

Evaluation of Some Physiological Parameters in Type 2 Diabetes Mellitus Patients With Hypertension and Non-Hypertension According to Body Mass Index

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ABSTRACT: Diabetes mellitus (DM) is a common metabolic disorder characterized by high blood sugar levels due to decreased insulin sensitivity, inadequate insulin synthesis, or a mix of the two. Insulin resistance (IR) causes adipocytes to release uncontrolled fatty acids, resulting in elevated amounts of unbound fatty acids in the bloodstream. The purpose of this study is to evaluate numerous biochemical markers in the serum of T2DM patients and comparing them to those without hypertension. **Material and method:** The current study had 60 T2DM patients split into two groups: 30 with HP and 30 without HP. Patient samples were gathered from the Diabetic Research Centre at Al-Mustansiriyah College University in Baghdad, Iraq, between January and April 2021. The two groups were compared with thirty healthy control volunteers. **Results:** The results of this study revealed that there is a significant difference in (Age, WHR, BMI, HbA1c, FBS, TC, TG, LDL, VLDL, HDL, C-peptide, HOMA-IR, and Cortisol), while there is no significant difference in urea and creatinine between patients without HP and control. On the other hand, there is an essential difference in all parameters determined in this study between T2DM with HP and control. Finally, there's an important variance in WHR, FBS, urea, creatinine, C-Peptide, HOMA-IR, and cortisol, but there is little variation in the other parameters identified in the study. **Conclusion:** According to the findings of this study, the association between Type 2 diabetes. and HP is proportional; patients with PH have higher WHR and FBS, which can be attributed to higher body fats; urea and creatinine levels are significantly higher in patients with HP due to kidney damage caused by high pressure; there is an immediate connection between age and T2DM infection; and BMI and WHR are two of the most influential risk factors for T2DM-related injury. The lipid profile parameters have been linked to T2DM because an increase in body fat raises the BMI and WHR and causes insulin resistance, which leads to T2DM; the renal function variables will increase as a response to damage to the kidney's nephrons; the level of C-peptide will increase as the body attempts to maintain a level of sugar in the normal range; and HOMA-IR will increase as resistance to insulin occurs in the body. The final result is that Cortisol concentration is altered by numerous inhibitory medications, resulting in low levels. More research on this area is needed to enhance findings, identify new techniques to controlling T2DM, and develop a trustworthy diagnostic procedure.

Keywords: T2DM, Dyslipidemia, Hypertension, HOMA-IR, Cortisol in T2DM



1. INTRODUCTION

Diabetes mellitus (DM) is one of the major chronic illnesses which places either when the beta cells of pancreas does not manufacture enough insulin or when the human body can't efficiently utilize the insulin it produces. Insulin is a peptide hormone which regulates blood sugar. Hyper glycaemia, also named increased blood pressure, is a general impact of uncontrolled DM and through the time drives to serious harm to many of the human body's systems, particularly the nerves and blood vessels.[1].Diabetes mellitus (DM) gives rise to a range of occurrences, encompassing both micro and macro-vascular problems. It explains a significant prevalence of illness or disease[2]. There is a lot of reasons and risk factors for T2DM including (age, wrong nutrition, hormonal, obesity, genetic and low level physical activity) all of these factors may cause T2DM.

Over than 50% of individuals with diabetes mellitus (DM) have hypertension (HTN), which has a crucial role in the development of both micro and macro-vascular complications in DM. Patients who have both diabetes mellitus (DM) and hypertension (HTN) have a four folds greater danger of developing cardiovascular disease (CVD) matched to individuals who do not have diabetes and have normal blood pressure [3].

Diabetes is a chronic ailment that can cause various complications like vision loss, kidney disease, low red blood cell count, heart problems, cognitive impairments, and reduced ability to do daily tasks independently, eventually impacting a person's overall well-being. Glycosylated hemoglobin (HbA1c) is measured to examine and treat persons with diabetes mellitus [4]. HbA1c assesses and appraises the extended-term control of glucose levels and anticipates the probability of microvascular complications in patients suffering from diabetes. The HbA1c level in the blood sample provides information about the average lifespan of red blood cells and serves as a measure of glycemic management over time. The prolonged effects of DM might potentially impair other organs, leading to various physiological changes in the body depending on the severity and length of the disease [5].

