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Multimorbidity in Diabetes Mellitus: Association with Oxidative Stress and Glycemic Control

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Abstract: Diabetes mellitus (DM), characterized by chronic hyperglycemia from insulin deficiency or resistance, has different subtypes including type 1 diabetes and type 2 diabetes that design study based on a cross-sectional observational study which aimed to examine the relationship between oxidative stress (plasma malondialdehyde (MDA) and glycemic control (glycated hemoglobin (HbA1c), in (80) adult diabetic patients in Iraq, and studied the prevalence of complications and multimorbidity , the Results indicated that there was a statistically significant moderate positive correlation between MDA and HbA1c levels ($r = 0.38$, $p = 0.0005$) suggesting that chronic hyperglycemia, which contributes to oxidative damage and diabetic complications , Nearly half were complication free, while some had neuropathy, retinopathy, and/or Ischemic heart disease and according to logistic regression , age, male sex, and duration of diabetes were all shown to be risk factors for poor glycemic control , these finding highlight the need to manage oxidative stress and glycemic control in order to reduce diabetes-related morbidity.

Keywords: Diabetes mellitus, oxidative stress, malondialdehyde, glycated hemoglobin, hba1c, diabetic complications, multimorbidity, glycemic control, reactive oxygen species, cross-sectional study.

INTRODUCTION

Diabetes mellitus (DM) is a syndrome characterized by hyperglycemia. It is a complex process of carbohydrate, lipid, and protein metabolism, primarily resulting from a relative or complete deficiency of insulin secretion from pancreatic beta cells or from defects in insulin receptors, depending on the subtypes treated: type 1 diabetes (DM1), type 2 diabetes (DM2), MODY, and gestational diabetes mellitus (GDM) (American Diabetes Association. 2011; World Health Organization, 2016; Atlas, D. 2015) Together, these disorders form part of a heterogeneous group of disorders that share a hyperglycemic phenotype and the interplay of genetic, environmental, and lifestyle factors. 10–12 Various globally recognized bodies involved in the study and monitoring of diabetes, such as the World Health Organization (WHO), the International Diabetes Federation (IDF), and the American Diabetes Association (ADA), consider this disease a pandemic due to its high incidence and prevalence, with more than 366 million people suffering worldwide (Zimmet, P. Z. *et al.*, 2014; Keval, H., & Britain, G. 2016; Keval, H., & Britain, G. 2016; Chen, X. *et al.*, 2025) However, some European and North American studies have shown the presence of undiagnosed diabetes in approximately 50% of patients who declare themselves healthy (Ceriello, A. 2000; Giugliano, D. *et al.*, 2008; Brownlee, M. 2001) In 2011, between 346 (WHO) and 366 (IDF) people were reported to have type 2 diabetes, representing approximately 6.4% of the global population. An estimated 552 million people will develop type 2 diabetes by 2030, equivalent to 14 million new cases each year (Kahn, S. E. *et al.*, 2014) Although the relationship between oxidative stress and diabetes has been studied and documented, the precise mechanisms by which this process occurs have been widely questioned (Santiago-Balmaseda, E. *et al.*, 2023; Singh, A. *et al.*, 2022) There is a discussion about whether the rise in reactive oxygen species in diabetes causes the manifestation of long-term disease-related complications or, on the other hand, if such complications and impaired metabolic control bring about oxidative damage and enhance its later manifestations. As such, the focus of the present work was the identification of the pathophysiological aspects of oxidative stress and the link it has to diabetes (Anandan, S., & Urooj, A. 2018; Yu, S. H. *et al.*, 2015) Under particular conditions, the production of reactive oxygen species (ROS) in the organism exceeds the limit of antioxidant defence mechanisms (ADMs) and causes a redox disorder known as oxidative distress (OD) (Halliwell, B., & Gutteridge, J. M. 2015; Rathod, S. *et al.*, 2025) The intensity and duration of the resulting pathological states may negatively affect various body tissues and lead to the slow reduction of vital functions and, in the context of the present discussion, the development

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of chronic diabetes complications where this paper aims to assessment results Multimorbidity in Diabetes Mellitus: Association with Oxidative Stress and Glycemic Control.

