Biochem. Cell. Arch. Vol. 21, No. 1, pp. 491-499, 2021	www.connectjournals.com/bca	*ISSN 0972-5075*
DocID: https://connectjournals.com/03896.2021.21.491		*eISSN 0976-1772*

AGE AND GENDER IMPACT ON GLYCAEMIC CONTROL, RENAL FUNCTION AND OXIDATIVE STRESS PARAMETERS IN IRAQI PATIENTS TYPE 2 DIABETES MELLITUS

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(Received 6 July 2020, Revised 13 September 2020, Accepted 29 September 2020)

ABSTRACT : Type 2 daibetes mellitus (T2DM) is a global concern boosted by both population growth and ageing, the majority of affected people are aged between (40- 59 year). The objective of this research was to estimate the impact of age and gender on glycaemic control parameters: Fasting blood glucose (FBC), glycated hemoglobin (HbA1C), insulin, insulin resistance (IR) and insulin sensitivity (IS), renal function parameters: urea, creatinine and oxidative stress parameters: total antioxidant capacity (TAC) and reactive oxygen species (ROS). Eighty-one random samples of T2DM patients (35 men and 46 women) were included in this study, their average age was 52.75±9.63 year. Current study found that FBG, HbA1C and IR were highly significant (P<0.01) increased by increasing age. The lowest level of FBG was in the age group 30-39 years, which was a high significant (P<0.01) lower than other age groups 40-49, 50-59 and ≥ 60 years. The highest level of HbA1C was in advanced age group ≥ 60years, which was significantly (P<0.01) highest than other groups 30-39, 40-49 and 50-59 years. The highest level of IR was in the older age group ≥ 60 years, which was significantly (P<0.01) highest than other age groups 30-39, 40-49 and 50-59 years. Insulin hormone level showed no significant (P>0.05) differences between age groups. Insulin sensitivity decreased in older age group ≥ 60years compared with the other age groups with a highly significant differences. The results shows a highly significant (P<0.01) increasing in levels of urea and creatinine with increasing age. The lowest level of urea was found in 30-39 and 40-49 year compared with other age groups, highest levels of creatinine were in 50-59 and ≥ 60 age groups, which were significantly (P<0.01) highest than 30-39, 40-49 years age groups. In present study, the levels of TAC decreased by age. Third age group 50-59 showed the lowest level of TAC, which was significantly (P<0.05) lower than other age groups 30-39, 40-49 and ≥ 60 years. Statistical analysis showed that the level of ROS was significantly (P<0.05) increased in advanced age groups 50-59 and ≥ 60years compared with other age groups 30-39 and 40-49 years. Statistical analysis revealed a significant (P<0.05) increased in levels of FBG in women compared with men, while insignificant differences (P>0.05) found in the HbA1c and insulin levels. A highly significant (P<0.01) increased in IR value was also found in women compared with men. Also, statistical analysis show that IS value was significantly decrease in women compared with men. The statistical analysis showed a non-significant differences for increasing levels of urea in women compared to men, while current finding showed a highly significant (P<0.01) increase in creatinine levels in men as compared with women. The present study showed insignificant increasing in the mean of TAC in men compared to women. While, the mean of ROS was significantly (P<0.05) increase in women compared to men.

Key words : Glycaemic control parameters, total antioxidant capacity, reactive oxygen species, type 2 diabetes mellitus, urea, creatinine.

How to cite : Hawraa Sabah Al-Musawi, Makarim Qassim Al-Lami and Ali H. Al-Saadi (2021) Age and gender impact on glycaemic control, renal function and oxidative stress parameters in Iraqi patients type 2 diabetes mellitus. *Biochem. Cell. Arch.* **21**, 491-499. DocID: https://connectjournals.com/03896.2021.21.491