Insulin resistance (IR) boosts the liberation of un-bound fatty acids, resulting in raised concentrations of circulating un-bound fatty acids. This, in turn, triggers the production of very low-density lipoprotein (VLDL) particles those are wealthy in triglycerides in the liver, ultimately leading to an increase in (HDL) (LDL) particles that are rich in triglycerides [6]. The elevation of triglycerides within lipid particles alters their metabolic processes. [7]. Elevated lipid deposition in the pancreas impairs its ability to respond to elevated concentrations of sugar in the blood and diminishes the production of insulin. HOMA-IR is the best indicator to detect insulin resistance in people with T2DM [8] C-peptide is a commonly employed indicator of the functionality of pancreatic beta cells. The production of this substance is equivalent in quantity to the naturally occurring insulin, but it is excreted at a more consistent pace and for a longer duration. C-peptide levels in persons with type 2 diabetes mellitus (T2DM) generally fall within the normal to elevated range. [9]. Cortisol, a glucocorticoid produced by the adrenal cortex, has a significant impact on the metabolism of glucose, fat, and protein. Hyper-cortisolism is linked to several disorders, such as diabetes, obesity, hypertension, osteoporosis, and cardiovascular disease. The incidence of hyper-cortisolism in diabetes patients exceeded that in the general population [10].

The aim of the present study is to estimate some bio-chemical factors and parameters in the serum of T2DM and as matched with T2DM participants with and without hypertension.

2. Material and method

2.1 The Study Population

The current study designed to identify the biochemical difference between DM patients and healthy people and the difference between DM with HP compared with DM without HP patients. So the patients participant In the study were divided into 2 patients groups, 30 patients in group of patient with DM who have high BP and 30 patient with DM who have normal BP Diabetes Research Center Al-Mustansiriyah University in Baghdad / Iraq for the time from January 2021 to April 2021, the sum of patients in this study were 60 participant patient. Those 60 patients in the two groups compared with 30 healthy participant who have not DM

2.2 Inclusion criteria

The study included patient having T2DM and one group included hypertension more than 9/13 mmHg, all groups has been divided after take the health condition and results parameters from the physician responsible on the patients.

2.3 Exclusion criteria

All patients that suffer from renal failure or cardiovascular disease, anemia and smokers are excluded.

2.4 Anthropometric study

patients and control participants has been going to measure the gender, age, weight, height waist and hip to evaluate BMI and WHR, BMI measurement studied by the utilize of the mathematical equation, it is calculated by dividing the weight by the square of height. WHR is measured by dividing waist circumference by the hip circumference.

2.5 Sample collection

Ten milliliter venous blood samples were collected from patients with T2DM and control A volume of 3 milliliters was placed in a EDTA for determination of HbA1c%. The remaining blood was putted in a gel tube and left at a temperature (22-26) °C for 45 minutes to separate the clot, then, the collected blood centrifuged at 3000 rpm for 10 minutes to separate serum. The collected serum then used to evaluate the biochemical parameters (TC, TG , HDL, LDL, VLDL, FBS, urea, Creatinine, C-peptide and cortisol).

2.6 Biochemical tests

The evaluation of C-peptide and cortisol were done by using direct ELISA technology by the using of the information provided from (Sunlong / China) kit absorbance were determined to be 450 nm and the standard curve calculated by the using of standard concentration and it is dilutions provided with the kit.

Other chemical parameters (TC, TG, HDL, LDL, VLDL, FBS, Urea and Creatinine) were evaluated by the using of kits provided from (Human company / Spain) each parameter was measuring in a different wave length as it is provided in the kits.

