**INTERNATIONAL RESEARCH JOURNAL OF PHARMACY**

www.irjponline.com

ISSN 2230 – 8407

Research Article

# EFFECT OF AGE AND GENDER ON SOME BIOCHEMICAL, HORMONES AND ADIPOCYTOKINES PARAMETERS IN IRAQI TYPE 2 DIABETES MELLITUS PATIENTS

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Article Received on: 18/09/18 Approved for publication: 20/11/18

**DOI: 10.7897/2230-8407.0912286**

**ABSTRACT**

Older age is very closely correlated to risk for developing type 2 diabetes. In the present study we evaluated the effect of age and gender on biochemical, hormones and adipocytakines parameters: Fasting blood sugar, HbA1c, insulin, Insulin resistance, Blood urea, serum creatinine, calcium, phosphorus, parathyroid hormone, calcitonin, vitamin D, adiponectin and tumor necrosis factor-α. Eighty random samples of type 2diabetes patients and a control group which included 20 healthy subjects. The average age was 45.18 ± 1.18year. The blood was collected for study the biochemical, hormones and adipocytakines parameters. The results: The age of all patients was 45.18 ± 1.18year compared with the control 38.56 ± 2.21year showed significant ($P<0.05$) differences between them. With gender according to no significant differences were found between male 51.95% and female 48.05% in patients' group and control 55.56%, 44.44% respectively. The finding showed increasing levels of FBS with increasing age. The lowest level of FBS was in 20-29 year, significantly ($P<0.05$) lower than the other age categories, increasing levels of HbA1c was found with increasing age. Serum insulin and IR levels revealed a significant ($P<0.05$) increase in 40-49 and 50-59 years. Increasing levels of Blood urea with increasing age. Parathyroid hormone and vitamin D were significantly ($P<0.05$) increased in age category 20-29 year. Increase in levels of FBS, Blood urea, Serum creatinine and calcitonin levels in men than women. The results of the present study showed the impact of type 2 diabetes on age and gender.

**Key words:** adiponectin, insulin, calcitonin, TNF-α, parathyroid hormone.

## INTRODUCTION

The increasing prevalence of Type 2 diabetes mellitus (T2DM) worldwide is reaching epidemic proportions and is becoming a major public health problem[1]. Insulin secretion depends on disease status and duration and can vary from delayed but markedly elevated in response to a glucose challenge, to absolutely diminished [2]. In Iraq, the prevalence of DM among adults is 10.4%, which means that around three million Iraqi individuals are suffering from DM [1]. Insulin is synthesized in the rough endoplasmic reticulum of theβ-cells. The actions of insulin on adipose tissue; skeletal, cardiac, and smooth muscle; and the liver. The net effect of the hormone is storage of carbohydrate, protein, and fat. Insulin receptors are found on many different cells in the body, including cells in which insulin does not increase glucose uptake[3]. HbA1c: Glycation is the nonenzymatic addition of a sugar residue to amino groups of proteins. Human adult hemoglobin usually consists of HbA (97% of the total), HbA2 (2.5%), and HbF (0.5%). HbA1c is formed by the condensation of glucose with the N-terminal valine residue of each β-chain of HbA to form an unstable Schiff base. HbA1c is the major fraction, constituting approximately 80% of HbA1[4]. If not treated, and addressed medically, nephropathy progresses into chronic kidney disease (CKD). This association of T2DM and CKD complicates the treatment of T2DM clinically [5]. Serum urea and creatinine are known to be raised with hyperglycemia in uncontrolled diabetics and usually correlate with severity of kidney damage. Creatinine is the breakdown product of creatinine phosphate is released from skeletal muscle at a steady rate. It is filtered by the glomerulus, and a small amount is also secreted into the glomerular filtrate by the proximal tubule [6]. The reduction in serum calcium level in type 2 diabetes mellitus is most probably due to hyperglycemia which increases calcium and phosphorus excretion in urine which is proportional to the degree of glucosuria, hypercalciuria by osmotic diuresis caused stimulation of bone resorption caused by secondary hyperparathyroidism [6]. In response to urinary calcium loss, PTH secretion is mildly but significantly stimulated to maintain serum calcium concentrations[5]. Phosphorus is an element that plays an important role in many physiologic systems. Phosphate is a component of cell membranes and biological macromolecules including proteins, nucleotides, carbohydrates and lipids. Eighty-five percent of phosphorus resides in bone (mostly as hydroxyapatite), 14% is present in cells and less than 1% is represented in plasma. Acid-base balance, hormones and vitamin D modulate intestinal absorption and renal reabsorption of phosphorus. Parathyroid hormone (PTH) inhibits renal reabsorption of phosphorus, and growth hormone decreases renal excretion. Vitamin D increases renal reabsorption[6]. Parathyroid hormone (PTH) in response to reduced calcium levels resulting in an increase in bone resorption and subsequently normalization of calcium levels. There are conflicting reports related to the role of PTH on glucose hemostasis [7]. Calcitonin is a 32 amino acid hormone secreted by the C-cell of the thyroid gland. The role of calcitonin in maintaining the serum calcium and stimulate renal vitamin D production. Calcitonin has an immediate effect on decreasing osteoclast activity and has been used for treatment of hyperkalemia [8]. The main defects that determine the development of T2DM are insulin resistance, pancreatic β-cell dysfunction and systemic inflammation. Multiple studies strongly suggest a role of vitamin D in the wellbeing of β-cells, insulin production and secretion, tissue sensitivity to insulin and the susceptibility to T2DM. An inverse relationship betweenT2DM and vitamin D is suggested by cross-sectional and prospective studies pointing to a direct link between the risk of T2DM and vitamin D [9]. Adipocytokines, such as adiponectin and tumor necrosis factor-a (TNF-a) are participating in the regulation of insulin sensitivity