INTRODUCTION

Type 2 Diabetic Mellitus is a metabolic disease in which there are high blood sugar levels over a prolonged period. Diabetes management is affected by gender and age, where women and elderly of ≥ 60 years are extremely affected because they are suffer from multiple medical conditions involving heart and kidney leading to limitations and insufficiencies of medical treatment (ADA, 2019). The purification of blood from insulin depend on receptors of insulin and enzyme that degrading it and deficient of these two molecules will lead to impaired in insulin purification and then hyperinsulinemia and this will

lead to development of insulin resistance (Farris *et al*, 2004). The levels of insulin were determined by the balance between the production and clearance of insulin (Corkey, 2012). Insulin Resistance is known as a state in which target tissues have diminished sensitivity to insulin, leads to elevate both blood glucose and insulin levels (Nan *et al,* 2012). Previous studies found that impairment of IS may caused by hyperglycemia and hyperinsulinemia themselves (Yki-Jarvinen, 1992).

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. Generally, urea and creatinine are elevated with increasing blood glucose level in unchecked diabetics and usually associated with severity of kidney damage. Creatinine is a product of creatinine phosphate breakdown which is released from skeletal muscle at a settled rate (Bamanikar *et al*, 2016). Oxidative stress is defined as a disruption in balance between reactive oxygen species (ROS) and antioxidants systems produced upon oxidative damage (Rashid *et al*, 2013).

Reactive oxygen species are a number of short-lived reactive molecules and free radicals containing one or more unpaired electrons derived of molecular oxygen which are critical for life of aerobic organisms, which generated during physiological or pathophysiological oxidative metabolism in mitochondria such as: O^{-2} and hydrogen peroxide (H_2O_2) (Sies, 1999; Hancock *et al*, 2001). Abundance of ROS or a faulty in intracellular defenses against ROS will result in pathogenesis of diabetes by give rise to oxidative damage to bio-molecules like lipids and proteins (Yang *et al*, 2012).

Antioxidants are substances that have the ability to neutralize free radicals caused by oxidation processes or suppress oxidation processes that occur under the impact of ROS, also are engaged in defense mechanism of the organism against the pathologies kinked to the free radicals attack (Kalaivanam *et al*, 2006). In general antioxidants parameters include superoxide dismutase (SOD), catalase (CAT), ceruloplasmin, glutathione peroxidase (GPx), glutathione reductase (GSH) and total antioxidant capacity (TAC) (Ferrari *et al*, 2011). Various methods can be used to evaluate the anti-oxidant status through measuring TAC. The measurement of TAC includes cumulative action of all antioxidants found in the plasma and body fluids, so it providing a completed parameter rather than the simple gathering of the measurable antioxidants. The evaluation of TAC provides assessment for all the known and unknown antioxidants and their synergistic interaction, thus giving an insight into the rigorous balance *in vivo* between antioxidants and oxidants (Pieme *et al*, 2017). Despite that free radicals level are agreed to be increase in diabetic patients (Srivatsan *et al*, 2009), the antioxidants level in diabetic patients has been found to stay the same (Giugliano *et al*, 1996), decrease (Song *et al*, 2007; Picchi *et al*, 2010), or increase (Kharroubi *et al*, 2015).

In T2DM, despite the fact that genes are proved to be related to risk of the disease, absent of exercise, obesity, indigent dietary habits, Insufficient sleep and other risk factors have been engaged in the etiology of disease (Nicklas *et al*, 2005; Ferrari, 2008).

Aim of the study

The aim of this study was to evaluate the impact of age and gender on the glycaemic control parameters, renal function, antioxidants and oxidant parameters in T2DM patients attending to the diabetes and endocrine care center of Marjan Teaching Hospital, Hilla province, Iraq.

MATERIALS AND METHODS

Subjects and the study design

Participants of present study composed of 81 patients (35 men and 46 women) with T2DM attending to the Diabetes and Endocrine care center of Marjan Teaching Hospital, Hilla province, Iraq. All participants were taken consent and were guided to fast for 10–12 hours before starting to collect blood samples. The medical history and clinical data of the studied patients were collected to record duration and complications of disease such as nephropathy, retinopathy hypertension, feet ulcer and cardiovascular diseases.

