients in obesity is 40.12 and 41.34 in the control group. 58.2% are smokers in the obesity group, and 44.4% in the control group. It was found that there is a significant difference in BMI and Waist Hip Ratio (WHR) between the 2 groups ($p<0.05$). Other parameters were almost similar between the two groups because the grouping was done from the whole sample randomly.

Table 1: Baseline characteristics of the patients in both the groups and the significance between the two groups

Parameters	Obesity Group n = 55	Control group n = 45	*p*-value
Age (years), mean±sd	40.12±13.23	41.34±14.35	0.0845
Gender Males (n,%) Females (n,%)	 26 (47.3) 29 (52.7)	 21 (46.7) 24 (53.3)	0.2
Duration of diabetes (months); mean±sd	32.57±7.5	31.4±7.2	0.36
BMI (kg/m^2)	34.2±1.67	24.16±1.09	0.037
Waist Hip Ratio (cm; mean±sd)	41.35±1.12	29.25±1.34	0.036
Smoking History (n,%)	32 (58.2)	20 (44.4)	0.058

Table 2 shows the parameters of the patients after a follow-up period. The fasting blood glucose is seen as high in the obesity group (154.23±4.65), and HbA1c % is slightly high in the obesity group. HDL levels are high in the control group (59.23±3.67) and LDL is seen high in the obesity group (229.35±6.5). Blood pressure is high in the "Obesity" group compared to the control group. Complications like proteinuria, hypertension, atrial fibrillation, and frequent pulmonary infection are seen as high in the obesity group compared to the control group. The study found that there are significant differences between the two groups in Fasting Blood Glucose, Total Cholesterol, LDL, SBP, and cardiopulmonary complications like Atrial Fibrillation, Frequent Pulmonary Infection, and Hypertension ($p<0.05$).

Table 2: Parameters of the patients in both the groups and the significance between the two groups

Parameters	Obesity Group n = 55	Control group n = 45	*p*-value
Fasting Blood Glucose (mean±sd)	154.23±4.65	128.23±4.78	0.0412
HbA_{1c}%	6.9±1.2	6.5±0.9	0.051
Total Cholesterol (mg/dl)	5.6±0.7	4.6±0.4	.041
HDL	52.25±4.78	59.23±3.67	0.0695
LDL	229.35±6.5	202.12±7.7	0.036

Complications			
1. Atrial Fibrillation	22 (40)	13 (28.88)	0.0257
2. Proteinuria	16 (29.09)	17 (37.78)	0.065
3. Frequent Pulmonary Infection	32 (58.18)	15 (33.34)	0.0487
4. Hypertension	28 (50.90)	15 (33.34)	0.0325
5. Diabetic foot	6 (10.9)	8 (17.78)	0.074
6. Visual symptoms	12 (21.82)	11 (24.45)	0.086
Blood Pressure			
SBP	138.23±4.34	119.12±1.25	0.04
DBP	82.56±1.89	80.05±0.8	0.062