and glucose. Adiponectin, the most abundant adipocytokine, was found to be decreased in conditions such as obesity, insulin resistance, type 2 diabetes, macrovascular complications and coronary artery disease (CAD) [10]. Adiponectin is protein synthesized and secreted predominantly by adipocytes into peripheral blood, accounting for 0.01% of the total plasma protein in human [11]. TNF- α is a pleiotropic cytokine that plays a central role in inflammation and apoptosis. It modifies the inflammatory reactions and immune reactions in response to injury and infection. TNF- α plays also a necessary and beneficial role as mediator of host resistance to infection and tumor formation[10]. This study was conducted to estimate the prevalence and identify potential determinants of T2DM patients attending a Diabetes Center in Baghdad, Iraq, 2017.

## MATERIALS AND METHODS

A cross-sectional study conducted on a systematic random sample of T2DM patients attending from AL-Kindi particular community for diabetes and heftiness treatment of Baghdad. The average age was 45.18 ± 1.18 year with range from 20-60 years old. In addition, a control group which included 20 healthy subjects in terms of non-diabetic. Consent was taken before participation in this study from all subjects. And many parameters were measured from blood samples for patients and control groups. The diagnosis of T2DM was based on the ADA (2016). The Diabetic Center in Eastern side of Baghdad during the period from December 2016 till May 2017. Laboratory investigations included FBS, HbA1c, insulin, IR, B.urea, serum creatinine, ca, p, PTH, calcitonin, vit. D, adiponectin and TNF-α. Venous blood sample 10 ml has been collected from the studied subject and serum has been collected and kept at -20°C until used. The study was carried out as per International conference of Harmonization-Good Clinical Practices Guidelines (ICH-GCP) or as per Declaration of Helsinki guidelines.

### Measurement of parameters

FBS, B.urea, s.creatinine, ca, and p were spectrophotomertrically estimated using commercial kits. Cobas electrochemilumine scenceimmunoassy (ECLIA) e411 and e111 apparatus were used to carry out HbA1c, insulin, PTH and calcitonin according to manufacture recommended procedure by using specific kit for each hormone. Vit. D, adiponectin and TNF-α were measured using enzyme-linked immunosorbent assay (ELISA) kits. The homeostasis model assessment (HOMA) was used to calculate insulin resistance (HOMA-IR) [FPI x FBS/405], where FPI is fasting plasma insulin concentration (μU/ml) and FPG is fasting plasma glucose (mg/dl).

**Statistical analysis**: The Statistical Package for Social Sciences (SPSS) version 18 (SPSS Inc., Chicago, IL, USA) used for data entry and analysis. Last significant difference-LSD was used to significant compare between mean. P≤0.05 was considered significant.

## RESULTS AND DISCUSSION

The mean ±SE age of all patients was 45.18 ± 1.18year compared with the mean ±SE age of control 38.56 ± 2.21year showed significant (P<0.05) differences in age between them. Regarding to the gender, the results reveled that non-significant differences were found between male 51.95% and female 48.05% in patients' group and control 55.56%, 44.44% respectively, and this result is in agreement with Mohammed, Z.J [12].