Collection of blood sample and preparation

Fasting venous blood samples were collected from all participants. Whole blood was pushed into EDTA tubes for determination of HbA1c concentration. For serum preparation, remaining blood pushed into disposable gel tubes was allowed to clot at room temperature for (10-15 minutes) and then centrifuged at (2000 × g) for approximately (10-15 min), and stored the obtained serum at -20^{0}C for further analysis of FBG, insulin, urea, creatinine, TAC and ROS.

Biomarkers analysis

Measurement of fasting blood glucose (FBG)

Enzymatic colorimetric method of Barham and Trinder (1972) has been employed to estimate FBG (mg/dl) used the Linear kit, Spain.

Measurement of Glycated Hemoglobin (HbA1c)

The HbA1c level was measured by an automated Epithod®616 Analyzer (DxGen /Korea) based on the

boronate affinity principle (ADA, 2017).

Measurement of Insulin Hormone

Insulin hormone has been inspected by using (CALBIOTECK/USA) ELISA kit specific for human insulin which relay on the standard sandwich enzyme-linked immune-sorbent technique (Kao *et al*, 1994).

Calculation of insulin resistance & insulin sensitivity

Insulin resistance has been assessed by determining of homeostasis model estimation of insulin resistance (HOMA-IR) and calculate by using the following equation (Stumvoll and Gerich, 2001):

$IR = (I_0 \times G_0) / 405$

I_0: Fasting insulin level. G_0: Fasting glucose level.

The quantitative insulin sensitivity check index (*QUICKI*) is derived utilizing the inverse of the sum of logarithms of fasting serum insulin and FBG (Katz *et al*, 2000).

$IS = 1 / (\log_{(\text{fasting insulin } \mu IU/ml)} + \log_{(\text{fasting glucose mg/dL})}$

Measurement of urea

Estimation of serum urea (mmol/L)was done by Berthelot's method using Linear kit, Spain (Friedman and Young, 2000).

Measurement of creatinine

Randox kit (Randox, UK) was used to estimate creatinine (mmol/L) based on the formation of colored complex comes when creatinine reacts with picrate in alkaline solution (Henry, 1974).

Measurement of total antioxidant capacity (TAC)

Cupric ion reducing antioxidant capacity (CUPRAC) method used to estimate TAC, this method measure the capacity of an antioxidant in the reduction of an oxidant, which changes color when reduced (Apak *et al*, 2010).

Measurement of Total Reactive Oxygen Species (ROS)

Reactive oxygen species was determined using a novel method, developed by Erel (2005). This method measure color intensity formed as a result of oxidation the ferrous ion–o-dianisidine complex to ferric ion by the oxidant found in the serum of T2DM.

Statistical analysis

The statistical analysis has been performed using SPSS 23 version. Data of study were expressed as (mean ± SD) using T-test. The normality of the distribution of all variables has been assessed using student′s Anova test. P values less than (0.05) is considered significant.

RESULTS AND DISCUSSION

The impact of age on the studied parameters

The mean±SD age of all patients was 52.75±9.63 year. Subjects were divided into four age groups: (30-39, 40-49, 50-59, ≥ 60), the percentage of each group showed in Fig. 1, the most represented age group was (50-59) and (≥ 60) years with percent 30.9%, 37%, respectively. The impact of age has been studied on some of the parameters that are closely related with T2DM, including: glycaemic control parameters, renal function parameters, oxidant and antioxidant parameters.

The possibility of developing T2DM increases with age. Several factors engaged in the pathophysiology of glucose intolerance in the elderly patients. The major factors are that aging prompt decrease IS and alter or insufficient compensation of β-cell functional against of increasing IR (Chang and Halter, 2003). Minimize in the proliferation capacity of β-cell and boost sensitivity to apoptosis are the states associated with aging (Maedler *et al*, 2006).

