Is hearing impairment in diabetic patients correlated to other complications?

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Abstract

Purpose Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia that results by relative or absolute insulin deficiency. Hearing disorders is common otological disorders in diabetic patients. This study aimed to investigate the frequency of hearing impairment among DM patients and its association with diabetes complications and blood sugar control.

Methods This analytical cross-sectional study was conducted from 2016 to 2017 on 81 patients with type 2 diabetes mellitus (T2DM), aged 40–65 years who were referred to Yazd diabetic research center. Air conduction pure tone hearing thresholds were obtained for each ear at frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz. We defined hearing impairment as the pure-tone average ≥ 25 dB hearing level of pure-tone thresholds at low frequencies (500; 1000; and 2000 Hz) and high frequencies (4000 and 8000 Hz). The demographic data and diabetes complications frequency were gathered. All statistical analysis was done in SPSS 22.

Results The mean ($\pm$ SD) age of participants was 56.38 ± 5.68 years (range 40–65 years), 32(39.5%) were males and 49(60.5%) were females. The prevalence of hearing loss in high frequency in right ear was higher in male (p value = 0.047). The grade of diabetic retinopathy and nephropathy were significantly associated with hearing impairment in high frequency in both ears (p value < 0.05). Finally, the results showed that even after adjustment of confounding variables using logistic regression analysis there were no relationship between hearing impairment and variables in both ears.

Conclusion The hearing impairment was associated with diabetes complications as retinopathy and nephropathy. The association was significant in high frequency.

Keywords Audiometry · Diabetes mellitus · Hearing impairment · Complications

Introduction

Along with advances in diabetes mellitus (DM) and complications research, there is an increasing attention to hearing disorders in DM patients. Previous studies indicated

the relationship between DM and hearing loss [1]. DM is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia that results by relative or absolute insulin deficiency [2]. The prevalence of DM all over the world is increasing rapidly [3]. It is estimated

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that the number of individuals with DM will increase to 592 million by 2035 [4].

The vascular and neural changes in the cochlea are likely the cause of hearing changes in patients with DM, also thickening of capillary walls (especially in the stria vascularis) and loss of outer hair cells [5].

The hearing loss in most of DM patients may not be due to noise exposure and high frequency sensori-neural hearing loss is predominant. [6–8] Some studies demonstrated that diabetes effects on hearing are more frequent among patients younger than 50 years old [9–11]. So endocrinologists need to control hearing in DM patients, in addition to other common diabetic complications. Although some recent studies showed hearing loss is related with diabetes [12–14] but some reports revealed no relation between DM and hearing impairment [15]. This study aimed to investigate the frequency of hearing impairment among DM patients and its association with diabetes complications and blood sugar control. It is important because type 2 diabetes mellitus (T2DM) is a public health problem, which significantly and negatively affect the quality of life when complicated with hearing loss [16].

Methods

Study population and data collection

This analytical cross-sectional study was conducted from January 2016 to April 2017 on T2DM patients, referred to Yazd diabetic research center. A total of 81 from 139 studied patients were selected by consecutive central-based sampling. The inclusion criteria were: endocrinologist confirmed diagnosed T2DM and age between 40 and 65 years old. The exclusion criteria consist of: history of working in noisy environments, creatinine ≥ 1.6 , use of ototoxic drugs (Aminoglycoside antibiotics, Steroids, Cisplatin), past history of ear diseases, head trauma, meningitis, allergy, occupational noise (occupational noise induced hearing loss causes sensorineural hearing loss (SNHL) in industrial workers who are continuously exposed to high frequency noise due to degeneration in hair cells and associated nerve fibers) and cardiovascular disease. A demographic checklist contains; noise exposure history, medical history, diabetes duration, treatment history, and complications.

