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THE EFFECT OF INSULIN AND METFORMIN ON THE PREVALENCE AND SEVERITY OF TOOTH WEAR IN TYPE2 DIABETIC PATIENTS

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ABSTRACT

Purpose: Investigating the effect of insulin and metformin on the prevalence and severity of tooth wear in patients with type 2 diabetes.

Patients and methods: This cross -sectional study was conducted on194 Egyptian adult diabetic type 2 patients, age group (50-70) using quota sampling method, assessing the prevalence and severity of tooth wear in adults of the included region. Three-stage stratification was done by sex, age and type of diabetes, then classified in to two groups: ***Group A:*** 105 patients treated with insulin regimens without metformin and stop metformin at least 5 years ago. ***Group B:*** 89 patients treated with metformin only. Measuring the tooth wear by Smith and Knight Tooth Wear Index (TWI).

Results: Teeth Wear index (TWI) was significantly positively correlated to age and duration of diabetes in all groups. Treatment with metformin was a significant positive predictor of TWI. TWI was 1.857 higher on average for those who use metformin as compared to those who use insulin.

Conclusion: There was a significant difference between different TWI as regard age and duration of diabetes**.** Any factor changes the oral salivary PH and viscosity will effect on the tooth wear severity.

KEYWORDS: Type 2 diabetes, tooth wear, insulin, metformin, tooth wear index.

INTRODUCTION

Tooth wear is an oral condition with multifactorial etiology, irreversible loss of hard tooth structure, not being considered caries process, trauma, or resorption.[1] It is a serious oral health issue that affects the dentition, occlusion, and tempromandibular joint of patients throughout their lives. The most significant function that is impacted by tooth wear is eating, as worn teeth cannot adequately bite and chew food. As a result, elderly individuals suffer and

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seek dental treatment for tooth wear.[2] All tooth wear types (attrition, abrasion, erosion, and abfraction) are diagnosed in all age groups. However, it is more prevalent and more severe in older people.[3]

Type 2 diabetes (T2DM) is a heterogeneous disease in which clinical presentation and disease progression may vary considerably and accounts for 90-95% of all diabetics and the risk of developing T2DM increases with age, obesity, and lack of physical activity. The traditional paradigm of T2DM occurring only in adults is no longer accurate, as it may occurs in all age-groups. It encompasses individuals who have relative insulin deficiency and have peripheral insulin resistance. 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 caused by hyperglycemia, such as dehydration or unintentional weight loss. Nevertheless, even undiagnosed patients are at increased risk of developing microvascular and macrovascular complications.[4]

In 2021, Egypt has 10.9 million adults living with diabetes, 62% of them were undiagnosed and this number is predicted to rise to 20 million by 2045.[5]

The first-line therapy for T2DM depends on comorbidities, patient-centered treatment factors, and management needs but will generally include metformin and comprehensive lifestyle modification. Pharmacotherapy should be started at the time T2DM is diagnosed unless there are contraindications; for many patients this will be metformin monotherapy in combination with lifestyle modifications.[6]

Metformin has taken a pivotal position in the field of diabetes treatment due to its good efficacy, excellent safety, limited side effects, and good cost performance. It is a hydrophilic drug, and its hydrophilicity limits its permeability through lipid membranes. Therefore, its passive diffusion through the cell membrane is very limited. Its distribution mainly depends on tissue-specific transporters.[7]

The mechanism works Metformin by increasing peripheral glucose uptake, reducing intestinal glucose absorption, increasing insulin sensitivity, and decreasing fasting plasma insulin levels, thereby reducing blood glucose concentrations without causing hypoglycemia. In addition, Metformin can inhibit gluconeogenesis by activating AMP-activated protein kinase.[8]

Moreover, the high level of metformin in the intestinal wall exerts an insulin-dependent effect, which is the main cause of excessive lactic acid. The risk of lactic acidosis increases with the degree of renal impairment and the patient's age.[7]