About more than half of patients diagnosed with T2DM are over 60 years of age, also diabetes prevalence peaks in subjects 65-74years of age. National Health and Nutrition Examination Survey data from 2006 revealed that 23.1% of all patients who are ≥60 years of age have diabetes (Morley, 2008). The study conducting by Cho *et al* (2018) has been supports the current finding, they found that patients aged 45-64 were the most diagnosed age group with T2DM.

The impact of age on glycaemic control parameters in T2DM patients

Table 1 illustrate the impact of age on the means of glycaemic control parameters (FBG, HbA1C, insulin, IR and IS) in T2DM patients. Current study found that FBG, HbA1C and IR were highly significant ($P<0.01$) increased by increasing age. The lowest level of FBG was in the age group 30-39 years, which was a high significant ($P<0.01$) lower than other age groups 40-49, 50-59 and ≥ 60 years. The highest level of HbA1C was in the advanced age group ≥ 60 years, which was significantly ($P<0.01$) highest than others age groups 30-39, 40-49 and 50-59 years. The highest level of IR was found in the older ≥ 60years age group, which was significantly ($P<0.01$) highest than others age groups: 30-39, 40-49 and 50-59 years. Insulin hormone level showed no significant ($P>0.05$) differences between age groups. the values of IS showed a highly significant ($P<0.01$) decrease in the older age group ≥ 60 years compared with the other age groups.

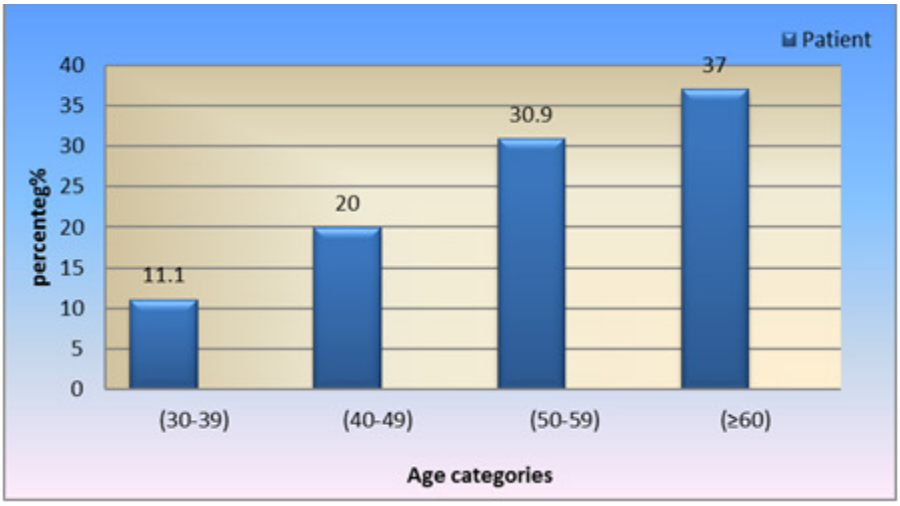

Fig. 1 : Distribution of T2DM patients by age groups.

The main reason for the boost of glycaemic control parameters in elderly patients is the progressive diminish of glucose tolerance. particularly, there is an age-related weakness in insulin-mediated glucose uptake. During the aging process, there is an elevation in oxidative stress and reduce in the neuro-hormones dehydroepandrogesterone and insulin-like growth factor-1, all of which effect action of insulin (Barbieri *et al*, 2001). It is well known that T2DM has often been undiagnosed for several years because hyperglycemia gradually occurs and is often not serious enough for the patient to recognize the classic symptoms of diabetes at the earlier stages. The findings can be clarified on the basis that the risk of type 2 diabetes rises with age, obesity and lack of physical activity (ADA, 2015).

The HbA1c is useful as it reflects chronic hyperglycaemia, with several advantages over FBG and OGTT (ADA, 2014). The HbA1c level can be influenced by a variety of blood conditions including haemoglobinopathies, haemolytic anemia and other types of anemia (Fox *et al*, 2015). The increased proportion of HbA1C with advanced age in the studied patients is agreement with Mohsen (2016). The present findings might be due to the fact that the HbA1C is greatly affected by elevated sugar levels. Similarly, Joung *et al* (2018) showed that the HbA1c level was higher in older than in younger patients with comparable glucose profiles, and it was more exact diagnostic test than the FBG in older patients.

