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Saliva Tgfb1 Level in Patients with Type 2 Diabetes Mellitus and Primary Hypertension on Dental Caries

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ABSTRACT

Background: The purpose of this study is to analyze the relationship and differences in salivary Tgfb1 levels in patients with type 2 diabetes mellitus (T2DM) and primary hypertension (PH) with dental caries patients.

Methods: The research design used is a clinical experimental approach. Salivary examination of T2DM and PH patients was carried out by laboratory staff at the Matakali Health Center and assisted by the research team, then continued with the examination of TGFβ1 levels at the microbiology laboratory of Hasanuddin University, Indonesia, which became a research partner. Saliva TGFβ1 levels were measured with a commercial Human TGFβ1 kit ELISA Assaygenie. Sampling using purposive sampling technique. Test analysis with Chi Square and independent sample T-test. The sample size in this study was 60 samples, namely 30 T2DM patients, 30 PH patients aged 18-40 years. Analysis is Chi Square and independent T-test.

Results: The results of this study when viewed from the distribution of tooth brushing habits in T2DM patients, namely the frequency of brushing teeth is not good (1x a day) and dental caries is 56.7%, while PH patients are 63.4%. This shows that the frequency of tooth brushing affects the occurrence of dental caries in T2DM and PH patients. Likewise, when viewed from the sex distribution of T2DM in males 60% and females the lowest 40%. Gender distribution in patients with PH & dental caries with the largest proportion of male 53.3% and the lowest female 46.7%. Salivary TGFβ1 levels of patients with T2DM & Caries, PH with dental caries were 577.85 pg/ml (0.042) and 386.3894 pg/ml (0.024). Then continued with testing the effect of TGFβ1 on T2DM and PH patients with dental caries, namely T2DM patients (p. 0.042) and PH patients (p. 0.024). This shows that there is a significant effect between salivary TGFβ1 levels of T2DM and PH patients on dental caries. Likewise, it was found that there was a significant difference between T2DM and PH in dental caries by looking at the average value of salivary TGFβ1 on PH was 386,3894pg/mL while salivary TGFβ1 on T2D was 577,8546pg/mL. It can also be seen from the standard deviation value of T2DM deviation is 173.04621, while HTP is 95.93092.

Conclusion: There is associated and difference of Salivary TGFβ1 levels of patients with T2DM and PH at the age of 18-40 years with dental caries. The higher the salivary TGFβ1 level, the higher the risk of dental caries.

Keywords: TGFβ1 levels, Saliva, Type 2 diabetes mellitus, Primary hypertension, Dental caries

Background Diabetes mellitus (DM) is a disease that has multiple risk factors that are important in the development of cardiovascular disease. Therefore, diabetes mellitus has a relationship with hypertension.^[1] Diabetes mellitus can cause dysfunction in various cells and different tissues, including tissues in the oral cavity such as the salivary glands. Decreased salivary flow rate can also occur in patients with poorly controlled glycemia. The high risk of DM in the oral cavity, causing oral injury, decreased speed and quality of wound healing.^[2-3] In addition, a history of hypertension, xerostomia has an important role in increasing the risk of dental caries.^[4] Dental caries results from the demineralization process which causes damage to the hard tooth tissue. Diabetes mellitus is one of the predisposing factors that affect the occurrence of dental caries due to uncontrolled blood glucose levels causing high levels of glucose in saliva.^[5] Likewise, hypertension is a degenerative and the sufferer must take antihypertensive drugs. Antihypertensive drugs have systemic side effects and effects on the oral cavity, one of which is to reduce the amount of salivary flow so to facilitate the occurrence of dental caries.^[6]

Growth factor beta1 (TGFβ1) has a close relationship in the physiopathogenesis of dysregulated hypertension in patients with diabetes mellitus.^[7-8] In the process of embryogenesis, salivary glands, TGFβ1 expression is responsible for disruption of one of the glandular branches in the oral cavity and has an important role in regulating the proliferation and differentiation of epithelial cells. This can affect the homeostatic process in the oral mucosa.^[9] This has been proven in studies using experimental animals suffering from diabetes mellitus. The results explained that in these animals, the production of TGFβ isoforms in the salivary glands was impaired.^[10] Diabetes is diagnosed by testing the level of sugar or glycated hemoglobin in the blood. T2DM, also known as adult-onset diabetes, is characterized by high blood pressure, insulin resistance, and insulin deficiency.^[11]