2.7 Study design

The study model has been designed to show the study map that used in this study

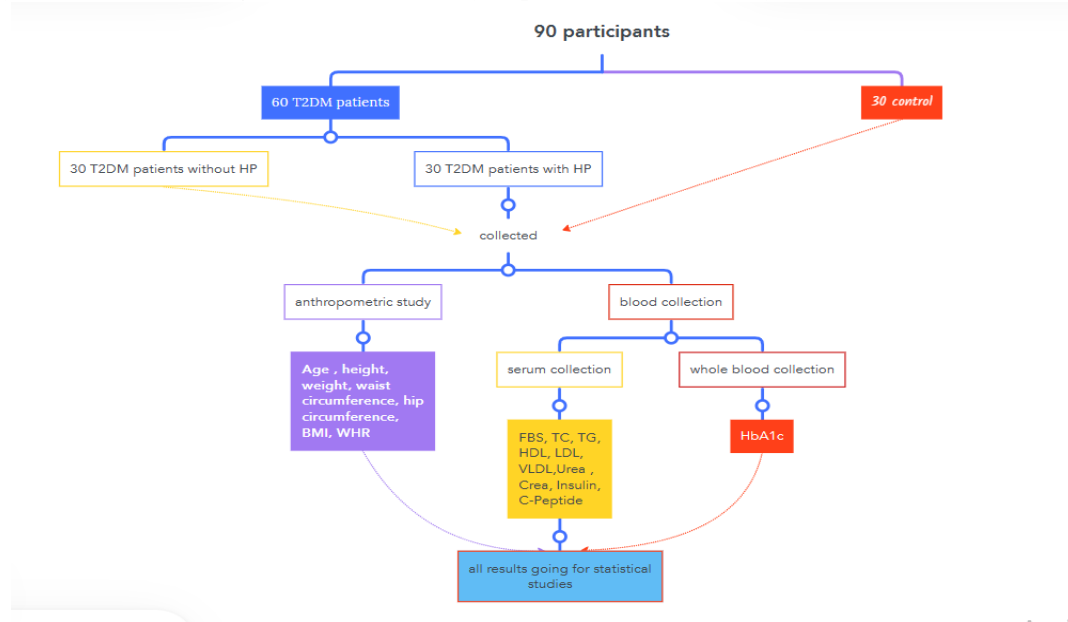


FIGURE 1. - study design

2.8 Statistical analysis

The data has been analyzed using IBM statistics SPSS 26 version. The descriptive statistics for each parameter included the calculation of the mean and the standard deviation (SD). The T-test was employed to compare the chemical variables between patients and control groups and two groups of patients between each other at a significance level of probability ($P < 0.05$) [11].

3. Results

3.1 Anthropometric and biochemical parameters between control and T2DM without HP

The mean and SD for the studied parameters used the statistical study and the results showed that there is a significant increase in age ($P < 0.05$) between patients (49.3 ± 4.7) as compared with control (38.7 ± 7.4), there is significant difference ($P < 0.05$) in BMI between patients (29.47 ± 5) as compared with control (25.89 ± 3.5), there is a significant increase ($P < 0.05$) in WHR between patients (0.97 ± 0.051) as compared with control (0.86 ± 0.055) there is a significant increase ($P < 0.05$) in the level of FBS in patient (155.7 ± 27.7) as compared with control (96.7 ± 5.0), there is a significant increase ($P < 0.05$) in the level of HbA1c% in patients (8.65 ± 1.45) as compared with control (4.8 ± 0.31) there is a significant difference ($P < 0.05$) in lipid profile (TC, TG, HDL, LDL, VLDL) between patient (231.8 ± 53.9 216.8 ± 65 38 ± 4.37 154.1 ± 52.8 44.6 ± 16.3) as compared with control (158.9 ± 28.8 , 93 ± 9.2 , 52.7 ± 5.47 , 82.5 ± 30.4 , 18.6 ± 1.8) respectively, there is a non-significant increase in the level of urea between patients (33.9 ± 9.3) as compared with control (30.1 ± 9.2), there is a non-significant difference in the level of creatinine in patients (0.79 ± 0.19) as compared with control (0.73 ± 0.22), there is a significant increase ($P < 0.05$) in the level of C-peptide between patients (3.85 ± 1.2) as compared with the control (1.82 ± 0.33), there is a significant difference in the level of HOMA-IR between patients (3.56 ± 1.2) as compared with control (2.07 ± 0.37) in the last, there is a significant decrease ($P < 0.05$) in the level of cortisol between patient (56.23 ± 10.75) as compared with control (100.1 ± 6.7)

The result of the study shown in table 3-1.