Insulin has the advantage of being effective in management of T2DM where other antidiabetic drugs are not and should be considered as part of any combination regimen when hyperglycemia is severe, especially if catabolic features (weight loss, hypertriglyceridemia, ketosis) are present and It is common practice to initiate insulin therapy for patients who present with blood glucose levels ≥ 300 mg/dl or A1C >10% or if the patient has symptoms of hyperglycemia (i.e., polyuria or polydipsia) or evidence of catabolism (weight loss).[6]

Diabetes increases the risk of oral disease directly (e.g., gingival inflammatory response) and indirectly (e.g., decreased saliva production due to medication). [9] It has also been reported that oral health may have an impact on T2DM risk and its metabolic control, suggesting a complex bidirectional link between T2DM and oral diseases. [10]

Mohiti[11] found that diabetes mellitus causes a reduction in saliva pH and increases saliva viscosity, which can cause qualitative and quantitative changes in saliva and oral health.

Patients with diabetes are among the most common patients for whom dentists use oral

health prevention and promotion techniques to attain optimal oral and overall health. As a result, dental professionals should be aware of the prevalence and severity of tooth wear, as well as the underlying reasons that contribute to it and its link to Diabetic patients, by investigating the effects of oral hypoglycemic drugs on salivary flow rates and protein composition in patients with type2 diabetes.[2,12]

So, this study was conducted to investigate the effect of insulin and metformin on the prevalence and severity of tooth wear in patients with T2DM.

METHODS

Study design

This cross sectional, descriptive study was conducted at fixed prothodontics department, faculty of dentistry, Tanta university and Endocrinology and Diabetes department, EL-Maadi Armed Forces Medical Complex to investigate the effect of insulin and metformin on the prevalence and severity of tooth wear in patients with type 2 diabetes. Diabetic patients were diagnosed by the medical doctor with diabetes duration at least from 10 years or more by history taken from patients in the hospital.

Inclusion criteria:

Based on the dental clinical examination, patients were selected according to the following criteria

1. Egyptian adult, type 2 diabetic patients, age group (50-70).
2. Wiliness to consent and comply with the study protocol.
3. No clinical abnormalities, or an unusual medical history.
4. Good oral hygiene with moderate health condition of the supporting bone.
5. Apparent wear (attrition, erosion, abrasion) either localized or generalized.

Exclusion criteria:

1. Adult who cannot respond to questionnaire.
2. Patients free fromTMJ joint problem.
3. Patients free from bruxism or bite alignment problems.
4. Non highly acidic food intake or acidic beverage.
5. No clear abrasion due to mal use of dental brush.
6. Patents free from other systemic diseases

Study sample

Adults' Egyptian participants were selected in the study survey based on a sample size calculation with the following criteria: there was a 5% margin of error, a 0.05 alpha level, and a 75% expected tooth wear prevalence.[13]

An estimated 194 participants were needed for this study. The method used for this study was the quota sampling method, assessing the prevalence and severity of tooth wear in adults of the included region. A three-stage stratification was done by sex, age and type of diabetes (type2 was selected).

Diabetic patients were classified in to two groups according to the type of treatment:

Group A: 105 patients treated with insulin regimens without metformin and stop metformin at least 5 years ago.

Group B: 89 patients treated with metformin only.

Dental calibration

The dentist was trained for clinical examination with tooth wear index using, The Smith and Knight Tooth Wear Index (TWI) is a globally accepted and commonly used index for determining tooth wear.

TWI is useful for diagnosing problems. It can evaluate the severity of wear on each surface by calculating the amount of surface area involved and the depth of the surface loss. Regardless of the

kind of dental wear, each tooth was measured for wear on all four surfaces (buccal, cervical, lingual, and incisal-occlusal). Each tooth received only one diagnosis.[14]

Cohen's kappa coefficient was 0.65 of intra-examiner reliability was achieved before launching the study. Patients were examined in the clinic. Data were collected within three-month 2021

Data collection

Patients who agreed to participate in the study were recruited by a dentist based on inclusion/exclusion criteria and completed self-administered questionnaires.

Questionnaires

The dentist conducted a face-to-face interview using a validated self-administered questionnaire that covered sociodemographic data such as age, gender, educational level, and occupation.[15]

Clinical examination

Study participants were checked visually in dentist chairs with a mouth mirror and adequate illumination. Teeth were washed and dried before to the dental examination, with plaque and residue removed with a cotton swab.