MATERIAL AND METHOD

This study was designed as a cross-sectional observational study to investigate the associations among multimorbidity in diabetes mellitus, oxidative stress, and glycemic control among patients attending different hospitals across Iraq during the period from March 2024 to April 2025 therefore was in our paper The major objective was to measure the relationship between oxidative stress markers, namely plasma malondialdehyde (MDA) levels, and glycemic control by glycated hemoglobin (HbA1c) among diabetes mellitus patients where As a secondary objective, the study aimed to examine the rate of diabetic complications and multimorbidity while recognizing risk factors contributing to poor glycemic control. The research only concentrated on the adult population who had diabetes mellitus (types 1 and 2) and had been confirmed by Glucose Tolerance Test (GTT) or by HbA1c measurement following the recommendations by the American Diabetes Association (ADA) established criteria moreover The respondents were intentionally sampled among both genders and aged 40-75 years (80 patients) to increase the applicability to middle-aged and elderly individuals most exposed to diabetes complications however Inclusion criteria required verified diagnosis of diabetes mellitus and willingness to participate by presenting written informed consent and supply of blood samples and Patients were included irrespective of duration of disease to obtain a representative sample spanning new-onset to long-standing disease. Stringent exclusion criteria were used to remove confounding factors affecting oxidative stress or glycemic indices consequently were patients presenting acutely infected or inflamed at the time of sampling were removed since the condition may spuriously raise markers of oxidative stress accordingly Pregnant females were removed except for those presenting gestational diabetes mellitus who were identified and analyzed separately, were in study Patients receiving antioxidant supplementation or medication that potentially modulates oxidative stress, e.g., corticosteroid in addition to Patients presenting advanced chronic diseases not related to diabetes mellitus, e.g., end-stage renal failure or advanced liver disease, were also excluded since such diseases have independent influences on the metabolic and oxidative stress pathways as well as patients who cannot or are not willing to provide consent or adhere to study protocols were removed to preserve the integrity of the study and according to Data were obtained by structured interview and examination of the patients' medical records at the participating hospitals in Iraq, both tertiary care and district health care hospitals, to yield a representative patient population so demographic information such as age at presentation, gender Detailed, marital status, and occupation were obtained in a systematic manner also The clinical presentation consisted of the duration of diabetes and symptoms and gestational diabetes while that Diabetic complications by clinical assessment and by consensus diagnostic criteria were delineated separately and consisted of peripheral neuropathy, retinopathy, ischemic heart disease (IHD), nephropathy, and diabetic foot. Blood samples were taken following fasting for biochemical analysis; HbA1c levels were obtained by standardized immunoassay or high-performance liquid chromatography (HPLC) methods and gave both contemporaneous and historical indices of glycemic control, based on The status of oxidative stress was evaluated by plasma malondialdehyde (MDA) concentrations by the thiobarbituric acid reactive substances (TBARS) spectrophotometric method and represents an established indirect marker of lipid pero- xidation.

Statistical analysis

- Statistical evaluations were performed utilizing IBM SPSS
- Continuous variables were expressed as means accompanied by standard deviations
- categorical variables
- The association between oxidative stress and glycemic control was tested based on through Pearson’s correlation coefficient.
- Logistic regression analyses
- Odds ratios

RESULTS

Table 1: Patient Demographics and Clinical Characteristics

Characteristic	Details
Age (years)	54.1 ± 10.2
Age Range	40 - 72

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Sex Distribution	Female: 46 (57.5%), Male: 34 (42.5%)
Duration of DM Raw Sample	['5 years', '5 years', 'first visit', '1 year', '3 weeks', '1 year', 'first visit', '6 months', '2 years', '5 years']
Duration of Diabetes (years)	7.4 ± 5.6
Duration Range	0.0 - 26.0
BMI	Not available
Occupation Distribution	housewife: 38 (47.5%), retired: 15 (18.8%), employee: 6 (7.5%), teacher: 5 (6.2%), military: 5 (6.2%), jeweller: 2 (2.5%), policeman: 2 (2.5%), executive: 2 (2.5%), mercer: 2 (2.5%), driver: 1 (1.2%), nurse: 1 (1.2%), officer: 1 (1.2%)
Marital Status Distribution	married: 56 (70.0%), widowed: 21 (26.2%), single: 2 (2.5%), divorced: 1 (1.2%)

