



Saliva Tgfβ1 Level in Patients with Type 2 Diabetes Mellitus and Primary Hypertension on Dental Caries



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Abstract

This study aims to analyze the relationship and differences in salivary Tgfβ1 levels in patients with type 2 diabetes mellitus (T2DM) and primary hypertension (PH) with dental caries patients. 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. It is associated with and difference in 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

dental caries;
primary hypertension;
saliva;
TGFβ1 levels;
type 2 diabetes mellitus;

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1 Introduction

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 (Sahakyan et al., 2010). Diabetes mellitus can cause dysfunction in various cells and different tissues, including tissues in the oral cavity such as the salivary glands (Mahardika et al., 2021; Saraswati et al., 2021). Decreased salivary flow rate can also occur in patients with poorly controlled glycemia. The high risk of DM in the oral cavity causes oral injury and decreased speed and quality of wound healing (Deshpande et al., 2010; Rojo-Botello et al., 2012). In addition, a history of hypertension, and xerostomia has an important role in increasing the risk of dental caries (Sreebny & Schwartz, 1997). 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 (Al-Maskari et al., 2011). Likewise, hypertension is 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 to facilitate the occurrence of dental caries (Mokoginta et al., 2016).

Growth factor beta1 (TGFβ1) has a close relationship with the physiopathogenesis of dysregulated hypertension in patients with diabetes mellitus (Derhaschnig et al., 2002; Yadav et al., 2011). 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 (Bernardi et al., 2018) 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 (Lamers et al., 2007). Diabetes is diagnosed by testing the level of sugar or glycated haemoglobin in the blood. T2DM, also known as adult-onset diabetes, is characterized by high blood pressure, insulin resistance, and insulin deficiency (Adashi & Reshick, 1986).

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 (Adashi & Reshick, 1986; Lamers et al., 2007). During salivary gland embryogenesis, TGFβ1 expression is responsible for glandular branch disorders and has an important role in regulating epithelial cell proliferation and differentiation, affecting 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 (Loh, 1993).

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 between Saliva TGFβ1 levels in patients with T2DM and PH with dental caries (Bradshaw & Lynch, 2013; Ewoldsen & Koka, 2010).

2 Materials and Methods

The research design used is a clinical 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, and 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, and 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 TGF β 1 levels at the microbiology laboratory of Hasanuddin University, Indonesia, which became a research partner. Saliva TGF β 1 levels were measured with a commercial Human TGF β 1 ELISA Kit (MyBio Source). Sampling using a purposive sampling technique. Test analysis with Chi-Square and independent sample T-test.

3 Results and Discussions

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%. 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 TD2M in males 60% and females the lowest at 40%. Gender distribution in patients with PH & dental caries with the largest proportion of males 53.3% and the lowest female 46.7%.

Salivary TGF β 1 levels of patients with T2DM & Caries this shown in 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 TGF β 1 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 TGF β 1 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 looking table 5, the average value of salivary TGF β 1 on PH was 386,3894pg/mL while salivary TGF β 1 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.

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 (Dental caries)	Mean T2DM (Dental caries)	Mean PH (Dental caries)	p-value T2DM (Dental caries)	p-value PH (Dental 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				
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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		

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 males than females. 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 1 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 such as inferior or salivary flow velocity, changes in the buccal mucosal epithelium or even changes in salivary composition (Derhaschnig et al., 2002; Lourenco et al., 2008).

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 (Bellamy et al., 2009; Kahn, 2000). 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-cleaning effect that may contribute to the increased prevalence of dental caries (Lindholm et al., 2005; Mishra, 2016). 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 (Rao et al., 2009).

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 high contributes 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 (Akhurst & Hata, 2012; Wylie-Sears et al., 2014; Zeisberg et al., 2003)

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 (Masriadi, 2018; Masriadi & Azis, 2019; Masriadi et al., 2021; Masriadi, 2019) 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 (Lee & Bae, 2002).

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 (Stefoni et al., 2002; Ivanović et al., 2006). 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 (Seay et al., 2005).

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 TGF β 1 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 (Djukic et al., 2015; Dodds et al., 2000).

TGF β 1 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 (Pasomsub et al., 2021; Landry et al., 2020). 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 (Lee & Bae, 2002). Diabetes Mellitus Diabetes Mellitus is a degenerative disease that is generally associated with genetic and environmental factors (Masriadi & Muriyati, 2022). Diabetes mellitus is a disease that has received worldwide attention because its incidence continues to increase (Masriadi et al., 2022).

4 Conclusion

Based on the results of research on salivary TGF β 1 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 TGF β 1 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, and bacterial factors that cause dental caries.

Acknowledgements

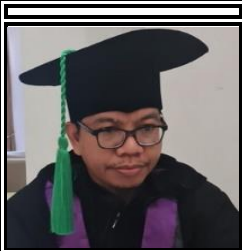





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