The Smith and Knight Tooth Wear Index was used (TWI): [16]

To detect the severity of tooth wear:

Score	Surface	Criteria
0	*B/L/O/I*	No loss of enamel surface characteristics.
	C	No loss of contour.
1	*B/L/O/I*	Laos of enamel surface characteristics.
	C	Minimal loss of contour.
2	*B/L/O/I*	Loss of enamel exposing dentine for less than one third of surface.
		Loss of enamel just exposing dentine.
	C	Defect less than I mm deep.
3	*B/L/O/I*	Loss of enamel exposing dentine for more than one third of surface.
		Loss of enamel and substantial loss of dentine.
	C	Defect less than 1-2 mm deep.
4	*B/L/O/I*	Complete enamel loss - pulp exposure - secondary dentin exposure.
		Pulp exposure or exposure of secondary dentine.
	C	Defect more than 2mm deep - pulp exposure - secondary dentine exposure.

B: buccal; L: lingual; 0: occlusal; I: incisal; C: cervical.

Statistical analysis

For statistical analysis, the data were computed using the statistical package for social science program (SPSS version 21.0). Frequencies and percentages, as well as averages and standard deviation, were included in the univariate analysis. The TWI score of each tooth was used to determine the mean tooth. In addition, the chi-square test was employed to compare the research variables at different levels.

The relationship between medium- and high-risk levels of tooth wear was studied using ordinal logistic regression. The test statistic was odds ratios (OR), with 95 percent confidence intervals (CIs), and statistical significance was defined as p 0.05.

RESULTS

A total of 194 patients with diabetes with duration of diabetes more than or equal to 10 years were enrolled in this study, 105 (54.12%) treated with insulin regimens without metformin and stop metformin at least 5 years ago, and 89 (45.88%) of them treated with metformin regimens. The baseline clinical characteristics were shown in **(Table 1)**.

There was a significant difference between different TWI as regard age and duration of diabetes as shown in **(Table 2)**. Teeth Wear index (TWI) was significantly positively correlated to age and duration of diabetes in all groups, insulin group and

TABLE (1): Comparison between Insulin and Metformin Groups

		Insulin Group (n=105)	Metformin Group (n=89)	t/X^2	P
Age (Years)		59.33±5.63	57.36±5.62	2.436	0.016*
DM Duration (Years)		15.48±3.21	14.21±2.65	2.956	0.004*
Stop Metformin (Years)		8.99±2.68	---	---	---
Years on Metformin (Years)		6.46±2.69	---	---	---
Male (%)		57 (54.3%)	47 (52.8)	0.042	0.837
Tooth wear Index (TWI)	**0 (%)**	28 (26.7%)	14 (15.7%)	10.397	0.034*
	1(%)	33 (31.4%)	19 (21.3%)		
	2 (%)	24 (22.9%)	23 (25.8%)		
	3(%)	17 (16.2%)	28 (31.5%)		
	4(%)	3 (2.9%)	5 (5.6%)		

TABLE (2): Comparisons between Tooth Wear Index in all groups, Insulin and Metformin Groups