Table 2: Distribution of Patients According to Symptoms and Diagnosis

Symptoms or Complications at Diagnosis	**Number**	**Percentage**
polyuria	37	46.2%
polyuria, thirst, dry mouth	10	12.5%
fatigue, dizziness	5	6.2%
checking during CVA	3	3.8%
gestational DM	3	3.8%
during routine checking	3	3.8%
polyuria, fatigue	3	3.8%
dry mouth, polyurea, thirsty	2	2.5%
fatigue, dizziness, polyuria	2	2.5%
polyuria, thirsty, dry mouth	2	2.5%
UTI checking	1	1.2%
routine checking	1	1.2%
headache	1	1.2%
during routine checking before eye surgery	1	1.2%
weight loss, polyuria	1	1.2%
polyuria, weight loss	1	1.2%
thirsty, dry mouth, fatigue	1	1.2%
polyuria, thirsty, dry mouth	1	1.2%
fainting attack, weight loss	1	1.2%
dizziness, polyuria, weight loss	1	1.2%
How Diagnosed	**Number**	**Percentage**
GTT	75	93.8%
HbA1c	5	6.2%

Table 3: Glycemic Control Status

Parameter	**Value**	
HbA1c Monitoring per Year	0.7 ± 1.3	
Reading HbA1c >7% Last Year	**Number**	**Percentage**
0	56	70.0%
Yes	18	22.5%
No	4	5.0%
Unknown	2	2.5%
Current HbA1c Status	**Number**	**Percentage**
HbA1c >7%	18	23.1%
HbA1c ≤7%	60	76.9%
HbA1c of Research	**Value**	
Mean ± SD	0.0962 ± 0.0240	
Range	0.0606 - 0.1500	

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Table 4: Results Related to MDA (µmol/L) of Research

Statistic	Value
Mean ± SD	3.2905 ± 0.5244
Median	3.3930
Range	1.8468 - 4.7244
Sample Size	80

Table 5: Correlations Between Oxidative Stress Markers and HbA1c

Parameter	Value
Correlation Coefficient (r)	0.3807
P-value	0.0005
Sample Size	80
Interpretation	Significant moderate positive correlation

Table 6: Diabetic Complications Prevalence

Complication Combination	Number	Percentage
0 (No complications)	39	48.8%
peripheral neuropathy	6	7.5%
retinopathy, peripheral neuropathy	5	6.2%
peripheral neuropathy, retinopathy	5	6.2%
impotence, IHD	3	3.8%
peripheral neuropathy	3	3.8%
IHD, retinopathy, peripheral neuropathy	3	3.8%
peripheral neuropathy, diabetic foot	3	3.8%
IHD	3	3.8%
peripheral neuropathy, impotence, retinopathy	2	2.5%
albuminuria	2	2.5%
peripheral neuropathy, albuminuria	2	2.5%
albuminuria, retinopathy, peripheral neuropathy, IHD	2	2.5%
impotence, retinopathy	1	1.2%
nephropathy, retinopathy	1	1.2%

Table 7: Logistic Regression Evaluation of Risk Factors (Outcome: Poor Glycemic Control - HbA1c >7%)

Risk Factor	Coefficient	Odds Ratio	Interpretation
age (years)	0.0294	1.0299	Increased risk (OR = 1.03)
gender encoded	0.2778	1.3202	Increased risk (OR = 1.32)
duration years	0.1752	1.1915	Increased risk (OR = 1.19)