Anthropometric measurements including weight and height measurements were obtained using standardized techniques. Height was measured in centimeters using a wall-mounted measuring tape to the nearest centimeter. Subjects were requested to stand upright without shoes with their back against the wall, heels together and eyes directed forward. Weight was measured in kilograms using a digital scale that

was kept on a firm horizontal surface. Subjects were asked to wear light clothing and weight was recorded to the nearest 0.5 kg. BMI was calculated as weight in kilograms divided by height in meters squared (Kg/m^2). The guideline of the United States National Institute of Health (NIH) use the following BMI classification: BMI $< 18.5 \text{ kg}/\text{m}^2$, underweight; BMI 18.5 to 24.9 kg/m^2 , normal weight; BMI 25.0–29.9 kg/m^2 , overweight; BMI 30–34.9 kg/m^2 , obesity class I; BMI 35–39.9 kg/m^2 , obesity class II; and BMI $\geq 40.0 \text{ kg}/\text{m}^2$, obesity class III. All of laboratory examinations were done in Yazd diabetes research center laborator at first visit. HbA1c was determined by high performance liquid chromatography (ToSoHG8). Micro-albuminuria, Triglyceride (TG), Cholesterol, High-density lipoprotein (HDL), low-density lipoprotein (LDL), Creatinine and Urea levels were measured with Biosystem kits (Spain, European), using the auto-analyzer BA-400 (Biosystems, European).

Ophthalmologic examination including visual acuity (by means of snellen charts), intraocular pressure (using Applanation Tonometry), fundoscopy (utilizing slit lamp and non-contact lenses) and indirect ophthalmoscopy were also completed. If required, fluorescein angiography was ordered. All the relevant examinations were completed by an ophthalmologist. Based on their optic fundi findings, they were classified into five groups: No retinopathy, Mild NPDR, Moderate NPDR, Severe NPDR, PDR.

Diabetic nephropathy was graded as: 1) no micro-albuminuria (albumin concentration $\leq 30 \text{ mg}/\text{L}$), 2) micro-albuminuria (albumin concentration 30–300 mg/L and 3) macro-albuminuria (albumin concentration $\geq 300 \text{ mg}/\text{L}$) [17]. The nephropathy grading was done by a nephrologist.

Audiometric measure

The measurements were done by a licensed audiologist using a calibrated audiometer of American National Standard Institute (ANSI) in a sound-treated booth that met accepted standards. Also an Otolaryngologist examined all of patients. Air conduction pure tone hearing thresholds were obtained for each ear at frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz. Higher frequencies are perceived as higher pitches. To produce low frequency pure tone means, we averaged pure tone thresholds measured at 500, 1000, and 2000 Hz for each ear. To produce high-frequency pure tone means, we averaged pure tone thresholds measured at 4000 and 8000 Hz for each ear.

Participants were classified as having impairment if the average of the pure-tone thresholds (PTA) measured at 500, 1000, 2000, 4000 and 8000 Hz in either ear $\geq 25 \text{ dB}$ hearing level [18]. Hearing loss evaluation described as follows: normal ($\leq 25 \text{ dB}$), mild (26–40 dB), moderate (41–55 dB), severe (56–70 dB), very severe (71–90 dB), profound (91–120 dB) and deaf (no hearing). [19]

Statistical analyses

Data were analyzed using the SPSS version 22 for windows computer software package (SPSS Inc., Chicago, IL, USA). With one proportion estimation formula, using hearing loss prevalence 19%, type one error; 0.05, type two; 20 and 10% differences the calculated sample size was 84. Frequency, percent, mean and standard deviation (SD) were used for population description.

To measure the participant characteristics association with hearing impairment the simple linear regression for continuous and logistic regression for categorical variables and post hoc analysis when necessary, which were adjusted using Scheffe applications was done.

Logistic regression was used to determine the studied factors (age, sex, diabetes duration, and diabetes complications) on distribution of the dichotomous outcomes (normal, impaired hearing).

The level $p < 0.05$ was taken as the cutoff value for significance. All of the calculations were statistically analyzed using the Statistical Package for statistical package for the social sciences (SPSS) ver. 22.

Data availability The dataset(s) supporting the conclusions of this article is available in the [Yazd Diabetes Research Center] repository.