### 1. Effect of age on the studied parameters

### Effect of ageon glucose related parameters

Effect of age on glucose related parameters in T2DM patients is illustrated in table (1). The finding showed clear trend of increasing levels of FBS with increasing age. The lowest level of FBS was in the age category 20-29 year which was significantly (P<0.05) lower than the other age categories 30-39, 40-49, and 50-59 years. Also, a clear trend of increasing levels of HbA1c was found with increasing age. The lowest level of HbA1c was in the age category 20-29 year which was significantly (P<0.05) lower than the other age categories 30-39, 40-49, and 50-59 years. Serum insulin levels showed a significant (P<0.05) increase in the age categories 40-49 and 50-59 years as compared with the age categories 20-29 and 30-39 years. Also, levels of IR revealed a significant (P<0.05) increase in the age categories 40-49 and 50-59 years as compared with the age categories 20-29 and 30-39 years.

In the current study, the incidence of hyperglycemia increased with age. These results are agreed with Joung K H *et al* [13]. Zhou *et al*. [14] mentioned that the incident of T2DM was mainly in middle-aged adults Chinese 30-59 years. Results from large trials have also suggested that aggressive control in older DM patients[15]. Other study suggested that age of T2DM is probably significant predictors for development of severing hyperglycemia in these patients [12]. It is well documented that T2DM frequently goes undiagnosed for many years because hyperglycemia develops gradually and at earlier stages is often not severe enough for the patient to notice the classic diabetes symptoms. The results may be explained on the ground that the risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity [16]. The HbA1c is widely accepted and used as the most reliable test for assessing chronic glycemic condition. Also, HbA1c results vary with red cell dynamics and assay methods [17]. The increased percentage of HbA1c in the studied patients with advanced age is in agreements with Mohsen IH [18]. The current finding may be due to the fact that the glycosylation of hemoglobin is greatly affected by elevated sugar levels. In contrast, in a Korean population, the HbA1c level was higher in older than in younger patients with similar glucose profiles, and it was more diagnostically accurate than the FBG level in older patients [13]. Insulin levels could be higher if all patients were at an early stage of disease diagnosis. In the current study, the level of insulin increased with age. The present result regard the increase level of insulin with the age is in agreement with the results of Kharroubi AT [19] who found that reduced activity of insulin or reduced pancreatic synthesis (type II), circulating antibodies to insulin, delayed release of insulin or the absence of inadequacy of insulin receptors can be related to age. While Henquin J *et al*[20] mentioned that a significant difference in mean insulin and glucagon contents in T2DM subjects below and above 65 years ($P \leq 0.01$). This due to the fact that both β- and α-cell masses have been found to decrease slightly with aging in non-diabetic subjects**.** Conversely, autonomous, non-regulated insulin secretion is generally the cause of hypoglycemia. It is well documented that the patients with T2DM may have insulin levels that appear normal or elevated. However, the higher blood glucose levels in these patients would be expected to result in even higher insulin values had their β-cell function been normal[16]. Insulin resistance is explained as a condition in which target tissues had decreased sensitivity to insulin, lead to raise both blood insulin and glucose levels [21]. The results of the present study show that patient with T2DM had significantly higher IR with advanced of age and this elevation in IR were association with increased insulin level. These results are in agreement with previous studies Mohsen IH [18] which reported elevation of insulin hormone levels in patient with T2DM and this elevation associated with insulin IR status levels. Previous study Ha KH *et*

*al*[22] reported that in 2005, 70.6% of people with T2DM had IR, whereas 46.1% of those people had β-cell dysfunction. So they suggested that IR plays a more important role than β-cell dysfunction in the pathophysiology of participants with newly diagnosed T2DM.