Table 1. - T-Test result for the studied parameters between control and T2DM without HP patients

The studied parameters	Mean ±SD for T2DM without HP (N=30)	Mean ±SD for control (N=30)	p-value
Age, years	49.3±4.7	38.7±7.4	<0.001
BMI, Kg/m ²	29.47±5	25.89±3.5	<0.001
WHR	0.97±0.051	0.86±0.055	<0.001
FBS mg/dl	155.7±27.7	96.7±5.0	<0.001
HbA1c	8.65±1.45	4.8±0.31	<0.001
TC mg/dl	231.8±53.9	158.9±28.8	<0.001
TG mg/dl	216.8±65	93±9.2	<0.001
HDL mg/dl	38±4.37	52.7±5.47	<0.001
LDL mg/dl	154.1±52.8	82.5±30.4	<0.001
VLDL mg/dl	44.6±16.3	18.6±1.8	<0.001
Urea, mg/dl	33.9±9.3	30.1±9.2	0.127
Creatinine, mg/d	0.79±0.19	0.73±0.22	0.333
C-peptide ng/ml	3.85±1.2	1.82±0.33	<0.001
HOMA-IR	3.56±1.2	2.07±0.37	<0.001
Cortisol ng/ml	56.23±10.75	100.1±6.7	<0.001

3.2 Anthropometric and biochemical parameters between control and T2DM with HP

The mean and SD for the studied parameters used the statistical study and the results showed that there is a significant increase (P<0.05) between patients (49.7±7.4) as compared with control (38.7±7.4), there is significant difference (P<0.05) in BMI between patients (30.6±4.97) as compared with control (25.89±3.5), there is a significant increase (P<0.05) in WHR between patients (1.01±0.055) as compared with control (0.86±0.055) there is a significant increase (P<0.05) in the level of FBS in patient (195.1±56.4) as compared with control (96.7±5.0), there is a significant increase (P<0.05) in the level of HbA1c% in patients (8.4± 1.48) as compared with control (4.8±0.31) there is a significant difference (P<0.05) in lipid profile (TC, TG, HDL, LDL, VLDL) between patient (253±41, 230±72.5, 37±4.38, 150.3±46.5, 45.2±14.8) as compared with control (158.9±28.8, 93±9.2, 52.7±5.47, 82.5±30.4, 18.6±1.8) respectively, there is a significant increase (P<0.05) in the level of urea between patients (59.9±7.9) as compared with control (30.1±9.2), there is a significant difference (P<0.05) in the level of creatinine in patients (1.27±0.41) as compared with control (0.73±0.22), there is a significant increase (P<0.05) in the level of C-peptide between patients (3.4±0.84) as compared with the control (1.82±0.33), there is a significant difference (P<0.05) in the level of HOMA -IR between patients (3.4±0.95) as compared with control (2.07±0.37) in the last, there is a significant decrease (P<0.05) in the level of cortisol between patient (34±7.12) as compared with control (100.1±6.7).

Table 2. - T-Test result for the studied parameters between control and T2DM with HP patients

The studied parameters	Mean ±SD for T2DM with HP (N=30)	Mean ±SD for control (N=30)	p-value
Age, years	49.7±7.4	38.7±7.4	<0.001
BMI, Kg/m ²	30.6±4.97	25.89±3.5	<0.001
WHR	1.01±0.055	00.86±0.055	<0.001
FBS mg/dl	195.1±56.4	96.7±5.0	<0.001
HbA1c	8.4± 1.48	4.8±0.31	<0.001

TC mg/dl	253±41	158.9±28.8	<0.001
TG mg/dl	230±72.5	93±9.2	<0.001
HDL mg/dl	37±4.38	52.7±5.47	<0.001
LDL mg/dl	150.3±46.5	82.5±30.4	<0.001
VLDL mg/dl	45.2±14.8	18.6±1.8	<0.001
Urea, mg/dl	59.9±7.9	30.1±9.2	<0.001
Creatinine, mg/d	1.27±0.41	0.73±0.22	<0.001
C-peptide ng/ml	3.4±0.84	1.82±0.33	<0.001
HOMA-IR	3.4±0.95	2.07±0.37	<0.001
Cortisol ng/ml	34±7.12	100.1±6.7	<0.001

3.3 Anthropometric and biochemical parameters T2DM patients (with and without HP)

The mean and SD for the studied parameters going for statistical study and the result showed that there is a significant difference ($P<0.05$) in FBS between T2DM with HP (195.1±56.4) as compared with T2DM without HP (155.7±27.7), there is a significant increase ($P,0.05$) in the level of Urea and Creatinine between T2DM with HP (59.9±7.9, 1.27±0.41) as compared with T2DM without HP (33.9±9.3, 0.79±0.19) respectively, there is a significant difference ($P<0.05$) in the level of cortisol between T2DM with HP (34±7.12) as compared with T2DM without HP (56.23±10.75) from the other hand, there is non-significant differences between all other parameters for the comparison between T2DM with and without HP. The result of the study shown in table 3-3.

