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Metformin lowers both liver and kidney tests in women with diabetes melts type 2 in the mid-Euphrates of Iraq

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SUM-

Introduction: Diabetes is a metabolic disease characterised by hyperglycaemia resulting from defects in insulin secretion, action, or both. It is currently the third most detrimental chronic illness to human health. The prevalence of diabetes is increasing globally due to factors such as improved living standards, urbanization, industrialization, and an ageing population. According to the WHO, the present global prevalence of diabetes is approximately 422 million, and this figure is projected to rise to 600 million by 2040.

Method: A retrospective cross-sectional study was conducted on 200 women with type 2 diabetes mellitus (T2DM). The participants were divided into two groups based on their utilisation of metformin. The Met group (MG) comprised 50 women who had been administered 500 mg of metformin twice daily, while the non-Met group (NMG) consisted of 50 women who did not use metformin.

Result: The mean diabetes duration was 8.54 ± 3.25 years. Significant differences in age, social status, and education were found between metformin and non-metformin groups ($P < 0.05$). Binary analysis of renal biomarkers showed that irregular BUN and serum creatinine levels might affect the non-metformin group ($P < 0.05$). A stratified analysis revealed that lack of Met. Use may confound the link between high S. Creatinine and T2DM effects, while T2DM duration may confound the B. urea-S. Creatinine relationship.

Conclusion: Metformin has a potential role in reducing high levels of renal and hepatic markers through several pathways, including improving insulin sensitivity, reducing oxidative stress and modulating inflammation. In addition, its effects on cellular metabolism and mitochondrial function may contribute to its ability to protect renal and hepatic tissue from damage.

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INTRODUCTION

Diabetes is a disease that affects the body's metabolism. Characterized by hyperglycaemia caused by defects in secretion of insulin, action, or both issues [1]. It is currently the third most harmful chronic illness to human health. Improved living conditions, urbanisation, industrialisation, and an ageing population all help to explain the global increasing disease prevalence. The WHO estimates that 600 million diabetes will develop by 2040 from the about 422 million diabetics present today. This fast increase emphasizes the urgent necessity of worldwide awareness campaigns, preventive programs, and the improvement of healthcare systems to properly control and reduce the influence of diabetes. Reducing the spread of this chronic illness mostly depends on lifestyle changes, early identification, and the facilitation of reasonably priced treatment [2]. In the absence of substantial intervention, the strain on healthcare systems and the quality of life for millions will persistently worsen [3]. Many studies have looked at the complicated link between type 2 diabetes and liver and renal function. These organs are essential for the metabolic activities of the body; hence their malfunction might aggravate the course and degree of diabetes-related problems [4,5]. The complication of diabetic involves a complex interplay of various factors, including hyperglycaemia, hypertension, and inflammation, which can ultimately lead to glomerular and tubular dysfunction, therefore it consider as the primary cause for development of chronic kidney and liver diseases [6,7] .

Metformin is reducing gluconeogenesis, increasing glucose absorption in skeletal muscle, fatty acid oxidation in adipose tissue, and peripheral insulin sensitivity and by AMPK-dependent and AMPK-independent pathways, metformin targets hepatocytes and reduces hepatic glucose production in T2D [8]. AMPK switches cells from anabolic to catabolic, limiting ATP-consuming synthetic pathways and restoring energy balance in hepatocytes. By encouraging β-oxidation of free fatty acids and/or lowering their de novo synthesis, these modifications can help to lower hepatic lipid accumulation [9].

The aim of this study was to investigate correlations between metformin with renal and liver function tests in women with type 2 Diabetes

METHODS

A retrospective cross-sectional study was carried on 200 T2DM women age (41 - 60) years. Between January

2, 2023, to December 1, 2024, the data were collected from numerous government and commercial hospitals or institutions from Al-Kindi Hospital in Baghdad, Marjan Hospital in Babylon, and Al-Hajjah Hospital in Karbala in addition to the private clinic. The woman participants were divided into two groups according to their use of metformin. The Met group (MG) comprised 50 women who had used metformin. The Met group (MG) comprised 50 women who were administered 500 mg of metformin twice daily, while the non-Met group (NMG) consisted of 50 women who did not use metformin.

Inclusion criteria: Type 2 DM patients aged between 30 and 65 years old, who consented to and permitted their enrolment in the study.

Exclusion criteria: Women who were pregnant, individuals with type I DM, those with chronic liver or kidney disease, CVD, hepatitis, or any other liver or kidney diseases, which were not included in this study.

Ethical approval: A request has been submitted to the hospitals mentioned above, to obtain approval to read patients' tympanics and obtain the information we need.

Statistical Analysis

All categorical variables were expressed as frequencies and percentages, and comparisons between groups were performed using the Chi-square test or Fisher's exact test, as appropriate. For non-normally distributed numerical variables, the Mann-Whitney U test was applied. Correlation analyses were conducted using Pearson's or Spearman's correlation coefficients, depending on the data distribution. Statistical analyses were performed with a confidence interval of 95%, and all results were interpreted accordingly.