**Effect of age on renal function tests in T2DM**

Effect of age on renal function parameters in T2DM patients is illustrated in table (2). The finding showed clear trend of increasing levels of B.urea with increasing age. The highest level of B.urea was found in the advanced age categories 40-49 and 50-59 year as compared with the other age categories at significant level (P<0.05). While, no significant (P<0.05) differences were found in s.creatinine and calcium levels among the different age categories. Levels of phosphorus revealed a significant (P<0.05) increase in the age categories 30-39, 40-49 and 50-59 years as compared with the age category 20-29 years. The incidence of elevated B. urea levels with age is agree with Bamanikar SA *et al*[6] who reported increased B. urea level in mean age 58.4±7.77 years. The present results may be due to that the patients with T2DM had significantly higher FBS with advanced of age as shown previously. These results indicate that there is strong relationship between blood sugar level and urea level because hyperglycemia is one of the major causes of progressive renal damage and an increase in urea level is seen when there is damage in the kidney or the kidney is not functioning properly. This finding corroborates with the findings of other studies which reported that hyperglycemia is one of the major causes of progressive renal damage [6]. Murtadha *et al*. [23] suggested there was strong positive correlation between age and urea level, also showed high level of urea in both types of diabetes. The current finding that no significant differences in the level of s.creatinin with advanced age, is agreement with Bamanikar SA *et al* [6] who reported that the association between hyperglycemia and the serum creatinine levels showed a weaker link. While it is disagreement with previous study which reported that s.creatinine level is influenced by age and the association between the age and creatinine levels in diabetes due to the risk of developing end stage renal disease (ESRD) [23]. Creatinine is the breakdown product of creatinine phosphate is released from skeletal muscle at a steady rate. Serum creatinine correlates quite well with the percent of the body that is skeletal muscle. It is filtered by the glomerulus, and a small amount is also secreted into the glomerular filtrate by the proximal tubule [24]. Overall, the explanation behind the current results is that the patients participating in this study may had complications of kidney disease (nephropathy) but the disease did not develop to the ESRD. The present finding that no significant differences in the level of calcium with advanced age, is in agreement with Marwa AT and Amar M [25]. The current finding could be attributed to that no significant differences were found in the calcium levels between T2DM patients and healthy controls. The incidence of elevated phosphorus levels with age is similar to that reported by a previous study with Christakos S *et al* [26] who found that serum phosphorus levels are not as tightly regulated as serum calcium, and it rises with high phosphorus diet. On the other hand, it has been reported that in the T2DM, there was no significant correlation between the level of blood glucose and the serum level of phosphorus and calcium[26]. The current study is disagreed with Fang L. and Li X [27] who reported that the calcium and phosphorus level don't change in mild vit. D deficiency in T2DM patients. Since the ingestion of a large amount of phosphate can increase serum phosphate by increased phosphate absorption through paracellular way.

**Effect of age on calcium regulating hormones in T2DM**

Effect of age on calcium regulating hormones in T2DM patients is illustrated in table (3). The finding showed that the levels of PTH were significantly (P<0.05) increased in first age category 20-29 year compared with the other age categories 30-39, 40-49, and 50-59 years. Concerning calcitonin levels, no significant (P<0.05) differences were found between the age categories. While the levels of vitamin D were significantly (P<0.05) increased in first age category 20-29 year compared with the other age categories 30-39, 40-49, and 50-59 years. PTH and calcitonin are the major regulators of cellular calcium and phosphate transport, while vitamin D provides appropriate concentrations of these minerals through its gastrointestinal tract and perhaps renal actions [8]. The results of PTH are in agreement with Rahimi Z [7] who reported that high level of PTH is associated with abnormal glucose metabolism in early stage of disease and is related with the prevalence of diabetes mellitus. And they suggested that diabetic patients should be evaluated for hyperparathyroidism because of the higher incidence of diabetes in patients with primary hyperparathyroidism. It was estimated that primary hyperparathyroidism in diabetic patients is approximately 3 fold higher than the general population. While PTH secretion is impaired in patients with poorly controlled diabetes mellitus and advancing patients age [7]. The present result support this study, it is clear from the results of the current study that hyperparathyroidism has been described in early stage of diabetic disease, and low calcium in addition to low PTH observed during poor blood glucose control with increased age and disease progression. In the present study, with advanced age of the T2DM patients no significant differences were found in calcitonin levels. This result is in agreement with Daniels GH *et al* [28]. Calcitonin role in glucose metabolism regulation isn't completely clear. On the other hand, the main action of calcitonin is the decreasing of calcium serum concentration, mainly due to the calcium sediment in bones and reduction of bone tissue resorption [29]. The current finding may be explained on the ground that the calcium level was not significantly different with progress of the age in T2DM patients. Therefore, the level of calcitonin is not significantly different with advanced of the age. Although no significant differences were found between the age categories reared 1, 25(OH)2 D level, a clear vitamin D deficiency was observed in all age categories in the present study. These results are agreed with 30 who reported that the prevalence of hypovitaminosis D reaching epidemic proportions and, in this regard, hypovitaminosis D seems to be a predisposing factor for development of type 2 diabetes. A low vitamin D status is known to induce secondary hyperparathyroidism that causes the overflow of calcium into adipocytes, thereby increasing lipogenesis [31]. The primary action of 1, 25(OH)2 D is to enhance intestinal calcium absorption and to promote osteoclast function, thereby keeping calcium and phosphorus homeostasis and bone health. Lack of vitamin D has been involved in the pathogenesis of several acute and chronic illnesses including musculoskeletal disorders, type 1 diabetes and type 2 diabetes [32]. Vitamin D is deficient even in those countries having sufficient sunlight and day lengths. Elderly people are especially low in their vitamin D status as their skin cannot photosynthesize vitamin D properly [33].