Table 3. - T-Test result for the studied parameters between T2DM with and without HP

The studied parameters	Mean ±SD For T2DM with HP (N=30)	Mean ±SD for T2DM without HP (N=30)	p-value
Age, years	49.7±7.4	49.3±4.7	0.788
BMI, Kg/m ²	30.6±4.97	29.47±5	0.363
WHR	1.01±0.055	0.97±0.051	0.004
FBS mg/dl	195.1±56.4	155.7±27.7	<0.001
HbA1c	8.4± 1.48	8.65±1.45	0.529
TC mg/dl	253±41	231.8±53.9	0.92
TG mg/dl	230±72.5	216.8±65	0.454
HDL mg/dl	37±4.38	38±4.37	0.483
LDL mg/dl	150.3±46.5	154.1±52.8	0.769
VLDL mg/dl	45.2±14.8	44.6±16.3	0.882
Urea, mg/dl	59.9±7.9	33.9±9.3	<0.001
Creatinine, mg/d	1.27±0.41	0.79±0.19	<0.001
C-peptide ng/ml	3.4±0.84	3.85±1.2	0.108
HOMA-IR	3.4±0.95	3.56±1.2	0.594
Cortisol ng/ml	34±7.12	56.23±10.75	<0.001

For anthropometric studies the results shows that there is a significant difference in age between the T2DM with and without HP as compared with control. This result is in agreement with another studies like Suastika et al [12], who said that age is one of the most effected risk factors for T2DM infection, when people get older the functionality of the body and organs will be less affected than in younger people, from the other hand there is non-significant difference between people with and without HP because patient will suffer from high HP after the infection with T2DM so the primary disease (T2DM) occurs in the same age period.

There is a significant difference in the level of BMI and WHR between T2DM patients with and without HP as compared with control. This result is even agreed with the studies of Yasser et al. [13], BMI and WHR are the most accurate parameters for the determination of body obesity, the elevated levels of BMI and WHR clarify that the appearance of T2DM is related with the accumulation of body fats and going to affect various functions in the body, Insulin resistance is responsible for a substantial portion of the raised fasting sugar levels in the bloodstream. The emergence of insulin resistance in obesity can be related to the constrained ability of enlarged adipocytes to handle and metabolize glucose. This condition may also occur in muscle, liver, and β -pancreatic cells when there is an accumulation of lipids [14]. There is a significant difference in WHR between T2DM with HP and T2DM without HP and that is back to the reality of raising the WHR increase the concentration of fats and the heart will need to bump more blood to make oxygen reaches the body cells and organs [15].

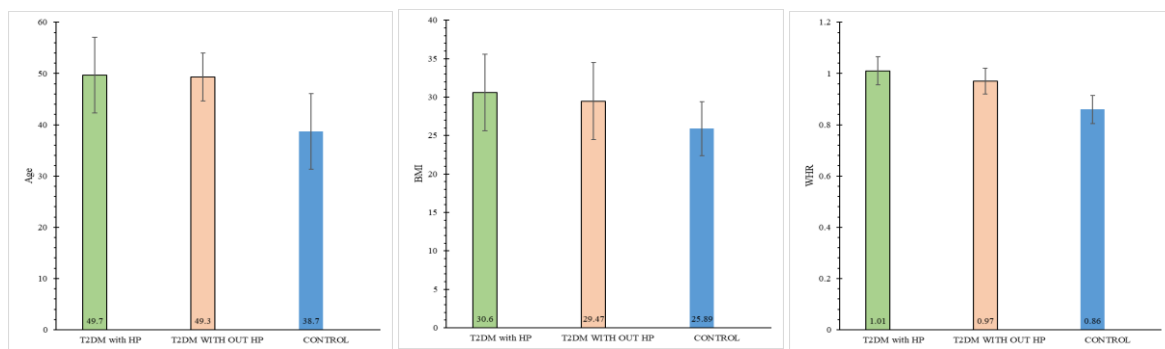


FIGURE 2. - mean and SD for Age, BMI and WHR among control, T2DM with HP and T2DM without HP