RESULTS

Patients Demographics Characteristics

The study was conducted on a total of 100 diabetic women, comprising 50 who were on metformin and 50 who were non-metformin users. The mean age of the participants was 51.5 ± 9.04 years. The mean duration of diabetes was 8.54 ± 3.25 years. Significant statistical differences were observed between the metformin and non-metformin groups in terms of age, social status, and education ($P < 0.05$). The demographic characteristics and biochemical parameters of the participants are presented in **Tab. 1.**

Subsequent adjustments for these confounding factors were made to ensure the reliability of the findings. The analysis revealed that patients with elevated serum creatinine levels who were not on metformin exhibited a stronger association with adverse T2DM outcomes, and similarly, abnormal blood urea nitrogen levels were more prominently linked to renal dysfunction in patients with a prolonged course of T2DM. These findings underline the need of addressing renal biomarkers and confounding variables when evaluating metformin use and its impact on T2DM therapy, and further longitudinal studies are warranted to validate these correlations and examine potential pathways. As illustrated in **Tab. 2.**, there is a clear indication that aberrant liver function-related indicators, particularly higher ALP and AST levels, are substantially correlated with NMet use ($P < 0.05$). Furthermore, the stratified analysis underlines the potential confounding effects of age and duration on these correlations. These data imply that both renal and hepatic function markers play a vital role in evaluating the prevalence and risk factors related with NMet use. Further research is necessary to explore these correlations in greater detail and to find underlying processes that may contribute to these reported effects.

DISCUSSION

Diabetes is a health problem that affects how the body uses energy. It is also expensive, and it is thought that by 2030, the Arab area will have the second-highest number of patients with the disease. This shows that we need to do more to stop it, improve healthcare and tell more people about it. It will be very important to deal with lifestyle factors such as food, physical activity and early diagnosis if we are to manage the growing burden of

Tab. 1. Distribution of demographic characteristics of studied sample.

	Range	N (%)	P value
Age (years)	40-50	84 (42)	<0.05
	51-60	116 (58%)	
Duration (Year)	7 (1.75–12.00)	7.50 (1.5–13.5)	
Social Status	Single	20 (10)	<0.05
	Married	100 (50)	
	Widower	80 (40)	
Education	Illiterate	40 (20)	<0.05
	Primary	66 (33)	
	Secondary	60 (30)	
	College	34 (17)	
RFT			
BUN (mmol/L)	5.40 (4.41–6.79)	6.14 (4.90–9.06)	<0.05
UCr (mmol/d)	7.43 (4.64–12.12)	5.87 (3.89–8.49)	<0.05
LFT			
ALT (U/L)	19 (14–27)	16 (12–23)	<0.05
AST (U/L)	20 (16–24)	17 (14–23)	<0.05

BUN: Blood Urea Nitrogen; UCr: Urine Creatinine, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase

Tab.2. The Odds Ratio (OR) and 95% Confidence Interval (CI) for abnormal renal and liver function indexes and NMet.

RFT		BUN (mmol/L)	UCr (mmol/d)
Age (years)	40-50	2.76 (1.71, 4.43)	0.58 (0.31, 1.09)
	51-60	1.87 (1.27, 2.74)	0.99 (0.98, 1.00)
Duration (Year)	<5 years	2.29 (1.35, 4.88)	9.59 (4.60, 19.99)
	>5 years	1.43 (0.99, 2.06)	4.13 (2.66, 6.41)
LFT		**ALP**	**AST**
Age (years)	40-50	0.21 (0.10, 0.46)	0.32 (0.16, 0.64)
	51-60	1.63 (0.85, 3.13)	1.32 (0.83, 2.11)
Duration (Year)	<5 years	0.45 (0.21, 0.96)	0.58 (0.30, 1.12)
	>5 years	0.82 (0.44, 1.53)	0.99 (0.61, 1.63)

this disease. Governments and health organisations must work together to make cheap treatment and education available so that the impact on people and economies in the region can be reduced [10,11]. The frequency of depression demonstrates significant variance between research studies, phenomena that can be related to a range of environmental, cultural, ethnic, and social factors. This study indicated that more than half of T2DM patients had significant depression. The median PHQ-9 score for diabetes patients was much higher than that of the control group, indicating that depression is more widespread among diabetics than non-diabetics (2022) found that depression was much more common in T2DM patients (63%) than in the control group (48%) [12,13].

There are a number of ideas that try to explain this link. One possible reason could be that higher levels of alkaline phosphatase might be a sign of low-level inflammation or oxidative stress. These are known to contribute to insulin resistance and problems with the cells in the pancreas that make insulin (beta cells).Alkaline phosphatase is also involved in the process that controls the amount of phosphate in the body. Problems in this process might affect how well the body controls blood sugar. More research is needed to understand the exact reasons for this and to see if measuring alkaline phosphatase in the blood could be a way to spot or assess type 2 diabetes early on [14]. This research could also assist in the identification of potential preventative measures or interventions to address the mental health challenges associated with diabetes. Furthermore, an understanding of the regional variations and contributing factors in Iraq may offer valuable insights into the broader global context of the relationship between diabetes and mental health. Collaboration between healthcare providers, researchers, and policymakers is imperative to implement effective strategies based on these findings [15].

CONCLUSION

Metformin's ability to influence gut microbiota composition and improve glucose uptake further supports its protective effects on kidney and liver health. Studies suggest that its multiple mechanisms not only mitigate damage, but also promote tissue repair and regeneration. In addition, its role in reducing advanced glycation end products (AGEs) and improving lipid metabolism adds another layer of protection against chronic kidney and liver disease.

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