**Effect of age on cytokines related with T2DM patients**

Table (4) shows effect of age on cytokines related with T2DM patients. The results documented that non-significant (P<0.05) differences were found in levels of serum adiponectin and TNF-α among all age categories of T2DM patients. Regarding the results of adiponectin, it is in agreement with other study 34 who reported that genetic polymorphisms, sex, and dietary factors, such as soy protein, fish oils, and carbohydrate-rich diets influence on circulating adiponectin, while no relationship was found between adiponectin and age. While the current finding it is disagreed with Kadowaki T *et al* [35] who reported that IR increases with age, which would predict the lower adiponectin levels in the elderly. In addition, adiponectin, by improving insulin sensitivity and hyperglycemia, might affect the

development or progression of diabetic microvascular complications. However, the relationship between microvascular complications and serum adiponectin level is controversial [10]. Also, other study stated that several single-nucleotide polymorphisms and mutations in the adiponectin gene had been reported to be linked to type 2 diabetes and hypoadiponectinemia in different ethnic groups [36]. Interestingly, our study has shown that the adiponectin levels were increased somewhat but not significantly with age, could be explained by the fact that the decline in sex steroidal hormones with age might rise the adiponectin levels in the elderly Kadowaki T *et al*[35] indicated that the falling in renal function with aging might reduce the adiponectin clearance by kidney. The finding that no effect of the age on the level of TNF-α in the T2DM patients is similar to that reported by Jung, U. J. and Choi, M [10] who mentioned that the mean levels of TNF-α were not significantly different according to age. Since in this study, the complication associated with T2DM patients were present in all age categories; therefore, no significant differences were found in the levels of TNF- α among the age categories. Other study reported that this cytokine contributes to the impairment of glucose homeostasis, insulin signaling and development of IR and cardiovascular complications [37]. Overall, the present findings could be attributed to there is relationship between the work of adiponectin and TNF-α as sources of protection and proinflammatory factor of the body regardless of the age.

**2. Effect of gender on the studied parameters**

**Effect of gender on glucose related parameters in T2DM patients**

The data present in table (5) shows the effect of gender on glucose related parameters in T2DM patients. The findings revealed a significant (P<0.05) increase in levels of FBS in men compared with women, while no significant differences (P>0.05) were found in the levels of HbA1c, insulin and IR. Concerning of the result of FBS, a similar result was reported by (24) who stated that FBS levels of men were significantly higher than those of women. In contrast, it is in disagreement with Hassan S A *et al*[38] who stated that no significant differences were found in this parameter between men and women in T2DM patients' group. Other study Willer AK *et al* [39] explained that the tests at baseline, individually or combined, FPG and 2hPG performed in boys and girls are alike. There is indicates that men and women have different attitudes and behaviors related to diabetes care. Where Women are more sensitive to illnesses, more able and likely to rest during an illness, and more willing to seek medical advice. Where found the women were have a greater interest and concern for diabetes and were more likely to perceive symptoms than men. However this study failed to take into account other factors such as stress at work or low mood due to lack of support from peers for the patient that could have led to the behavior pattern of the gender and which could have affected the results. Agreement with Hassan S A *et al* [38] who reported that the plasma HbA1c levels are not affected by gender, HbA1c levels of the studied cases did not show any significant differences between the men and women. In contrast found that HbA1c levels in women at reproductive age were elevation. Iron deficiency is common in women, and depleted iron stores affect glycation rates and elevate HbA1c. Also, this result is in disagreement with the results obtained by Ha KH *et al* [22] who studied the median HbA1c in men was also significantly higher than in women. In that study the proportion of participants with current smoking or current drinking status was higher in men than in women. On the other hand, the proportion of participants using antihypertensive and lipid-lowering drugs was lower in men than in women. While the current finding could be attributed to that the participants were not in same conditions above. In the present study there is no effect of the gender on the level of insulin. This result is in agreement with Willer AK *et al* [39] who reported that in T2DM, the impairment of insulin sensitivity and insulin secretion is substantial and similar in both sexes. Sex and gender differences are equally important in development, awareness, presentation, diagnosis, and therapy, as well as prevention of the lifestyle-associated disease T2DM. On the other hand, this result is in disagreement with Aregbesola A *et al*[40] who found a higher fasting plasma insulin level and HOMA-IR in males than in females. These variations could be due to some factors such as random testing, selection bias, and sex disparities in access to healthcare in some countries [39]. Also, there is no effect of the gender on the level of IR rate. Similar result has also been observed by Willer AK *et al*[39] who reported that in T2DM, the impairment of IR, insulin sensitivity and insulin secretion is substantial and similar in both sexes. The variations in these studies may be due to ethnicity in the analyses of gender difference in IR and T2DM prevalence and incidence. No significant differences between sexes which were found in this study may be due to the fact that a homeostatic model assessment of IR (HOMA-IR) using FBS and fasting serum insulin levels was employed to estimate IR, and as clear from the above results insulin level did not affect by differences in the gender.

