Psychiatric Morbidity and Glycemic Control in Type 2 Non Obese Diabetic Egyptian Patients

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Abstract: Context: Type 2 diabetes mellitus doubles the odds of suffering from depressive illness. **Objectives:** The present prospective randomized controlled study aimed to estimate the prevalence of anxiety and depressive disorders among a consecutive group of patients with type 2 non obese diabetes and assess its impact on glycemic control. **Subjects and Methods:** We selected 200 consecutive adult patients with type 2 non obese diabetes mellitus. Patients were divided into 2 groups according to HbA1c level: >7% defined group1 with poor glycemic control (n=140) and ≤7% defined group2 with good glycemic control (n=60). All patients were assessed using semi structured Sociodemographic data form, Hospital Anxiety Depression Scale, The Mini Mental State Examination and Mini international Neuropsychiatric Interview (MINI). **Results:** Anxiety and depressive scores (HAD) were significantly higher in group 1 patients than in group 2 .The prevalence rate of psychiatric disorders were as follow: major depressive disorders 30.7%, dysthymic disorders 15.7% generalized anxiety disorder 10.7%, panic disorder with or without agoraphobia 10%, social anxiety disorder10%, obsessive compulsive disorder 5.7%, post traumatic stress disorder 5(3.6%) in group1 patients and major depressive disorder 18.3%, dysthymic disorder 11.7%, generalized anxiety disorder 8.3%,panic disorder with or without agoraphobia 6.7% social anxiety disorder 6.7%, obsessive compulsive disorder 5%, post traumatic stress disorder 3.3% in group2 patients .Correlation coefficient were computed among hospital anxiety depressive scores (HAD) and HbA1c level, where significant positive correlation was found between these scores and HbA1c level in the diabetic patients indicating the negative impact of depressive and anxiety disorders on glycemic control among diabetics. **Conclusion:** Anxiety and depressive disorders were significantly more frequent in patients with poor glycemic control (more than one third) than in those with good glycemic control. There was a strong association between HbA1c and depressive and anxiety symptoms. The presence of depressive symptoms was associated with a significant worsening of glycemic control.

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1. Introduction

During the last years, the co-morbidity of mental disorders with chronic health conditions has emerged as a topic of considerable clinical and policy interest. Diabetes is considered one of the most psychologically demanding of the chronic medical illnesses because it requires strict daily management of the treatment by the patients themselves[1]. Lack of active involvement can lead to poorer outcomes and increased risk of complications. The presence of psychiatric co-morbidity can result in difficult clinical courses, because it may affect adherence to medication and self-care regimes[2],On the other hand, poor diabetes control might cause or exacerbate depression via direct effects on brain functions or indirectly through complications, functional impairment, or decreased quality of life[3].

Depression has been bi-directionally associated with diabetes mellitus[4]. Subjects who are depressed are more likely to develop type 2 diabetes mellitus either because of the metabolic abnormalities caused by the drugs used to treat depression or because of poor food choices and lack of physical activity that may accompany major depressive episode[5]. Among the anti-depressants, the ones that have non-adrenergic activity are the ones with the highest potential to cause metabolic abnormalities[6].

There has been a growing interest in the study of psychological distress and mental disorders in diabetes. Some epidemiological studies have found higher prevalence rates of depression and anxiety disorders in people with diabetes (PWD) compared with the general population[7,8].Studies evaluating the relationship between depression and diabetes have yielded mixed results. For example, the prevalence of depression in PWD ranges from 3.8%[7] to as high as 49.5%[8]. Many of the studies have relied on clinical or other convenience samples in describing depression and diabetes as co morbid conditions or in exploring the association of depression with clinical markers such as glycemic control, blood pressure, cholesterol, and triglyceride levels[9].