		TWI 0	TWI 1	TWI 2	TWI 3	TWI 4	F/X^2	P
Age (Years)	**All Groups**	54.64±3.84	56.38±4.95	60.48±4.87[1,2]	60.89±5.53[1,2]	65.75±5.92[1,2,3,4]	17.844	<0.001*
	Insulin Group	55.50±4.17	58.42±4.93[1]	62.75±3.65[1,2]	60.82±6.54[1]	69.33±0.58[1,2,3,4]	11.789	<0.001*
	MET Group	52.93±2.37	52.84±2.31	58.09±4.92[1,2]	60.93±4.96[1,2,3]	63.60±6.67[1,2,3]	16.630	<0.001*
DM Duration (Years)	**All Groups**	12.93±2.85	13.56±2.67	16.00±2.40[1,2]	16.96±2.19[1,2]	15.88±3.31[1,2]	19.299	<0.001*
	Insulin Group	13.32±3.28	14.39±2.74	17.58±1.88[1,2]	18.06±1.39[1,2]	16.00±4.35	14.301	<0.001*
	MET Group	12.14±1.51	12.11±1.85	14.35±1.67[1,2]	16.29±2.34[1,2,3]	15.80±3.11[1,2]	17.191	<0.001*
Stop MET (Years)	**Insulin Group**	9.11±2.75	8.88±2.53	10.45±2.52[2]	7.18±1.81[1,2,3]	7.67±3.79	4.460	0.002
Years with MET (Years)	**Insulin Group**	4.21±1.50	5.52±1.70[1]	7.13±2.31[1,2]	10.88±1.36[1,2,3]	8.33±3.21[1,2,4]	40.199	<0.001*
Male (%)	**All Groups**	21 (50%)	28 (53.8%)	25 (53.2%)	26 (57.8%)	4 (50%)	0.581	0.965
	Insulin Group	13(46.4%)	18(54.5%)	14(58.3%)	12(70.6%)	0(0%)	6.239	0.182
	MET Group	8 (57.1%)	10 (52.6%)	11 (47.8%)	14 (50%)	4 (80%)	1.907	0.753

[1]; Statistically Significant difference on comparing with TWI0 using post hoc test (LSD).

[2]; Statistically Significant difference on comparing with TWI1 using post hoc test (LSD).

[3]; Statistically Significant difference on comparing with TWI2 using post hoc test (LSD).

[4]; Statistically Significant difference on comparing with TWI3 using post hoc test (LSD).

metformin group **(Table 3)**. There was no significant between different TWI as regard gender **(Table 2)**.

In insulin group, TWI was significantly positively correlated to duration of metformin use before start insulin and no significant correlation between TWI and duration of stoppage of metformin **(Table 3)**.

Treatment with metformin was a significant positive predictor of TWI. The log odds of having more sever TWI was 1.857 higher on average for those who use metformin as compared to those who use insulin. Moreover, Duration of diabetes and age were significant positive predictor of TWI. For every one-year increase on Duration of diabetes and age, there is a predicted increase of 0.322 and 0.147 respectively in the log odds of a subjects having more sever TWI. Gender identification was not a significant predictor **(Table 4).**

TABLE (3): Spearman's rho Correlations between Studied parameters and TWI

	In all Groups		**In Insulin Group**		**In Metformin Group**	
	rs	**P**	**rs**	**P**	**rs**	**P**
Age (Years)	0.491	<0.001*	0.502	<0.001*	0.652	<0.001*
DM Duration (Years)	0.511	0.001*	0.562	<0.001*	0.636	<0.001*
Stop MET (Years)	---	---	-0.101	0.305	---	---
Years with MET (Years)	---	---	0.717	<0.001*	---	---

TABLE (4): Ordinal Logistic regression the dependent variable is TWI

		Estimate	**Std. Error**	**Wald**	**Sig.**	**95% Confidence Interval**	
						Lower Bound	**Upper Bound**
Threshold	**[Wear = 0]**	14.169	1.905	55.309	<0.001	10.435	17.903
	[Wear = 1]	16.062	1.976	66.087	<0.001	12.190	19.935
	[Wear = 2]	17.676	2.042	74.916	<0.001	13.674	21.679
	[Wear = 3]	20.456	2.173	88.603	<0.001	16.196	24.715
Location	**Age**	0.147	0.031	22.960	<0.001*	0.087	0.208
	DM Duration	0.322	0.060	28.940	<0.001*	0.204	0.439
	Group	1.857	0.307	36.613	<0.001*	1.256	2.459
	Gender	0.017	0.273	0.004	0.950	-0.517-	0.551

DISCUSSION

Although T2DM has been established as a risk factor for poor oral health, there have been few investigations on the relationship between dental health and T2DM features. Previous research had linked diabetes duration and severity to increased decaying, periodontal-affected teeth, tooth loss, decreased saliva production due to medication and tooth wear, as well as a deterioration in quality of life. [9,17]

A recent meta-analysis, on the other hand, found no significant link between poorly controlled T2DM and oral health; this discrepancy underscores the need for more research. [10]

There are just a few epidemiological studies that look at the link between diabetes and glycemic management, tooth loss, wear, and dental prosthetics for treating biting and chewing issues. [10]

Therefore, this current cross-sectional study was performed to assess the prevalence and severity of tooth wear in adult with T2DM.