**Effect of gender on renal function parameters in T2DM patients**

The results in table (6) shows the effect of gender on renal function parameters in T2DM patients. The finding showed a significant (P<0.05) increase in B.urea and S.creatinin levels in men compared with women, while serum levels of Ca and P showed no significant (P>0.05) differences between men and women. Plasma urea and creatinine are established markers of GFR. The present findings regarding B.urea and s. creatinine are similar to that reported by previous study [23]. As mention previously in this study, FBS was significantly increased in men compared with women, so the explanation behind the increased levels of B. urea may be due to the relationship between blood sugar level and urea level. Hyperglycemia is one of the major causes of progressive renal damage and an increase in urea level is seen when there is damage in the kidney, or the kidney is not functioning properly. On the other hand, Bamanikar SA *et al* [6] reported that a no significant effect of gender on B.urea level. The finding that increased level of s. creatinine in men compared with women, has been reported in previous study [6]. Men have higher serum creatinine levels likely due to increased protein intake and storage of creatinine as a waste product in muscle mass which is higher in men. On the other hand, Murtadha JH *et al* [23] stated that the lower serum creatinine is associated with high risk of type 2 diabetes, which might reflect a lower volume of skeletal muscle. The present finding that no significant differences in the level of calcium between men and women, is in agreement with Hassan S A *et al* [38]. In addition, the insulin stimulates $Ca^{+2}$ oscillations even in $Ca^{+2}$ free medium, insulin increases cytoplasmic $Ca^{2+}$ by mobilizing intracellular $Ca^{+2}$ stores [41]. The results observed in the present study may be explained on the ground that the level of insulin was not affected by the gender, causing that calcium not be affected by gender. Concerning of phosphorus level, a same finding was reported by previous study Shimodaira M *et al* [42] who suggested that serum phosphorus maintains different associations with age, race and diabetes, in men and women both. Higher serum P levels were associated with lower FBS levels in both genders. The current finding is do not agree with Lederer, E [43] who reported that the serum p is influenced by endogenous factors such as age and gender.

**Effect of gender on calcium regulating hormones in T2DM patients**

The data present in table (7) shows the effect of gender on calcium regulating hormones in T2DM patients. A non-significant

difference was found in levels of PTH in men compared with women, while a significant increased (P>0.05) were found in the levels of calcitonin in men compared with women. Serum levels of vit. D showed non-significant (P<0.05) differences between the two gender. In some studies that PTH level was higher in T2DM patients than the control but it was not significantly. PTH could increase intracellular calcium in skeletal muscle and adipocytes, which would consequently suppress glucose uptake by those tissues and induce IR [42]. Differences in the prevalence of vitamin D deficiency in males and females may contribute to the different degrees of association between PTH and vitamin D [44]. The major regulatory substances for phosphorus are PTH and vit. D. The major physiological PTH functions predominantly as a calcium regulating hormone with secondary effects on phosphate homeostasis [43]. It well documented that the number of parathyroid glands and their location did not differ between the men and women. It is clear from the results presented in the current study that all PTH-related parameters were not affected by gender, causing the PTH not to be affected by gender. Regarding the present result of calcitonin level, the current finding is in concordance with Al-Darraji SZ *et al* [30] who found that the sex was the most important determinant of elevated serum calcitonin concentrations in men. Also, other study Arnold JF. and Barton SL [8] observed a higher mean calcitonin values in men than women. They stated that this difference between men and women has been ascribed to a lower calcitonin secretion rate in women. Also, this result could be attributed to the maximum C-cell surface area in the adult thyroid gland is twice as high in men as in women, and it has been established that smoking can increase the number of neuroendocrine cells and the secretion of peptides such as calcitonin. Regarding the results of vit. D, it is in agreement with the result obtained by Harinarayan C V [45] who studied that the serum $25(OH)_2$ D3 levels were inversely associated with metabolic syndrome in both genders. While Willer AK *et al* [39] reported significant differences in vitamin D levels were detected between the male and female. Also, Abudawood M *et al* [46] stated that levels of Vitamin D were higher in males than females in both non-diabetic and T2DM patients. The study Rafiq S. and Jeppesen PB [33] mentioned that vitamin D can enhance the synthesis of insulin hormone and its release from the β-cells; hence, it plays a role in glucose metabolism. The finding may be due to the fact that insulin, IR, Ca and P levels were not affected by gender. So the link between Vit. D and these parameter led to this finding.