The level of FBS and HbA1c is significantly elevated in patients as matched with control and that is in agreement with studies like Elimam et al and Nazari et al [16, 17]. The level of FBS is directly proportional with the HbA1c level , level of FBS is elevated due to the impaired destruction of beta cell in pancrias, the level of HbA1c is elevated when BS is elevated and the poor control of glucose in body will cause a high elevation in the level of the two parameters. Hence HbA1c level measure the level of glucose in 3 months, it conecer as the pest parameter to diagnose and monitoring T2DM. there is a significant elevation in FBS in patient with HP, Fasting blood sugar (FBS) independently poses a risk for the onset of hypertension within a 5-year period in a healthy population without diabetes. The study also demonstrated a strong correlation between elevated fasting blood glucose (FBG) levels and the development of hypertension. These findings suggest that researchers should consider FBG as a potential risk marker for hypertension[18].

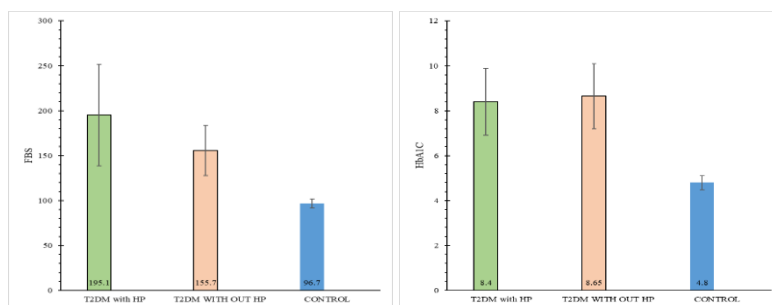


FIGURE 3. - mean and SD for FBS and HbA1c among control, T2DM with HP and T2DM without HP

The results obtained in the study show a significant difference in the level of (lipid profile) in patients as matched with control, this results is in agreement with revious studies like Shahwan et al and Hussain et al [19, 20],

In diabetes, blood lipid levels can be influenced by several factors due to the interplay between glucose and lipid metabolism. Consequently, any disruption in the process of glucose metabolism results in a disruption in the process of lipid metabolism, and vice versa[21]. Most of people with T2DM have insulin resistance as a main problem. Insulin resistance, when combined with hyperinsulinemia, is highly indicative of the future development of type 2 diabetes in individuals without diabetes[22]. Multiple studies have demonstrated that insulin impacts the production of liver apolipoprotein and adjusts the effect of lipoprotein lipase and cholesterol ester transport protein, leading to dyslipidemia in diabetes mellitus [23]. In addition, a lack of insulin decreases the functioning of hepatic lipase and other stages involved in the synthesis of physiologically active lipoprotein lipase. Hypertriglyceridemia commonly coexists with reduced levels of HDL cholesterol, which is a notable characteristic of aberrant lipid profiles observed in persons with diabetes. The lipid abnormalities associated with T2DM are characterized by elevated levels of TG and small, dense LDL particles, as well as reduced levels of HDL cholesterol[24]. The correlation between decreased levels of HDL cholesterol and heightened susceptibility to heart disease is firmly established, regardless of TG levels and other risk factors. The potential cause of hypertriglyceridemia may be attributed to heightened hepatic excretion of VLDL and sluggish removal of lipoproteins rich in triglycerides. This is primarily caused by elevated levels of substrates for triglyceride synthesis, namely FFA and glucose. The current investigation found substantial relationships between serum concentration of total cholesterol, triglycerides, LDL cholesterol, and hepatosteatosis, and blood concentrations of HbA1c [25]. The correlation studies indicate a strong link between high blood sugar levels (hyperglycemia) and the development of abnormal lipid levels (dyslipidemia). Our results corroborated a prior investigation indicating that the total cholesterol level tends to be within the normal range or close to it when glycemic control is sufficient, and a deterioration in control leads to an increase in the level. Hence, enhancing glycemic control could significantly diminish the likelihood of cardiovascular events in individuals with diabetes[26].