The study's findings revealed that tooth wear is common among older diabetes persons; as shown in table 2, there was a substantial difference in tooth wear index across age groups (50-70). This is in line with the findings of **Liu et al**, who surveyed 500 adults aged 18 to 55 in India and discovered a significant prevalence of tooth wear (88%) in the elderly. [3]

Srisilapanan et al., who researched The Prevalence and Severity of Tooth Wear in Type 2 Diabetic Patients and found that the average age was 56.5 (7.8), agreed with our findings. Nearly half of diabetic patients (44.1%) had the disease for more than five years. These findings corroborate our findings, which suggest that the age and duration of the disease have a major impact on the outcome.[2]

As shown in table3: In insulin group, TWI was significantly positively correlated to duration of metformin use before start insulin and no significant correlation between TWI and duration of stoppage of metformin so, Treatment with metformin was a significant positive predictor of TWI compared to those who use insulin.

Wetselaar et al evaluated the Tooth wear index in practice and to integrate the principles described in the European Consensus Statement to compose a renewed Tooth Wear Evaluation System (TWES) 2.0 and a new taxonomy, they found the etiology can be assessed by findings that a chemical and/or a mechanical cause which may cause the wear.[18]

Al- Mashhadane investigated the effects of oral hypoglycemic drugs on salivary flow rates and protein composition in patients with diabetes mellitus and found that diabetes mellitus can cause changes in salivary flow rates and protein concentrations, which can affect the oral health of these patients, while oral hypoglycemic drugs had no such effects. These findings contradict our findings. [19]

Mohiti et al conducted a case-control study comparing salivary viscosity and pH in three groups: controlled type 2 diabetic patients, uncontrolled T2DM patients, and healthy controls. It was concluded that diabetes causes a reduction in saliva pH and increases saliva viscosity, which can cause qualitative and quantitative changes in saliva and oral health. [11]

Therefore, any factor that alters the oral salivary pH and viscosity has an impact on the severity of tooth wear.

According to the results of our study, Treatment with metformin was a significant positive predictor of TWI. This expected to be a factor affecting on the salivary secretion and function, which may be related to its structural composition as metformin hydrochloride, a hydrophilic drug and/or its use may associate with lactic acidosis. [7]

Ahmadinia et al. had conducted a recent

systematic review and meta-analysis to study Association between T2DM and tooth loss, found that a positive association between T2DM and tooth loss in cross-sectional studies and no significant association between T2DM and tooth loss was found in cohort studies with increase the risk of oral disease in T2DM directly (e.g., gingival inflammatory response) and indirectly (e.g., decreased saliva production due to medication e.g., metformin). [9]

These results in agree with our findings that antidiabetic drugs may effect on salivary gland secretion and later lead to xerostomia and increase risk of developing dental erosion and attrition, due to loss of salivary protection of the teeth against acids, extrinsic or intrinsic factors which causing these conditions.

The current study analyzed the effect of two different medicines in treating T2DM and found that both had a significant influence on tooth wear index after omitting other factors that may enhance tooth wear (according to the research's exclusion criteria). Nevertheless, Metformin group had more sever TWI and metformin was a predictor TWI.

That means that a drug's chemical structure and character, might influence salivary pH, which can then affect the severity and frequency of tooth wear over time. Few studies were performed on this issue, so we recommend further studies to investigate the effect of antidiabetic drugs on the tooth wear severity and salivary secretion.

CONCLUSION

1. Diabetic patients exhibited a significant prevalence of tooth wear. Diabetes duration and patient age had strong impact on TWI.