**Effect of gender on cytokines related with T2DM patients**

Table (8) shows the effect of gender on cytokines related with T2DM. A significant (P<0.05) increased was found in the level of adiponectin in women compared with men, while non-significant (P>0.05) differences was found in the level of TNF-α between the two gender. Deregulation of adiponectin action is related in the development of T2DM [39]. This is in harmony with Al-Fartosy AJM *et al* [21] who found that the disparate circulating adiponectin concentrations by gender that is suggested to be lower in males. Their data obtained was show that females had a significantly higher adiponectin serum levels than males. At any particular body size or body weight, adiponectin concentrations are greater in women than in men. A possible explanation for this gender based difference in serum adiponectin levels could be due to the following reasons; first, is the different body fat distribution between males and females. The adipose tissue is the largest endocrine organ in the body, the adiponectin which is secreted by white adipose tissue and accounts for 0.01% of total plasma proteins. It has been reported that the number of fat cells and their size are possible determinants of adiponectin production rates since it is mainly secreted from adipocytes [21]. Second, the effect of sex hormones on the production of adiponectin rate. Testosterone has an inhibitory effect on adiponectin secretion. Interestingly, a series of published studies have reported an illogical high level of adiponectin in diabetic patients with severe insulin resistance [47]. The finding of TNF-α level is in agreement with previous study Zinman B *et al* [48] who reported that no differences between men and women regarding the serum TNF-α concentration with a higher prevalence of T2DM. Since in this study this parameter did not affected by the gender, so the level of TNF-α did not affected by gender.

**Table 1: Effect of age on glucose related parameters in T2DM patients**

| Parameters | Age category (year) | | | | LSD value |
|---|---|---|---|---|---|
| | 20-29 | 30-39 | 40-49 | 50-59 | |
| FBS (mg/dl) | 170.46 $^{b}$ ± 14.2 | 193.50 $^{a}$ ±74.70 | 223.58 $^{a}$ ± 20.6 | 227.82 $^{a}$ ± 19.5 | 40.261 * |
| HbA1c (%) | 5.92 $^{b}$ ± 1.32 | 8.29 $^{a}$ ± 0.45 | 9.09 $^{a}$ ± 0.36 | 9.29 $^{a}$ ± 0.42 | 2.379 * |
| Insulin (µu/ml) | 13.80 $^{b}$ ± 1.51 | 22.56 $^{b}$ ± 4.16 | 68.46 $^{a}$ ± 38.47 | 53.45 $^{a}$ ± 23.11 | 16.826 * |
| Insulin Res (IR) | 6.33 $^{b}$ ± 1.84 | 8.82 $^{b}$ ± 1.56 | 41.84 $^{a}$ ± 26.11 | 40.87 $^{a}$ ± 15.96 | 17.921 * |
| * (P<0.05) | | | | | |

**Table 2: Effect of age on renal function parameters in T2DM patients**

| Parameters | Age category (year) | | | | LSD value |
|---|---|---|---|---|---|
| | 20-29 | 30-39 | 40-49 | 50-59 | |
| B. Urea(mg/d) | 23.70 $^{c}$ ± 2.70 | 31.70 $^{b}$ ± 1.80 | 37.00 $^{a}$ ± 2.15 | 38.08 $^{a}$ ± 1.72 | 4.551* |
| S.Creatinine (mg/dl) | 0.716$^{a}$ ± 0.05 | 0.810$^{a}$ ± 0.29 | 0.836$^{a}$ ± 0.06 | 0.923$^{a}$ ± 0.06 | 0.275 NS |
| Ca (mg/dl) | 8.21$^{a}$ ± 0.47 | 8.37$^{a}$ ± 0.12 | 8.26$^{a}$ ± 0.13 | 8.37$^{a}$ ± 0.08 | 0.894 NS |
| P (mg/dl) | 3.55 $^{b}$ ± 0.05 | 4.13 $^{a}$ ± 0.12 | 4.03 $^{a}$ ± 0.12 | 4.17 $^{a}$ ± 0.09 | 0.352* |
| * (P<0.05), NS: Non-Significant. | | | | | |

**Table 3: Effect of age on calcium regulating hormones in T2DM patients**

| Parameters | Age category (year) | | | | LSD value |
|---|---|---|---|---|---|
| | 20-29 | 30-39 | 40-49 | 50-59 | |
| PTH (pg/ml) | 96.00 [a] ± 30.70 | 46.44 [b] ± 6.06 | 41.69 [b] ± 3.61 | 51.19 [b] ± 5.07 | 23.859 * |
| Calcitonin (pg/ml) | 1.640[a] ± 1.14 | 1.159[a] ± 0.21 | 2.08[a] ± 0.66 | 1.189[a] ± 0.23 | 1.135 NS |
| Vit. D (ng/ml) | 17.40 [a] ± 1.07 | 16.15 [b] ± 0.85 | 15.66 [b] ± 0.93 | 16.08 [b] ± 0.95 | 1.068 * |
| * (P<0.05), NS: Non-Significant. | | | | | |