Insulin play pivotal role in the regulation of glucose and its uptake from blood into sundry tissues such as muscle, liver and adipose tissue (ADA, 2014). The current study shows that the level of insulin insignificantly ($P>0.05$) reduced with age. Many physiological changes happen with age may contribute in impairment of insulin secretion and action, including changes in body composition, lack of physical fitness and hormonal changes (e.g. growth hormone, insulin-like growth factor, sex steroids and leptin), lipotoxicity and glucotoxicity secondary to sustain altitude of circulating free fatty acids and glucose. Also, the reason may attributed to impaired β-cell sensitivity of incretin hormone, which in turn spur insulin secretion. Consequently, both impaired β-cell compensation and IR result in elderly people developing T2DM (Morley, 2008).

Insulin resistance, a condition where insulin responsive tissues flop to increase glucose uptake in response to physiological concentrations of insulin leading to persistent hyperglycemia (Al-Fartosy *et al,* 2017). The current study records a significant increasing in IR value with age, a clear rise in the mean of IR were detected in age groups 50-59 and ≥ 60 years compared with 30-39 and 40-49 years. Generally, the major causes explained the age-related IR involving: anthropometric alteration, the environmental factors, neurohormonal changes, and boost oxidative stress (Barbieri *et al*, 2001). Current finding agrees with Mohsen *et al* (2016), who revealed an elevation in the levels of insulin in aging T2DM patient and this elevation associated with insulin IR status levels.

The impairment of (IS) may be resulted from hyperglycemia and hyperinsulinemia themselves (Yki-Jarvinen, 1992). Present study show that IS was elevated in ≥ 60 years age group compared with other groups. This is agreement with finding of Abu-Khumrah (2017) which show that IS increasing with age.

The impact of age on Renal function parameters in T2DM patients

Table 2 illustrate the influence of age on the means of renal function tests in T2DM patients. The results show a highly significant ($P<0.01$) increasing in levels of urea

Table 1 : Impact of age on glycaemic control parameters of T2DM.

Parameters	Diabetic group				P value
	30 - 39	40 - 49	50 - 59	≥ 60	
FBG (mg/dl)	168.33±15.31[a]	187.61±25.4[abc]	213.54±18.68[b]	234.13±38.11[c]	0.000**
HbA1c	7.87±0.68[a]	7.90±0.50[a]	8.06±0.59[a]	9.40±1.52[b]	0.000**
Insulin(µIU/ml)	18.93±4.44	16.77±4.51	16.66±5.37	16.25±3.64	0.73[NS]
IR	6.39±1.80[a]	7.61±1.30[a]	8.97±2.95[a]	11.64±3.46[b]	0.004**
IS	0.29±0.02[a]	0.29±0.02[a]	0.29±0.02[a]	0.27±0.03[b]	0.000**

Different letter refer to significant differences among groups, **(P<0.01), NS: Non-significant.

Table 2 : Impact of age on renal function parameters in T2DM patients.

Parameters	Diabetic group				P value
	30 - 39	40 - 49	50 - 59	≥ 60	
Urea (mmol/l)	4.36±0.59 [a]	4.74±0.94 [a]	6.63±0.76 G"	8.59±1.53 h	0.000**
Creatinine(mmol/l)	68.44±8.39 [a]	74.71±8.16 [a]	76.77±12.81[a]	98.23±19.63G"	0.000**

Different letter refer to significant differences among groups , **(P<0.01)

with increasing age. The lowest level of urea was found in 30-39 and 40-49 year age group compared with others age groups. Creatinine levels were also show a highly significant (P<0.01) increasing with aging, the highest level was in aged group ≥ 60 years, which were significantly (P<0.01) highest than other age groups 30-39, 40-49, 50-59 years.