Result

Among 139 patients, totally 81 were included. The mean age of participants was 56.38 ± 5.68 years (range 40–65 years), 32(39.5%) were males and 49(60.5%) were females. Demographics and clinical Characteristic of Participants with diabetes are summarized in Table 1. Figure 1 shows the average audiogram in both ears of studied patients. Tables 2 and 3 show the classification of low and high frequency hearing impairment in both ears. In studied patients, the frequency of hearing impairment was 38 (46.9%). The mean of DM duration ($\pm$ SD) was 12.48 ± 5.28 years (range 2–27 years). The results of the present study indicated that males had significantly higher prevalence of hearing loss in high frequency in right ear (p value = 0.047).

Totally, 48 patients (59.3%) suffered from complications of diabetes including: retinopathy in 38 individuals (46.9%), nephropathy in 23 patients (28.4%).

Subjects were classified by degree of diabetic retinopathy as follows: no diabetic retinopathy in 43 patients (56.6%), mild non-proliferative diabetic retinopathy in 10 patients (13.2%), moderate non-proliferative diabetic retinopathy in 13 patients (17.1%), severe non-proliferative diabetic retinopathy in 3 patients (3.9%) and proliferative diabetic retinopathy (PDR) in 7 patients (9.2%).

Table 1 The baseline characteristics of studied patients

Variables	Mean $\pm$ SD	Frequency (%)
Age(year) *	56.38 $\pm$ (5.68)	
Gender		
Male		32 (39.5%)
Female		49 (60.5%)
FBS	170.01 $\pm$ (69.3)	
LDL	93.3 $\pm$ (42.1)	
HDL	42.41 $\pm$ (11.17)	
TG	170.05 $\pm$ (91.6)	
HbA1C	8.56 $\pm$ (0.9)	
Diabetes duration (year)	12.48 $\pm$ (5.21)	
BMI(kg/m ²)*	29.15 $\pm$ (3.92)	
Type of medication (%)		
Insulin use (with or without oral agents)		42 (51.8%)
Oral agents only		35 (43.2%)
Retinopathy		
No		45 (55.6%)
Mild		10 (12.3%)
Moderate		15 (18.5%)
Severe		3 (3.7%)
PDR		8 (9.9%)
Nephropathy		
no micro-albuminuria		61 (75.3%)
Micro-albuminuria		16 (19.8%)
Macro-albuminuria		4 (4.9%)

Level of diabetic retinopathy was significantly associated with hearing impairment in high frequency in both ears (right ear, $p = 0.012$ and left ears, $p = 0.001$). Although in low

Fig. 1 The average audiogram of both ears in studied patients

Table 2 Health characteristics of population with diabetes classified by hearing impairment and normal in both ears in low frequency

	Right		p value	Left		p value
	Hearing- impairment	Normal		Hearing- impairment	Normal	
Age(year) (mean $\pm$ SD)*	56.56 $\pm$ 5.68	55.46 $\pm$ 5.81	0.524	56.18 $\pm$ 5.98	57.27 $\pm$ 4.18	0.548
Gender (%)			0.594			0.407
Male	27(39.)	5(38.5)		27(40.)	5(33.3)	
Female	41(60.3)	8(61.5)		39(59.1)	10(66.7)	
Health characteristics						
FBS	165.89 $\pm$ 67.85	191.23 $\pm$ 76.71	0.231	169.73 $\pm$ 74.82	171.20 $\pm$ 40.69	0.942
LDL	95.95 $\pm$ 42.00	79.47 $\pm$ 42.36	0.218	96.02 $\pm$ 41.52	80.37 $\pm$ 44.73	0.227
HDL	41.90 $\pm$ 11.29	45.11 $\pm$ 10.55	0.365	42.54 $\pm$ 12.03	41.80 $\pm$ 5.78	0.824
TG	172.15 $\pm$ 96.64	158.75 $\pm$ 53.90	0.643	175.21 $\pm$ 97.93	144.69 $\pm$ 38.01	0.247
HbA1C ≥ 7	8.41 $\pm$ 1.91	9.33 $\pm$ 2.02	0.124	8.61 $\pm$ 2.02	8.38 $\pm$ 1.67	0.685
Diabetes duration (year)	12.22 $\pm$ 4.95	13.76 $\pm$ 6.83	0.240	12.03 $\pm$ 5.06	14.40 $\pm$ 5.93	0.119
BMI(kg/m ²)*	28.82 $\pm$ 4.00	30.84 $\pm$ 3.08	0.191	28.95 $\pm$ 3.86	29.99 $\pm$ 4.22	0.391
Type of medication (%)			0.53			1.000
Insulin use (with or without oral agents)	34(52.3)	8(66.7)		35(54.7)	7(46.7)	
Oral agents only	31(47.7)	4(30.8)		29(45.3)	6(40)	
Retinopathy			0.032			0.337
No	38(59.4)	5(41.7)		37(59.7)	6(42.90)	
Mild	5(7.8)	5(41.7)		6(9.1)	4(28.6)	
Moderate	12(18.8)	1(7.7)		11(17.7)	2(14.3)	
PDR	6(95.3)	1(7.7)		6(9.7)	1(7.1)	
Severe	3(4.7)			2(3.00)	1(7.1)	
Nephropathy			0.249			0.543
no micro-albuminuria	50(82)	8(61.5)		47(78.3)	11(78.6)	
Micro-albuminuria	8(13.1)	4(30.8)		9(15)	3(21.4)	
Macro-albuminuria	3(4.9)	1(7.7)		4(6.7)		