Transforming growth factor beta1 (TGFβ1) has been implicated in the physio pathogenesis of hypertension and has also been reported to be dysregulated in diabetic patients^[10-11] During salivary gland embryogenesis, TGFβ1 expression is responsible for glandular branch disorders and has an important role in regulating epithelial cell proliferation and differentiation, affect oral mucosa homeostasis. In animal models that diabetes affects the production of TGF isoforms in the salivary glands so that it can be used as a basis for direct testing in humans.^[12]

There is a possible relationship between T2DM and PH with a decrease in the amount and quality of saliva. Impaired salivation can reflect changes in the oral tissues that cause dental caries. Based on this background, the researcher wanted to know the association and difference of Saliva TGFβ1 Level in patients T2DM and PH with dental caries.

Methods

The research design used is a clinal experimental approach. The population of the study was the community at the Matakali Health Center, Polewali Mandar Regency, who were patients with T2DM and PH and experienced dental caries aged 18-40 years. Inclusion criteria were T2DM patients who had HbA1c examination at the partner hospital of the Matakali Health Center, PH patients (grade 1), had dental caries, aged 18-40 years, did not smoke, recommended a sugar diet and reduced consumption of cariogenic foods 7 days before sampling saliva. The exclusion criteria were that the patient had a history of TB and HIV and diseases manifested in the oral cavity. The sample size is 60 people, namely 30 T2DM patients, 30 PH patients. The exclusion criteria were that the patient had a history of TB and HIV disease and the disease manifested in the oral cavity. The sample size is 60 people, namely 30 T2DM patients, 30 PH patients.

Salivary examination of T2DM and PH patients was carried out by laboratory staff at the Matakali Health Center and assisted by the research team, then continued with the examination of TGFβ1 levels at the microbiology laboratory of Hasanuddin University, Indonesia, which became a research partner. Saliva TGFβ1 levels were measured with a commercial Human TGFβ1 ELISA Kit

(MyBio Source). Sampling using purposive sampling technique. Test analysis with Chi Square and independent sample T-test.

Results

The results of this study when viewed from table 1, the distribution of tooth brushing habits in T2DM patients, namely the frequency of brushing teeth is not good (1x a day) and dental caries is 56.7%, while PH patients are 63.4%. This shows table 2, that the frequency of tooth brushing affects the occurrence of dental caries in T2DM and PH patients. Likewise, when viewed from the sex distribution of T2DM in males 60% and females the lowest 40%. Gender distribution in patients with PH & dental caries with the largest proportion of male 53.3% and the lowest female 46.7%.

Salivary TGFβ1 levels of patients with T2DM & Caries this shows table 3, PH with dental caries were 577.85 pg/ml (0.042) and 386.3894 pg/ml (0.024). Then continued with testing the effect of TGFβ1 on T2DM and PH patients with dental caries table 4, namely T2DM patients (p. 0.042) and PH patients (p. 0.024). This shows that there is a significant effect between salivary TGFβ1 levels of T2DM and PH patients on dental caries. Likewise, it was found that there was a significant difference between T2DM and PH in dental caries by looking table 5, the average value of salivary TGFβ1 on PH was 386,3894pg/mL while salivary TGFβ1 on T2DM was 577,8546pg/mL. It can also be seen from the standard deviation value of T2DM deviation is 173.04621, while PH is 95.93092.

Discussion

The sex distribution in T2DM with dental caries is 60% male and 40% female. The sex distribution of HTP and experiencing dental caries were 53.3% male and 46.7% female. The results of this study indicate that men suffer from more T2DM and PH with high rates of dental caries. However, in this study it was found that T2DM and PH patients who had high caries were higher in male than female. This happens because the number of samples selected is more male.

Further examination was carried out by looking at the salivary TGFβ1 level in T2DM and PH patients with dental caries. The results showed that the salivary TGFβ1 level for T2DM patients was considered normal, namely 171, 9659 pg/mL. The mean value of TGFβ1 level in T2DM patients was 577.8546 pg/mL (p. 0.042) while in PH patients it was 386.3894 pg/mL (0.024). This indicates that the level of TGFβ1 in T2DM and PH patients has a significant effect on the occurrence of dental caries.