A clear trend of increasing levels of urea with advanced age have been detected in present study. Present finding consistent with the finding of Murtadha *et al* (2016), who have been demonstrated a strong positive correlation between age and urea.

This finding may be due to the significantly higher FBG in elderly patients as previously mentioned, which indicates presence of strong relationship between blood glucose level and urea level because hyperglycemia is one of the main causes in progress kidney damage, so high levels of urea is usually seen in state of kidney damage or when kidney is not properly function. This finding supporting with a previous study, which demonstrated that hyperglycemia represented one of major causes of gradual kidney damage (Bamanikar *et al*, 2016). Furthermore, present study covenant with the results of Al-Attaby and Al-Lami (2018), who also recorded a significant increasing in the levels of urea with increasing age.

Regarding creatininie levels, the present study revealed a significant increasing in the creatinine level with advanced age. The creatinine levels closely related with the percent of the body, that is skeletal muscle. It is filtrated by mean of the glomerulus, and a teeny amount is also liberated to the glomerular filtrate through the proximal tubule (Argirova and Breipohl, 2002). Present finding is consistent with previous study which showed that levels of creatinine is influenced by age and these association between the age and creatinine levels in T2DM due to the hazard of developing the end stage renal disease (ESRD) (Murtadha *et al*, 2016).

Impact of age on antioxidant and oxidant parameters in T2DM patients

Table 3 illustrate the effects of age on the levels of TAC and ROS. In the present study the levels of TAC decreased by age. Third age group 50-59 showed the lowest level of TAC, which was significantly (P<0.05) lower than other age/groups/30-39, 40-49 and ≥ 60 years. Statistical analysis showed that the level of ROS was significantly (P<0.05) increased in advanced age groups 50-59 and ≥ 60 years compared with other age groups/ 30-39 and 40-49 years.

Antioxidants substances play a major role in preventing the formation and in scavenging of free radicals. This decrease in TAC levels may be due to its excess utilization in order to scavenge the free radicals produced in high amounts due to increased hyperglycemia. Argirova and Breipohl (2002) stated that decreasing levels of TAC with increasing age due to increased the oxidative stress, which may exert accumulative damage of cell contents that plays a role in decrease TAC levels and enhanced the progression of aging disease like T2DM. The current study agrees with the results of Al-aaraji (2017) study, which also showed a decrease in the TAC rate with age and reported a significant differences in TAC between age groups.

Reactive oxygen species showed a significant differences between age groups, the higher ROS levels were in age group 50-59 years and ≥ 60 years and lower ROS levels were in age/groups 30-39 and.40-49/years

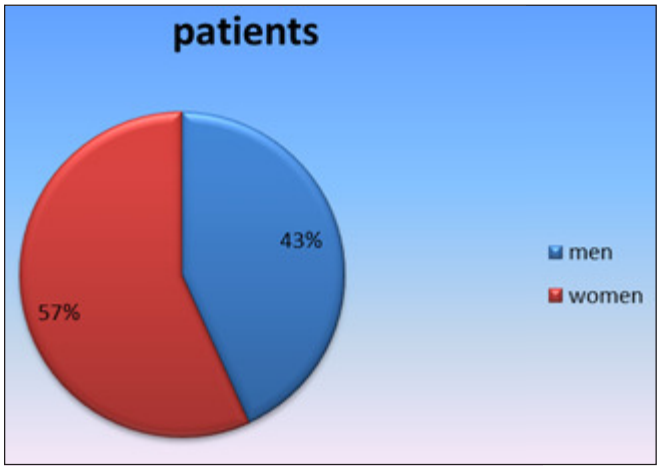

Fig. 2 : Distribution of T2DM patients according to gender.

may be due to high TAC levels in the last two age group; that decrease by increasing age because age considered as risk factor for developing T2DM, in which increased free radicals first related with an increase of antioxidant levels to provide more production against free radicals and with the disease progression the levels of antioxidant gradually reduced (Pourvali *et al*, 2016). Similar findings support the result of the current study, which also indicated an increase in ROS levels in elderly T2DM patients (Zhang *et al*, 2002).