*p value was calculated by T-Test

frequency, level of diabetic retinopathy was significantly associated with hearing impairment only in right ear ($p = 0.032$).

Subjects were categorized by degree of diabetic nephropathy as follows: no micro-albuminuria in 58 individuals (78.4%), micro-albuminuria in 12 patients (16.2%) and proteinuria in 4 patients (5.4%).

Level of diabetic nephropathy was significantly associated with hearing impairment in high frequency in both ears (right ear, $p = 0.027$ and left ears, $p = 0.032$). But no significant differences in diabetic nephropathy status were found by low frequency hearing impairment in both ears.

In the correlation analysis there were no significant association between BMI and means of low (p value: 0.41) and high frequency (p value: 0.51) in both ears.

Finally, for assess the relationship between hearing impairment and adjustment of confounding variables such as Age, duration of diabetes, cardiovascular factors (BMI, mean arterial pressure, fasting blood sugar, triglyceride, LDL cholesterol and HDL cholesterol), and factors associated with blood viscosity (hemoglobin) we used logistic regression analysis

for right and left ears (Tables 4 and 5). The results showed that even after adjustment of confounding variables there were no relationship between hearing impairment and variables in both ears.

† P value was calculated by Chi².

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Discussion

Most studies believe that T2DM can cause hearing impairment [8, 9]. A meta-analysis revealed that hearing loss has higher prevalence among diabetic patients compared with sex and aged-match non-diabetic patients [20, 21]. Some evidences showed that chronic hyperglycemia can cause vascular defects in stria vascularis and nerves and damage hearing ability [11, 20]. In current study, we evaluated the association of PTA variables in high and low frequency with age, weight, diabetes duration, microvascular complications and treatment modality among 81 T2DM patients.

Table 3 Health characteristics of population with diabetes classified by hearing impairment and normal in both ears in high frequency