2. Metformin therapy was found to be a strong predictor of TWI.

3. No correlation was found between TWI and duration of stoppage of metformin.

REFERENCES

1. Schlueter N, Amaechi B, Bartlett D, Buzalaf M, Cavalho T, Ganss C, et al. Terminology of Erosive Tooth Wear: Consensus Report of a Workshop Organized by the ORCA and the Cariology Research Group of the IADR. Caries Research. 2020; 54 (1): 2-6.
2. Srisilapanan P, Jindarat M, Roseman J. The Prevalence and Severity of Tooth Wear in Type 2 Diabetic Patients. Int J Dent. 2018; 2018: 3608158.
3. Liu B, Zhang M, Chen Y, Yao Y. Tooth wear in aging people: an investigation of the prevalence and the influential factors of incisal/occlusal tooth wear in northwest China. BMC Oral Health. 2014; 14: 65-70.
4. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2022. Diabetes Care. 2022; 45 (1): s17-s38.
5. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: 2021. Available at: https://www.diabetesatlas.org.
6. American Diabetes Association. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2022. Diabetes Care. 2022; 45 (1): s125-s143.
7. Feng J, Xiaohui W, Xiaochun Y, Irma A, Bernardo L, Marta M, et al. Mitochondria as an important target of metformin: The mechanism of action, toxic and side effects, and new therapeutic applications. Pharmacological Research. 2022; 177 (2022): 106114.
8. Wang YW, He SJ, Feng X, Cheng J, Luo YT, Tian L, et al. Metformin: A review of its potential indications. Drug Design, Development and Therapy. 2017; 11:2421-2429.
9. Ahmadinia A, Rahebi D, Mohammadi M, Ghelichi-Ghojogh M, Jafari A, Esmaielzadeh F. Association between type 2 diabetes (T2D) and tooth loss: a systematic review and meta-analysis. BMC Endocrinology Disodrders. 2022; 22: 100-110.
10. Laouali N, El fatouhi D, Aguayo G, Balkau B, Fagherazzi G. Type 2 diabetes and its characteristics are associated with poor oral health: findings from 60,590 senior women from the E3N study. BMC Oral Health. 2021; 315: 1-11.
11. Mohiti, A., Ghadiri-Anari, A. and Entezary, F. Comparison of pH and Viscosity of Unstimulated Saliva in Type 2 Diabetic Patients and Control Group. Journal Dental School. 2017; 35 (3):89-92.

12. Smith B, Robb N. Prevalence of tooth wear in 1007 dental patients. Journal of Oral Rehabilitation. 1996; 23 (4): 232–239.

13. Marró ML, Aránguiz V, Ramirez V L A. Prevalence of erosive tooth wear in Chilean adults, 2016: A cross-sectional study. Journal of Oral Rehabilitation; 47 (4):467–472.

14. Sterenborg B, Kalaykova s, Loomans B, Huysmans M. Impact of tooth wear on masticatory performance. Journal of Dentistry. 2018; 76: 98–101.

15. Al-Omiri M, Sghaireen M, Alzarea B, Lynch C. Quantification of incisal tooth wear in upper anterior teeth: conventional vs new method using toolmakers microscope and a three-dimensional measuring technique. Journal of Dentistry. 2013; 41: 1214 –1221.

16. López F, Cosano L , González J , LlamasCarreras J, Segura-Egea J. Clinical measurement of tooth wear: Tooth wear indices. Journal of Clinical and Experimental Dentistry. 2012; 4 (1): 48- 53.

17. Wu CZ, Yuan YH, Liu HH, Li SS, Zhang BW, Chen W. Epidemiologic relationship between periodontitis and type 2 diabetes mellitus. BMC Oral Health. 2020; 20: 204-219.

18. Wetselaar P, Wetselaar M, Katzer L, Ahlers M. Diagnosing tooth wear, a new taxonomy based on the revised version of the Tooth Wear Evaluation System (TWES 2.0). Oral Rehabilitation. 2020; 47:703–712.

19. Al- Mashhadane F. Effects of Oral Hypoglycemic Drugs on Flow Rate and Protein Composition of Saliva in Patients with Diabetes Mellitus. Al–Rafidain Dental Journal. 2011; 11: 297-302.