DISCUSSION

In type 2 diabetics, if glycaemic control improves, the oxidative stress indicators such as MDA will partially decrease.16 The result as well showed that MDA when compared to FBS and HbA1c correlated positively, thus, as fasting blood sugar increases, MDA and HbA1c increase as well so refer outcomes for the 80 subjects are listed in Table 1, found in the Results section (40 to 72 years of age), mean (SD) was 54.1 years defines them as middle-aged to elderly populations, usually affected by diabetes complications, patients distribution according to sex females constituting 57.5% , additionally was slightly more female-dominated, which is in agreement with the gender ratios in clinical diabetic cohorts; then, the average duration of diabetes was 7.4 years, with cases ranging significantly from just newly diagnosed to patients who have had the disease for up to 26 years as well as a smaller percentage came from a variety of jobs, including military, education, and public service, while a large number of housewives (47.5%) and retirees (18.8%) probably reflects sociocultural backgrounds furthermore patients looked when they were diagnosed and how diabetes was found even that Polyuria was the most common symptom, reported by almost half of the patients (46.2%) and either by itself or with thirst and dry mouth , Based on literature review Researchers have proven that oxidative stress plays an important role in the development of vascular complications in diabetes, especially type 2 diabetes. In diabetes, elevated levels of reactive

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free radicals (ROS) can be caused by a decrease or breakdown in antioxidants (CAT, SOD, and GSH). Thus, changes in these enzymes make tissues more susceptible to oxidative stress, which in turn leads to the development and increase of diabetes complications. Epidemiological studies have shown that death caused by diabetes is significantly explained by the increase in vascular disease compared to death caused by high blood sugar levels (Luger, M. *et al.,* 2018) on The other symptoms, such as lethargy and giddiness, and routine or opportunistic screenings during CVA evaluations, were present as witness to the usual hyperglyemic symptoms and incidental findings on the other hand Thus, in 93.8% of cases, diagnosis was primarily dependent on the GTT indicating adherence to classical criteria whilst HbA1c was used in a limited set where In our paper, we found GC status, yet the very important part of treatment for diabetes where patients have their HbA1c checked on average less than once a year, 0.7 times per year furthermore were found to be under control with respect to under HbA1c of 7%, another 23.1% had poor control (HbA1c >7%) , Still, 22.5% had bad readings, pointing to persisting problems with metabolic control for a good number of patients, about p value which found is dedicated to the oxidative stress marker malondialdehyde (MDA), a classic marker of lipid peroxidation and oxidative damage however The mean level of malondialdehyde in patients was 3.29 µmol/L, ranging from 1.85 mol/L to 4.72 µmol/L , which that A relatively wide range of oxidative burden could consider duration, presence of complications, or status of glycemic control, as mentioned therefore found in outcomes yielding a value for the Pearson correlation coefficient of 0.3807 with the p-value of 0.0005 Lastly as requirement which given in table 6 looks at the incidence and combinations of diabetic complications in the cohort and reveals almost half (48.8%) of the patients who had no documented complications, highlighting a possible group receiving early intervention , discussion our paper refer also to Peripheral neuropathy was the most common single complication observed (7.5%), often seen in combination with retinopathy (6.2%) or ischemic heart disease (IHD) more ever Complex multimorbidity combinations were also noted, including albuminuria, impotence, nephropathy, and diabetic foot, reflecting the multisystem impact of chronic diabetes, as discussed in our results. The relationship between multimorbidity in diabetes mellitus and oxidative stress was significant since oxidative stress is a major player in the generation of various types of complications associated with DM. (Luger, M. *et al.,* 2018; Maritim, A. C. *et al.,* 2003) as well as Increased levels of reactive oxygen species (ROS) due to hyperglycemia may cause chronic inflammation and tissue damage, strengthening multimorbidity in diabetic patients. In Oxidative Stress and Diabetic Complications, oxidative stress is stated to be related to diabetic cardiovascular complications (Qi, Y., & Wang, X. 2023; Pinilla, I. *et al.,* 2022).

CONCLUSION

Thus, it is concluded that there is a significant correlation between oxidative stress, as measured by malondialdehyde (MDA) levels, and the other parameters in the study. The second point in the conclusion regarding the moderate positive correlation between HbA1c and MDA emphasizes the role chronic hyperglycemia plays in facilitating oxidative damage, which perhaps leads to its onset.

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