The increase in salivary TGFβ1 levels is influenced indirectly by pathophysiological differences in blood glucose homeostatic disturbances and increased blood pressure, especially supported by other factors such as untreated dental caries. Although it is still not known with certainty whether the emergence of this pathology is due to the systemic profile of DM and hypertension or is caused by local manifestations as inferior or salivary flow velocity, changes in the buccal mucosal epithelium or even changes in salivary composition.^[13-14]

We know that diabetes mellitus is a systemic disease that manifests in the oral cavity. Patients with diabetes mellitus experience an increase in the number of bacteria in the oral cavity, causing abnormalities in the oral cavity. The most prominent complaint of oral conditions in people with diabetes mellitus is a decrease in salivary flow which causes dry mouth (xerostomia) and causes a high frequency of dental caries. Decreased salivary flow can increase salivary glucose and decrease the self-cleansing effect that may contribute to the increased prevalence of dental caries. In T2DM patients with poor oral hygiene, it will trigger plaque accumulation so that the self-cleansing effect of saliva is reduced, plaque is easy to stick causing demineralization and enamel damage so that dental caries is easy to occur.^[15]

The role of TGFβ1 in cardiovascular diseases such as hypertension is controversial. TGFβ1 plays a role in the development of cardiovascular-renal complications based on pathophysiological conditions in humans. Patients suffering from chronic diseases, such as hypertension, diabetes mellitus and hypercholesterolemia can result in end-organ damage (heart dysfunction, arteriosclerosis and chronic kidney failure). This gives a high contribution to the morbidity and mortality rates. Previous studies have shown that TGFβ1 is an important cause of fibrosis, extracellular matrix accumulation and epithelial/endothelial-mesenchymal transformation. All of these are pathogenic in the development of end-organ damage.^[16-18]

We know that the cause of hypertension is not only a decrease in organ function which is characterized by a decrease in arterial elasticity and blood vessel stiffness but can also be caused by multifactorial causes such as stroke, heart failure, chronic kidney disease, and visual impairment. [19-22] Several studies suggest that the role of TGFβ1 may protect or even lead to the development of this cardiovascular disease. This is because TGFβ1 is one of the immunomodulatory cytokines whose work affects many types of cells that make up the walls of heart blood vessels. Transforming growth factor TGFβ1 can play a role in cell migration, differentiation, proliferation and apoptosis. [23]

Djukic et al showed in a population of 387 hypertensive subjects that hypertension combined with diabetes promoted a significant reduction in salivary flow rate depending on the type of anti-hypertensive drug administered during treatment. Despite a decrease in salivary flow, here only 50% of patients in the diabetes mellitus group with hypertension reported frequent sensations of dry mouth, while it has been reported that the majority of patients exhibiting this disease association have xerostomia. [24]

People with diabetes and hypertension usually experience impaired wound healing. This condition may be caused by changes in the cytokine profile in saliva. The cell motility proteins involved are expressed in the saliva of patients with DM. Salivary TGFβ1 levels are higher when diabetes is associated with hypertension as indicated by the positive correlation between the presence of growth factors in saliva and fasting plasma glucose concentrations in the blood. [25-26]

TGFβ1 plays a role during the physiological development of glands involved in the proliferation and differentiation of epithelial cells and is one of the molecules responsible for the epithelial-mesenchymal cell transition in the pathological process of oral cancer formation. These results indicate that the oral effects induced by T2DM and PH are not associated with changes in epithelial cell proliferation, but other studies have described the involvement of other cells that may be a possible factor for oral carcinogenesis. Burzlaff et al observed that the most common cell types in the healthy oral mucosa were intermediate and superficial. Other studies have investigated the effect of type 2 diabetes mellitus on oral cells associated with cell maturation patterns. [27]

Conclusions

Based on the results of research on salivary TGFβ1 levels between type 2 diabetes mellitus (T2DM) and primary hypertension (PH) at the age of 18-40 years, it can be concluded that there is a very significant effect of salivary TGFβ1 levels in patients with type 2 diabetes mellitus and primary hypertension on dental caries. One of the limitations of this study is that several risk factors for dental caries cannot be controlled, such as oral hygiene, bacterial factors that cause dental caries.