	Right head		p value	Left hear		p value
	Hearing- impairment	Normal		Hearing- impairment	Normal	
Age(year)(mean $\pm$ SD) *	56.39 $\pm$ 5.89	52.33 $\pm$ 6.87	0.022	56.18 $\pm$ 5.98	57.27 $\pm$ 4.18	0.099
Gender (%)			0.227			0.047
Male	30(37)	2(2.5)		30(37)	3(2.5)	
Female	42(51.9)	7(8.7)		38(46.9)	11(13.6)	
Health characteristics						
FBS	173.89 $\pm$ 8.35	140.37 $\pm$ 17.49	0.019	172.76 $\pm$ 8.88	155 $\pm$ 13.7	0.452
LDL	91.5 $\pm$ 5.18	108.5 $\pm$ 13.91	0.258	89.2 $\pm$ 5.33	112.93 $\pm$ 10.11	0.065
HDL	42.57 $\pm$ 11.44	41.12 $\pm$ 9.07	0.732	42.94 $\pm$ 11.67	39.93 $\pm$ 8.28	0.379
TG	170.46 $\pm$ 10.68	166.62 $\pm$ 41.39	0.911	164.68 $\pm$ 11.27	196.52 $\pm$ 26.22	0.253
HbA1C $\geq$ 7	8.66 $\pm$ 1.98	7.76 $\pm$ 1.55	0.22	8.73 $\pm$ 1.97	7.66 $\pm$ 1.66	0.053
Diabetes duration	14.23 $\pm$ 5.06	12.62 $\pm$ 7.00	0.229	12.59 $\pm$ 5.24	11.83 $\pm$ 5.65	0.684
BMI(kg/m ²) *	28.94 $\pm$ 3.47	29.68 $\pm$ 1.13	0.777	28.94 $\pm$ 3.47	29.68 $\pm$ 1.13	0.777
Type of medication (%)			0.258			0.404
Insulin use (with or without oral agents)	30(39)	5(6.5)		30(39)	5(6.5)	
Oral agents only	39(50.6)	3(3.9)		34(44.2)	8(10.4)	
Retinopathy			0.012			0.001
No	40(52.6)	3(3.9)		38(50)	5(6.6)	
Mild	10(13.2)	0		10(13.2)	0	
Moderate	12(15.8)	1(1.3)		10(13.2)	3(3.9)	
PDR	3(3.9)	4(5.3)		2(2.6)	5(6.6)	
Severe	3(3.9)	0		3(3.9)	0	
Nephropathy			0.027			0.032
no micro-albuminuria	51(68.9)	7(9.5)		47(63.5)	11(14.9)	
Micro-albuminuria	12(16.2)	0		12(16.2)	0	
Macro-albuminuria	3(4.1)	1(1.4)		2(2.7)	2(2.7)	

*p value was calculated by T-Test

We showed that mean age of T2DM patients with high frequency hearing impairment is significantly higher than diabetic patients without hearing loss however this relationship in low frequency evaluation had not seen. Previous studies also showed contribution of aging and hearing loss in diabetic patients [8, 9].

In our study, hearing impairment between diabetic patients was not correlated with gender (except in high frequency evaluation of left ear that correlation was poorly significant (P value = 0.047)) but Sugimoto et al. [8] reported that gender was related to hearing in PTA. A meta-analysis showed that hearing impairment in diabetic patients was not influenced by gender [10].

Our findings showed that patients with high-frequency hearing impairments had higher levels of FPG in comparison with patients without hearing damage but HbA1C levels had not any significant difference between two groups. This is in line with findings of Kakarlapudi et al. that during a database review of medical records of 53,461 non-diabetic age-matched patients with 12,575 diabetic patients, reported

worsening of hearing loss among diabetic patients had not apparent correlation with HbA1C [22]. Moreover, Bainbridge et al. didn't find any association between hearing impairment and HbA1C in diabetic patients [15]. However contrary to our findings, a cross-sectional study of veterans with and without T2DM showed that diabetes severity based on current A1C had significant effects on hearing thresholds at a subset of frequencies in uncontrolled group in comparison with non-diabetic group [12]. These controversial issues should be addressed in future well-designed cohort studies to explore the correlation of glycemic control and hearing impairment among T2DM patients. Some studies reported the association between HbA1C and hearing loss [23]. Based on study by Kim et al [10, 14, 24] FPG and HbA1C are independent risk factors for microvascular complications and HbA1C variations which measures disparity between HbA1C and FPG, is a good marker for predicting diabetic complications.

Our study didn't show any significant effect of lipid levels on high and low-frequency hearing impairment in T2DM

Table 4 Relationship among hearing impairment and FBS, HbA1C, Retinopathy, Micro-albuminuria, sex, age, LDL, HDL, TG, BMI in right ear

variable	β	standard error	P value	Odds ratio (95%CL)
FBS	−0.001	0.010	0.934	0.999
HbA1C	−0.070	0.267	0.792	0.932
Retinopathy	−0.148	0.376	0.694	0.862
Micro-albuminuria	−0.371	0.885	0.675	0.690
Sex	0.137	1.058	0.897	1.146
Age	−0.041	0.099	0.674	0.959
LDL	0.015	0.011	0.177	1.015
HDL	−0.032	0.043	0.459	0.968
TG	0.001	0.008	0.854	1.001
BMI	0.001	0.138	0.993	1.001

patients. In this field, some other studies showed that abnormal lipid levels among T2DM patients contribute with sensory neural hearing loss [11, 12] and some of them believe that lipid levels do not affect hearing ability (13).