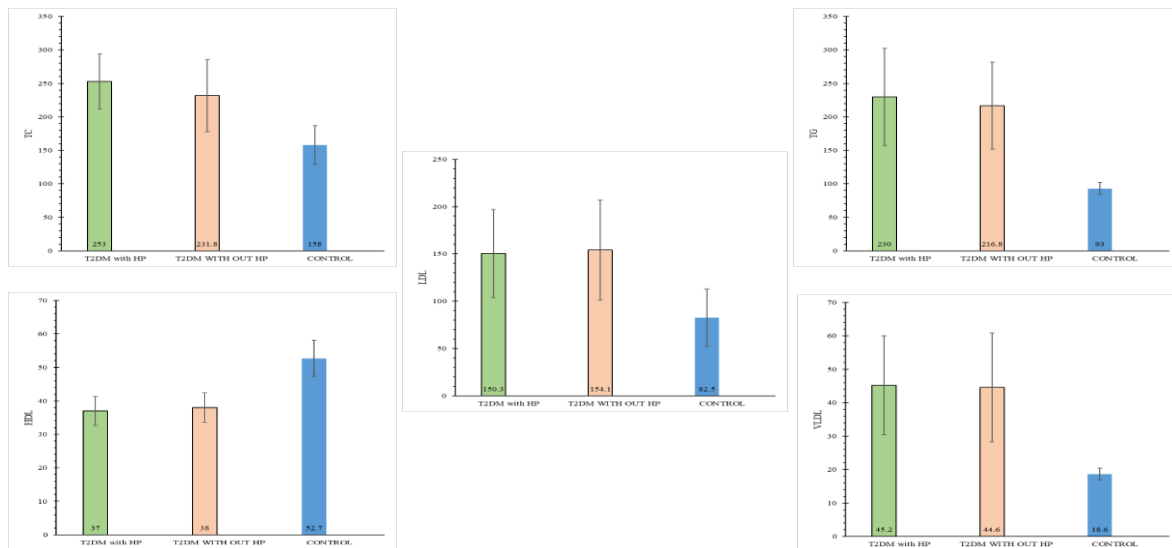


FIGURE 4. - mean and SD for Lipid profile (CG, CT, HDL, LDL and VLDL) among control, T2DM with HP and T2DM without HP

Level of urea and creatinine is significantly elevated in patients as matched with control, this result is in agreement with studies of Kene et al [27],

The kidneys would experience a failure to efficiently excrete serum creatinine, leading to an excessive elevation in its concentrations. Intensive therapy has the ability to significantly decrease increased HbA1c levels[28]. Nevertheless, the elevated concentrations of serum urea and creatinine, resulting from irreversible renal impairment, are challenging to reverse. Kidney damage in diabetes mellitus is a chronic and irreversible condition [29]. Elevated levels of serum urea and creatinine are reliable markers of glomerular injury, which is irreversible even with an intensive treatment plan. The only way to manage the growing glomerular damage and the subsequent rise in serum urea and creatinine levels is by early detection and action [30].

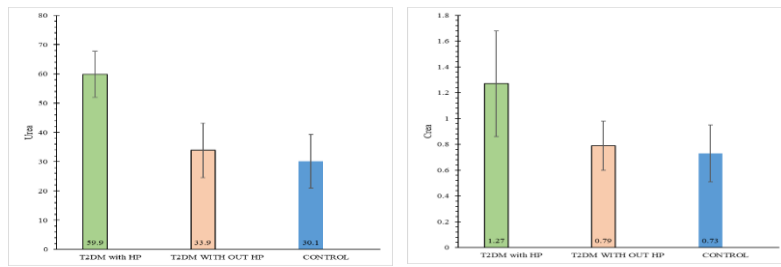


FIGURE 5. - mean and SD for urea and creatinine among control, T2DM with HP and T2DM without HP

The level of C-peptide and HOMA-IR were significantly increased in patients as matched with control and this results is in agreement with Jones et al [31].