**Table 4: Effect of age on adiponectin and TNF-α in T2DM patients**

| Parameters | Age groups (year) | | | | LSD value |
|---|---|---|---|---|---|
| | 20-29 | 30-39 | 40-49 | 50-59 | |
| Adiponectin (µg/ml) | 10.41[a] ± 1.88 | 10.80[a] ± 0.69 | 11.32[a] ± 0.72 | 11.84[a] ±0.70 | 1.984 NS |
| TNF-α (ng/ml) | 110.42[a] ± 20.08 | 105.84[a] ± 4.20 | 119.01[a] ± 11.20 | 107.52[a] ± 8.76 | 27.054 NS |
| NS: Non-Significant. | | | | | |

**Table 5: Effect of gender on glucose related parameters in T2DM patients**

| Parameters | Gender | | LSD value |
|---|---|---|---|
| | Men | Women | |
| FBS (mg/dl) | 234.70[a] ± 17.88 | 186.09[b] ± 11.96 | 42.811* |
| HbA1c (%) | 8.89[a] ± 0.33 | 8.88[a] ± 0.35 | 0.774 NS |
| Insulin (µu/ml) | 58.25[a] ± 25.49 | 40.81[a] ± 18.15 | 20.663 NS |
| Insulin Res. (IR) | 34.89[a] ± 17.07 | 21.59[a] ± 12.87 | 18.0954 NS |
| * (P<0.05), NS: Non-Significant. | | | |

**Table 6: Effect of gender on renal function parameters in T2DM patients**

| Parameters | Gender | | LSD value |
|---|---|---|---|
| | Men | Women | |
| B. Urea (mg/dl) | 37.42[a] ± 1.77 | 33.98[b] ± 1.33 | 2.071 * |
| S. Creatinine (mg/dl) | 0.976[a] ± 0.05 | 0.692[b] ± 0.03 | 0.127 * |
| Ca (mg/dl) | 8.40[a] ± 0.08 | 8.25[a] ± 0.09 | 0.664 NS |
| P (mg/dl) | 4.09[a] ± 0.09 | 4.11[a] ± 0.08 | 0.338 NS |
| * (P<0.05), NS: Non-Significant. | | | |

**Table 7: Effect of gender on calcium regulating hormones in T2DM patients**

| Parameters | Gender | | LSD value |
|---|---|---|---|
| | Men | Women | |
| PTH (pg/ml) | 47.51[a] ± 4.49 | 50.86[a] ± 6.04 | 5.732 NS |
| Calcitonin (pg/ml) | 2.29[a] ± 0.44 | 0.635[b] ± 0.04 | 0.772 * |
| Vitamin D (ng/ml) | 16.45[a] ± 0.88 | 16.07[a] ± 0.65 | 1.535 NS |
| * (P<0.05), NS: Non-Significant. | | | |

**Table 8: Effect of gender on cytokines related with T2DM**

| Parameters | Gender | | LSD value |
|---|---|---|---|
| | Men | women | |
| Adiponectin (µg/ml) | 19.87[b] ± 0.48 | 11.29[a] ± 0.62 | 1.189 * |
| TNF-α(ng/ml) | 113.13[a] ± 7.85 | 108.83[a] ± 6.78 | 17.592 NS |
| * (P<0.05), NS: Non-Significant. | | | |

## CONCLUSION

From the results of this study could be concluded: The risk of developing type 2 diabetes mellitus (T2DM) increases with age and gender, and the risk score of T2DM was higher in the elderly patients than in the younger patients. The decreased levels of vitamin D in the diabetic patients suggest that altered vitamin D and calcium homeostasis may play role in the development of T2DM. Vitamin D as an agent in diabetic management is rather appealing. Parathyroid hormone levels were low in the elderly patients

## ACKNOWLEDGEMENT

The authors gratefully acknowledge to all participant in this study and to all the staff members in AL-kindi Medical Directorate/Specialized Center of Endocrinology and Diabetes for their great help and to express thanks and gratitude to all staff members of the teaching laboratories in the medical city hospital in Baghdad.

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**Cite this article as:**

Aseel Khalid Thabah Al-Attaby and Makarim Qassim Al-Lami. Effect of age and gender on some biochemical, hormones and adipocytokines parameters in Iraqi type 2 diabetes mellitus patients. Int. Res. J. Pharm. 2018;9(12):23-30 http://dx.doi.org/10.7897/2230-8407.0912286

Source of support: Nil, Conflict of interest: None Declared