We found no significant differences in the proportions with or without hearing loss in both low and high-frequency thresholds by diabetes duration. It is consistent with evidences from general population [15, 16].

In present study, we observed no significant association between low or high-frequency hearing impairment and BMI among T2DM patients. It is in agree with the results of some studies that showed inconclusive association between BMI and hearing loss [15–17].

Diabetes treatment and its effect on hearing ability is a controversial issue. We found no significant association between modality of treatment (insulin or oral antidiabetic agents). Bainbridge [15] et al. reported that hearing loss is more common among patients with T2DM on insulin in low-frequency

Table 5 Relationship among hearing impairment and FBS, HbA1C, Retinopathy, Micro-albuminuria, sex, age, LDL, HDL, TG, BMI in left ear

variable	β	standard error	P value	Odds ratio (95%CL)
FBS	0.002	0.011	0.838	1.002
HbA1C	−0.274	0.303	0.365	0.760
Retinopathy	−0.432	0.491	0.379	0.649
Micro-albuminuria	−0.202	0.989	0.838	0.817
Sex	−0.790	1.294	0.541	0.454
Age	−0.186	0.130	0.153	0.831
LDL	0.028	0.014	0.041	1.029
HDL	−0.035	0.054	0.520	0.966
TG	0.000	0.009	0.957	1.000
BMI	0.009	0.161	0.954	1.009

thresholds. Patients on insulin usually have longer-lasting diabetes in comparison with patients on oral agents.

We showed in this study that hearing loss in high-frequency thresholds is significantly associated with the severity of retinopathy however we observed no difference in proportions with nephropathy levels. Some studies showed the association of diabetic retinopathy and hearing loss [18, 19]. Our findings corroborate other evidence about nephropathy [15]. Some studies reported that hearing loss is associated with creatinine levels in T2DM patients [13, 17].

The exact mechanism of hearing damage in diabetic patients is not clearly explained, yet. Some believes that it is a neuropathic process and others think that it is an ischemic phenomenon. Our findings that showed the associations of hearing loss with diabetic microvascular complications instead of macro vascular risk factors such as high cholesterol and low HDL levels, support the hypothesis that diabetes induced hearing loss is predominantly a neuropathic process. Findings of study that performed by Vaughan et al. is in agree with this report [20].

We should consider to limitations of this study. The most important one was the limited number of subjects that leads to low power of study in some variables. Socioeconomic factors had undeniable influences on occurrence of T2DM complications that had not evaluated in present study. Also, smoking history should be considered in further studies.

Conclusion

The hearing impairment was associated with diabetes complications as retinopathy and nephropathy. The association was significant in high frequency.

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Author's contributions “SJ carried out collect samples and wrote the final manuscript. NN participated in the design of the study, performed the statistical analysis and conceived of the study, and participated in its design and coordination and helped to draft the manuscript. MR carried out supervision stages of project and conceived of the study, and participated in its design and coordination and helped to draft the manuscript as well. SA conceived of the study, and participated in its design and coordination and helped to draft the manuscript as well. All authors read and approved the final manuscript.”

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Compliance with ethical standards

Conflict of interest No conflict of interest was declared.

Consent for publication “Not applicable.”

Ethics approval and consent to participate This study is adopted in Ethics Committee of Yazd Diabetes Research Center, based on the Helsinki.

Research ethics The proposal for this thesis research was presented to the Ethics Committee of Shahid Sadoughi University of Medical Sciences and approved by the Internal Medicine Department. The Ethics Committee approved the study with the number 17/113685 on August 27, 2014. The patients were informed about the objective and nature of the study, and each participant provided written consent prior to the study.

Abbreviations *DM*, Diabetes mellitus; *T2DM*, Type2 diabetes mellitus; *SNHL*, sensorineural hearing loss; *BMI*, Body mass index; *PTA*, pure-tone thresholds; *SPSS*, statistical package for the social sciences; (*PDR*), proliferative diabetic retinopathy; *FPG*, fasting plasma glucose

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