The increasing prevalence of IR and metabolic syndrome has sparked significant interest due to their rising incidence and the resulting cardiovascular events, which can lead to both death and morbidity, even in those without diabetes [32]. Therefore, it is crucial to promptly identify insulin resistance (IR) in individuals without diabetes, as part of a community-based approach to mitigate the future prevalence of type 2 diabetes mellitus (T2DM). It is worth noting that interventional studies have shown that preserving beta-cell function reduces the progression from pre-diabetes to diabetes[33]. It has been proposed that the preferred method for screening (IR) should be appropriate for a study involving a large population, necessitate only one blood sample, and exhibit a high degree of reproducibility and predictive capability. It was noted that levels of C-peptide were significantly elevated in patients with metabolic syndrome, regardless of gender[34]. The fasting C-peptide exhibits a substantial correlation with many indicators of metabolic syndrome in obese adults. Therefore, C-peptide can function as a versatile biomarker to identify persons at risk for (IR)[35], type 2 diabetes mellitus (T2DM), atherosclerosis, and metabolic syndrome. Current guidelines suggest initiating T2DM screening at the age of 45 and repeating it every 3 years. However, for persons at higher risk, screening should commence earlier and be conducted more frequently [36].

Level of cortisol is significantly lowered in patients with T2DM as compared with control, this results is not agreement with the other studies, most previous studies showed that cortisol levels is increased with T2DM [37]. Although the cortisol in general elevated with T2DM because of the elevating stress, there is a reason of the decrease in the level of cortisol in ours work, the decrease could be explained by the use of specific drugs that help to reduce blood glucose and reduce cortisol level. In the study of vincent et al [38] He states that the combination of steroidogenesis inhibitors can enhance the management of hypercortisolism. Previously, combinations of ketoconazole and metyrapone were primarily documented in patients with severe Cushing's syndrome (with a median urinary -free cortisol level 30- to 40-fold above the upper limit of normal) and life-threatening coexisting medical conditions.

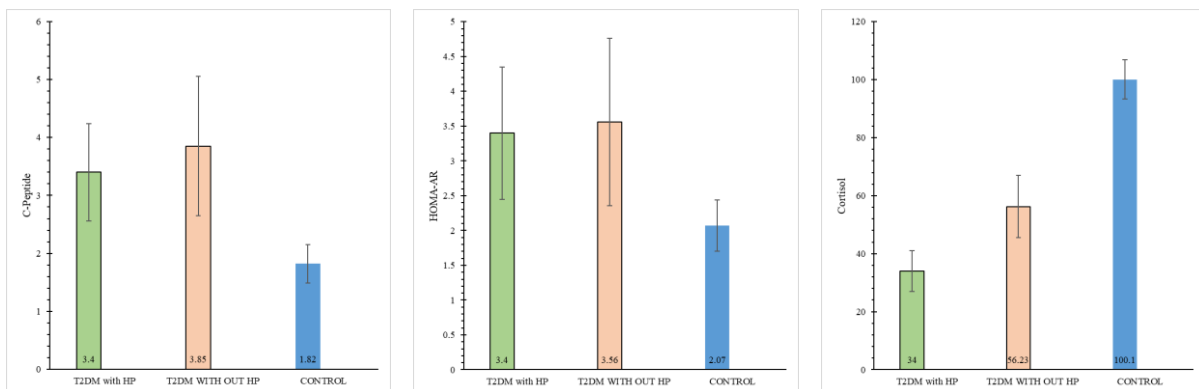


FIGURE 6. - mean and SD for urea and creatinine among control, T2DM with HP and T2DM without HP

4. Conclusion

Based on the findings gained in this study, it can be determined that the connection between T2DM and HP is proportional; patients with PH show higher WHR and FBS, which is back to the higher body fats; urea and creatinine are significantly higher among individuals with HP because of the disrupt damage in the kidney due to the high pressure; there is a direct connection between age and T2DM infection, The BMI as well as WHR are two of the most commonly identified risk variables for T2DM injury. lipid profile parameters are associated with T2DM because an increase in body fat will increase the BMI and WHR and, of course, the resistance to insulin that causes T2DM, renal function variables will be raised as a response to the damage that affects the nephrons of the renal level of C-peptide raised due to the body's try to maintain a level of sugar in the normal range, and HOMA-IR rises because the insulin resistance occurs in the body. The final result is that some inhibitory medicines affect cortisol levels, causing them to drop to low levels and

causing a deficiency in patients' physiological characteristics. More research should be conducted on this topic in order to improve results, discover novel approaches to control T2DM, and develop a reliable diagnostic method.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

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