Similarly, studies evaluating the relationship between depression and hyperglycemia in PWD have

yielded controversial results. Some studies suggested that depression is associated with hyperglycemia in people with both type 1 and type 2 diabetes[10,11], whereas other studies did not find any correlation at all[12]. Concerning anxiety disorders, prevalence studies using structured diagnostic interview have found elevated rates of anxiety disorders(generalized anxiety disorders and simple phobia) in patients with diabetes[13]. Although little is known about the effects of anxiety on metabolic control in patients with diabetes, severe anxiety may affect quality of life and by interfering with diabetes self-care may affect metabolic control indirectly. A study showed that an anxious emotional copying style was associated with increased stress, reduced regimen adherence and poorer glycemic control[14]. The psycho physiological effects of anxiety (often perceived as stress) on glycaemia in patients with diabetes also have been studied .the results of this research have been inconsistent with some studies reporting hyperglycemic responses to stress, while others reported no such response[14,15].

Aim of the work.

The purpose of this prospective randomized controlled study was to explore anxiety and depressive disorders among Egyptians with type 2 non obese diabetes and to examine the relationship of these disorders to glycemic control (glycosylated hemoglobin,HbA1c).

2. Patients and methods

Patients: During one year period(from August 2011 to Juli 2012), we selected 215 consecutive consented patients with type 2 non obese diabetes, at their routine consultation at the outpatient's clinic of internal medicine department at Benha University Hospitals, Benha, Egypt. From the overall sample, 13 patients refused to participate and 2 were omitted because of loss of contact. Patients were directly invited by 2 interviewers to participate in the study, they were informed that the objective was to assess the possible relationship between anxiety and depressive disorders and glycemic control. Hospital research ethical committee approved their consent. Patients were excluded from this study, if they were obese or refused to participate, and those who could not clearly understand the questions due to such associated problems such as dementia or sever visual disturbance. All patients were divided into two groups:1-Group 1:Included 140 patients with poor glycemic control(HbA1c was greater than 8.1%).2-Group 2: Included 60 patients with good(optimal) glycemic control(HbA1c was ≤7%).

Methods:

All patients were subjected to full history taking and complete clinical examination. Anthropometric examination was made and demographic data of the patients were collected on a semi-structured questionnaire. A demographic questionnaire recorded details of age, gender, occupation, marital status and education In addition, we recorded details of the duration of their diabetes (in years), current treatment regimen (diet, oral hypoglycemic, insulin or a combination) and extent of any complications involving eyes (retinopathy, maculopathy), kidneys (proteinuria) or feet (peripheral vascular disease, neuropathy, foot ulcers); each type of complication was coded as present or absent. Other significant co morbid illnesses were recorded as present or absent. The presence of other significant illness was verified physical examination and laboratory investigations. Levels of glycosylated hemoglobin (HbA1c)(HPLC, Bio-rad) was checked on the day of the assessment, and was recorded. Glycemic control was optimal if the HbA1c was ≤7% and suboptimal if it was between 7.1% and 8.0% and considered poor if the HbA1c was greater than 8.1%[16].

Psychiatric evaluation:

All patients were subjected to the following: The hospital anxiety and depression scale (HADS) was used to assess levels of anxiety and depression. The HADS had been developed for use in a hospital setting and contains14 self-report items, using a four pointier response Scale. All items focus on cognitive symptoms of anxiety and depression, in order to avoid contamination by somatic symptoms of anxiety and depression (e g weight loss or insomnia), which can have a physical cause, and are therefore not necessarily symptoms of depression. Scores of 11 or more on the HADS anxiety or HADS depression subscale are described as indicative of clinical anxiety or depression[17]. All patients completed the Arabic version of HADS[18].Mini-Mental State Examination (MMSE):The Mini Mental State Examination (MMSE) is a tool that can be used systematically and thoroughly to assess mental status it is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. The maximum score is 30. A score of 23 or lower is indicative of cognitive impairment. The MMSE takes only 5-10 minutes to administer and is therefore practical to use repeatedly and routinely. It is effective as a screening tool for cognitive impairment with older, community dwelling, hospitalized and institutionalized adults. Assessment of an older adult's cognitive function is best achieved when it is done routinely,