Discussion

Diabetes is caused by Obesity. In epidemic forms. A study by WHO reveals that in the past 40 years, the obese population has increased by 7-fold [23]. Obese people have high levels of impaired glucose tolerance (IGT, or prediabetes) which is ultimately a key risk factor for diabetes [24]. In addition to it, the rise in the number of cases of obesity and diabetes has laid impacts on infectious diseases. Obesity has dramatically spread all over the world taking Pathogenesis of obesity and diabetes is similar. They share a common IR pathway, pro-inflammatory and pro-thrombotic patterns, and oxidative stress (Ox-S) [25,26]. Obesity results in overnutrition stimulating dysregulated metabolic balance with subsequent accumulation of fat in non-lipid-storing organs like skeletal muscles, liver, and endothelium. It induces metabolic disorders like diabetes, IR, IGT, cerebrovascular disease, liver disease, and cardiovascular diseases. Endothelial dysfunction by obesity makes such mechanisms that trigger CVD and atherosclerosis [27, 28]. In obese patients, from an endothelial background, low nitric oxide (NO) bioavailability causes impaired endothelium-dependent vasodilation [28,29]. De Nigris et al. reveal that high glucose levels and endothelial cells which are stimulated by insulin on the pro-atherogenic pathway are vulnerable to [29]. Moreover, the onset of T2D is connected to altered “clock genes”. These are the precursors in developed metabolic complications. Shift in circadian clock genes increases the chances of metabolic disorders such as IR and obesity. Several pieces of evidence have marked the alteration in clock genes in obesity and diabetes. Parameters of glucose metabolism like insulin sensitivity, glucose tolerance, and glucagon, insulin, and glucose levels show circadian variations the whole day [30]. An alteration in the Circadian Locomotor Output Cycles Kaput (CLOCK) gene disrupts the feeding rhythm. It promotes inactivity, thereby leading to hypoinsulinemia, hyperlipidemia, and hyperphagia [31]. Obesity and diabetes are linked with insulin resistance (IR) and cardiovascular disorders both micro- and macrovascular. Its factors are laid in Oxidative stress processes [25]. Evidence of studies on endothelial cells reveals that Ox-S has a role in hyperglycemic phenotype and glucose variability [32, 33, 34]. Thus, obesity gets affected by Oxidative Stress having a high vulnerability to activate the oxidative pathways which were dysregulated by decreased mitochondrial function and degraded ROS scavenging. Nuclear Erythroid 2 related factor-2 (NFE2L2 or NRF2) which is a redox-sensitive transcription factor helps in the regulation of response elements of antioxidants (AREs). In diabetic patients, the active status of NRF2 is reduced which increases oxidative stress, and mitochondrial dysfunction thereby leading to the enhancement of endothelial dysfunction [35]. NRF2 prevents many human diseases like obesity and diabetes [36]. In diabetic

complications, elevated levels of circulating markers of lipid peroxidation were observed, reflecting oxidative damage in several tissues [37]. Pathogenesis of obesity and diabetes reveals that both common phenotype which is characterized by insulin resistance and inflammatory processes [38, 39]. Inflammatory markers associated with obesity and obesity-related diseases state that persistent low-grade inflammation response is a modifiable risk factor. The relationship between glycemic complex and adipose tissue inflammation is very complex. Dysfunctional adiposity is marked by an altered gene expression profile in obesity and type 2 diabetes [40]. A case-cohort study was performed by ARIC (Atherosclerosis Risk in Communities) on middle-aged diabetic and non-diabetic patients. It reveals that inflammatory factors play a key role in pathways that progress from obesity to diabetes. In this age group subjects, the obese population has a 6-fold greater risk of developing diabetes [41]. Parrizas et al. state that miR-192, which alters lipid homeostasis and adipocyte differentiation in obese people [42]; miR-193b, which maintains the production of adiponectin in white adipose tissue (WAT) and insulin resistance [43]as the markers of prediabetes. In fact, the downregulation of miR-192 in diabetes-induced patients states a therapeutic role in the prevention of diabetes [44]. Therefore, the prevalence of diagnosed diabetes mellitus increases with increased obesity.

Conclusion

The study has concluded that obesity can be considered a risk factor for diabetes which specifically impacts long-term cardio-pulmonary complications. It is found that obesity affects diabetic people much more than non-obese in terms of higher blood glucose and cardiopulmonary complications. There is no significant effect on other systemic complications due to obesity. The study also showed a significant impact on systolic blood pressure among obese diabetic individuals. The lipid profile also deteriorates due to obesity. The study enrolled patients from one center due to which there is a limitation of the number of patients. There is a need to conduct similar studies to bring more varied conclusions. However, this current study has brought forward an important finding which would contribute to clinical management through the inclusion of anti-obesity management in patients of diabetes with obesity.

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