Authors' contributions

Masriadi has full access to all data in this study and is responsible for the integrity of the data and the accuracy of the data analysis. Concept and design: Masriadi. National and institutional policies: Masriadi, Hasta Handayani, Risnayanti Anas. Laboratory support: Hasta Handayani Idrus, Nur Najma Tasyah and Tuti Alawiyah. Data acquisition, analysis, or interpretation: Muh Fajrin Wijaya, Sari Aldilawati, and Helwiah Umniyati

Funding

Nil.

Availability of data and materials

The database used to extract data from individual studies and the code associated with the table design cannot be uploaded to a public repository because the data provider (at the Matakali Health Center Ingredient) does not enter it because it is very confidential. Research data can be obtained by contacting the Chairperson in charge of Non-Communicable Diseases at the Matakali Health Center, Polewali Mandar Regency, South Sulawesi, Indonesia.

Declarations

Ethical policy and institutional review board statement

All procedures were carried out according to the ELISA examination method. Ethical clearance from the Institutional Committee Universitas Muslim Indonesia (No.5271/A/KEPK-UMI/III/2021) was obtained prior to the start of the study. National guidelines followed in accordance with the Declaration of Helsinki

Consent for publication

Not applicable

Competing interest

The authors declare they have no competing interest

Patient declaration of consent

Informed consent (written and oral) was obtained from all the parents and participants.

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Table 1. Toothbrushing habit with dental caries in T2DM and PH

Toothbrushing Frequency	T2DM (Dental Caries)		PH (Dental caries)	
	Frequency	Percent	Frequency	Percent
Good (2 x a day)	13	43.3%	11	36.6%
Bad (1x a day)	17	56.7%	19	63.4%
Total	30	100%	30	100%

Table 2. Criteria for samples of T2DM and PH patients with dental caries

Criteria		T2DM (Dental Caries)		PH (Dental caries)	
		Frequency	Percent	Frequency	Percent
Gender	Male	18	60%	16	53.3%
	Female	12	40%	14	46.7%
Total		30	100%	30	100%

Table 3. Salivary TGFβ1 Level Values

No.	T2DM (Dental caries)	PH (Dntal caries)	Mean T2DM (Dental caries)	Mean PH (Dntal caries)	p-value T2DM (Dental caries)	p-value PH (Dntal caries)
1	400,7598279	297,2079799				
2	521,2181	424,0061611				
3	766,3612504	328,9075252				
4	635,3364631	335,2474342				
5	922,7456739	364,8336765				
6	557,1442514	502,1983728				
7	808,6273108	411,326343				
8	584,6171906	542,3511302				
9	445,1391913	392,3066158				
10	369,0602826	347,9272524				
11	662,8094024	288,7547678				
12	426,1194641	599,4103118				
13	326,7942222	278,1882527				
14	707,1887658	305,6611919				

15	533,8979182	377,5134946	577.8546 pg/ml	386.3894 pg/ml	0.042	0.024
16	400,7598279	297,2079799				
17	521,2181	424,0061611				
18	766,3612504	328,9075252				
19	635,3364631	335,2474342				
20	922,7456739	364,8336765				
21	557,1442514	502,1983728				
22	808,6273108	411,326343				
23	584,6171906	542,3511302				
24	445,1391913	392,3066158				
25	369,0602826	347,9272524				
26	662,8094024	288,7547678				
27	426,1194641	599,4103118				
28	326,7942222	278,1882527				
29	707,1887658	305,6611919				
30	533,8979182	377,5134946				

Table 4. Effect of salivary TGFβ1 T2DM and PH with dental caries

	Frequency	Mean±SD	p-value
T2DM (Dental caries)	30	57,785±17,304	0.042
PH (Dental caries)	30	36,638±95,930	0.024

Table 5. Differences between T2DM, PH and dental caries

Patient	Mean±SD	Mean Differences	p-value
T2DM (Dental caries)	57,785±17,304	1.914	0.001
PH (Dental caries)	36,638±95,930		