The impact of gender on the studied parameters

The study included 81 patients, of whom 35 were men and 46 women. In the present study women's percentage was higher than men, as shown in Fig. 2.

The present study showed that prevalence of T2DM in women is higher than men. Estrogen and gonadal hormones alterations which changes of immune cells function represented a best justification for increasing disease probability in women than men, this agreed with (Zhang *et al*, 2002), who suggest that estrogen hormone control the liver production of glucose and in diabetic women this hormone boost the influx of glucose from liver. The results of current study along the lines of other studies (Stoian *et al*, 2015; Ferdi *et al*, 2018) that showed the higher percentage of T2DM patients in women.

Impact of gender on glycaemic control parameters in T2DM patients

Table 4 elucidates the impact of gender on glycaemic control parameters in T2DM patients. Statistical analysis revealed a significantly ($P<0.05$) elevated in levels of FBG in women compared with men, while insignificant differences ($P>0.05$) were found in HbA1c and insulin levels. A highly significant ($P<0.01$) increased in IR value was found in women compared with men. Also, statistical analysis show that IS value was significantly ($P>0.05$) decrease in women compared with men.

Regarding to FBG, a comparable results have been reported by previous studies conducting by Machado-Alba *et al* (2016), who stated that women are highly influenced by T2DM because they are less muscular, so does not prop high absorption of fixed glucose load. In contrast, result of present study is in conflict with Rohitash *et al* (2014), Al-Attaby and Al-Lami (2018) studies were reported that FBG levels of men were significantly increased compared with women.

Concerning to HbA1C, present study showed a somewhat increase in the HbA1C level in women than men. Generally, women have a lower hemoglobin level than men, and this may explain the increase in glycated hemoglobin in women compared to men. The current study agrees with Hassan *et al* (2016), Al-Attaby and Al-Lami (2018) studies, where confirmed that HbA1c levels were not influenced by gender. While the present finding conflict with the study conducted by Ha *et al* (2018), they reported that HbA1c levels in men were significantly higher than in women. In that study, it was observed that the percentage of participants, who were current smokers or continuing to drink was also higher in men than in women. Otherwise, the percentage of participants utilizing antihypertensive and lipid-lowering medications was lower in men compared with women. So, the current results could be attributed to that the patients were not in the conditions matching above.

Concerning the levels of insulin, the current result is in accordance with Al-Attaby and Al-Lami (2018), who demonstrated that no effect of gender on the levels of insulin in T2DM.

Insulin resistance showed highly significant increase in women than men, this is may be due to the high levels of FBG and insulin hormone in studied women, which already used to calculate the IR value. Moreover, women transition from the pre-menopause to post-menopause state with fundamental metabolic alterations and estrogen deficiency could be a contributing factor in increasing the IR value in women. These changes may be return to deficiency of estrogen in menopause. The transition from pre- to postmenopause is related with the emergence the metabolic syndrome such as high intra abdominal fat and glucose levels (Schubert *et al*, 2006). In contrast, current results were in disagreement with Aregbesola *et al* (2016) they found a higher levels of fasting serum insulin and HOMA-IR in men compared with females. These gaps between studies may be due to several factors such as casual testing, selection bias and gender disparity in gain access to healthcare center in some countries.

Table 3 : Impact of age on antioxidant and oxidant parameters in T2DM patients.

Parameters	Diabetic group				P value
	30 - 39	40 - 49	50 - 59	≥ 60	
TAC (mmol/l)	2266.97±617.70[a]	2259.12±358.68[a]	2027.99±486.19G"	2206.93±431.43[a]	0.010*
ROS (mmol/l)	154.84±25.53 [a]	161,98±16.11 [a]	179.31±20.03G"	200.06±18. 90G"	0.021*

Different letter refer to significant differences among groups, *(P<0.05) significant.

Table 4 : Impact of gender on glycaemic control parameters of T2DM.

Parameters	Mean ± SD		P value
	Men	Women	
FBG(mg/dl)	183.29±36.96	200.98±52.52	0.053*
HbA1C %	7.96±0.96	8.29±1.64	0.27NS
Insulin (µIU/ml)	15.82±8.03	18.62±9.46	0.08NS
IR	6.95±2.82	9.01±5.12	0.002**
IS	0.30±0.02	0.29±0.03	0.036*

SD: Standard Deviation, *(P<0.05) significant, **(P<0.01) high significant, NS: Non-Significant.

Table 5 : Impact of gender on renal function parameters in T2DM patients.

Parameters	Mean ± SD		P value
	Men	Women	
Urea (mmol/l)	5.79±2.55	6.39±2.42	0.44NS
Creatinin (mmol/l)	87.71±28.67	74.52±21.05	0.008**

SD: Standard Deviation, **(P<0.01) high significant, NS: Non-Significant.

Table 6 : Impact of gender on antioxidant and oxidant parameters in T2DM patients.

Parameters	Mean ± SD		P value
	Men	Women	
TAC (mmol/l)	2211.55±404.16	2182.23±344.67	0.60 NS
ROS (mmol/l)	166.12±26.67	181.46±49.80	0.042*

SD: Standard Deviation,*(P<0.05) significant, NS: Non-significant.

In current study, IS was significantly impaired in women compared to men, this observation may be because women have a somewhat excess levels of estrogen and progesterone, which are engaged in the impairment of IS in the entire body (Machado-Alba *et al*, 2016).

Impact of gender on renal function parameters in T2DM patients

The results in Table 5 elucidate the impact of gender on renal function parameters in T2DM patients. The statistical analysis showed a non-significant differences for increasing levels of urea in women compared to men, while current finding showed a highly significant (P<0.01) increase in creatinine levels in men as compared with women.

The finding of present study similar to previous study conducting by Bamanikar *et al* (2016), which reported a no significant impact for gender on the urea level. The finding of significantly increase creatinine level in men compared to women may be due to increase protein intake and storage of creatinine as a waste product in muscle mass and the presence of high muscle mass in men as revealed earlier (Bamanikar *et al*, 2016). On the other hand, Murtadha *et al* (2016) suggested that the lower creatinine levels is related with high risk of T2DM, which could reflect a lower skeletal muscle volume. The results of current study along the lines of Iraqi recent study (Fadheelah *et al*, 2020), which showed that creatinine level was greater in males than females.

Impact of gender on antioxidant and oxidant parameters in T2DM patients

Table 6 shows the impact of gender on TAC and ROS levels. The table shows increasing in the mean of TAC in men compared to women, but the statistical analysis revealed no significant (P>0.05) differences. While the mean of ROS was significantly (P<0.05) increase in women compared to men.

The result of the current study is consistent with the study of Kharroubi *et al* (2016), which also showed that there was no significant effect of gender on TAC. In the present study, the levels of ROS were significantly higher in women group than men group, this finding may be due to FBG levels were significantly increased in women compared with men. It is well documented that chronic exposure to high levels of glucose increases the production of ROS and generates oxidative stress in islet cells. Several suggested mechanisms binding hyperglycemia with increased ROS production. These mechanisms include increased glucose flux through the polyol pathway, formation of the advanced glycation end-products (AGEs) enhancing oxidative stress, mitochondrial synthesis of superoxide anion radical (O^{-2}) and NF-κB signaling pathway activation causing inflammatory reaction, thus ROS production increased in phagocytes (Gawlik *et al*, 2016).

CONCLUSION

Overall, the results of current study showed that glycaemic control parameters increased with increasing age, but this increasing was not significantly different.

Urea significantly increased in the older groups compared to the younger groups. The gender did not show any significant effect on any of the studied parameters. It is clear from the above that age and gender cannot be consider as a risk factor for the incidence of hyperglycemia and T2DM may be draw up by the effects of other physiological, genetics and epigenetic factors. This study is a part of a large study through which we gaze to find out the factors that pose a real risk in the development and exacerbation of T2DM in Iraqi patients.

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