systematically and thoroughly. Since its creation in 1975, the MMSE has been validated and extensively used in both clinical practice and research[19].The Mini-International Neuropsychiatric Interview, is a short structured diagnostic interview designed to explore each of the necessary criteria for the main diagnoses of DSMIV Axis1 was the principal diagnostic instrument, the Arabic version was used (Ghanem *et al.,*1999).Depressive and anxiety modules were used to establish current DSMIV depressive and anxiety disorders while being blind to glycemic status and psychopathological data of self reported hospital anxiety depression scale. The Sociodemographic features, history of current or previous psychiatric treatment and family history of psychiatric disorders were obtained in an ordinary clinical interview(20).

Statistical analysis:

All the data were recorded on investigative report form. These data were transferred to IBM card, using IBM compatible computer with statistical program (SPSS). Data was analyzed using the statistical software SPSS version 16. Continuous variables were expressed as means and standard deviation. Pearson Correlation co efficient was done to compare the effects of depression on glycemic control (HbA1c). A *P*-value ≤0.05 was considered statistically significant.

3.Results:

Two hundreds and fifteen consecutive patients were enrolled for the study .From the overall sample,13 refused to participate and 2 omitted because of loss of contact. The remaining 200 participated in the study. Patients were divided into two groups according to HbA1c level: >7 defined group1 with poor glycemic control, n=140(70%) and < 7 defined group2 with good glycemic control, n=60 (30%). The mean age of the subjects was 50.41±7.46 years. They were 69(34.5%)men and 131(65.5%) women. Table 1:shows Sociodemographic features of the sample (mean age, sex percentage, educational level, marital status and occupation). There was no statistical significant difference between both groups of patients (p> 0.05). Table 2: Shows the clinical characteristics of the sample. Where there was no statistical significant difference between both groups of patients as regard; duration of diabetes mellitus, body mass index, treatment, co morbid diseases, history of previous or current psychiatric treatment, and diabetic complications (p>0.05), except for diabetic neuropathy and retinopathy that were found to be more frequent in group1 than group2 (p <0.05), patients with poor glycemic control were found to be less compliant in diet regimen than patient with good glycemic control with statistical significant difference (p <0.05). Also it was found that 5% of all patients reported history of treatment of anxiety and/or depressive disorders and16% was under psychotropic medications (antidepressants and benzodiazepines). Hospital anxiety depressive scores (HAD) were significantly higher in group1 patients than in-group 2 (p<0.05) (Table 3). Depressive and anxiety disorders were more frequent in diabetic patients with poor glycemic than those with good glycemic control with statistical significant difference (p <0.05) .The prevalence rate were as follow: major depressive disorders 30.7%, dysthymic disorders 15.7% generalized anxiety disorder 10.7%, panic disorder with or without agoraphobia 10%, social anxiety disorder10%, obsessive compulsive disorder 5.7%, post traumatic stress disorder 5(3.6%) in group1 patients and major depressive disorder 18.3%, dysthymic disorder 11.7%, generalized anxiety disorder 8.3%,panic disorder with or without agoraphobia 6.7% social anxiety disorder 6.7%, obsessive compulsive disorder 5%, post traumatic stress disorder 3.3% in group2 patients, also it was found that 40% of group 2 reported no specific anxiety or depressive disorder in contrast to 13.6% of group 1 patients (Table 4).

Correlation coefficient were computed among hospital anxiety depressive scores (HAD) and HbA1c level, the result of the co relational analysis showed that significant positive correlation were found between hospital anxiety depressive scores (HAD) and HbA1c level in the diabetic patients (Table 5), indicating the negative impact of depressive and anxiety disorders on glycemic control in diabetic patients. Also. On computing these scores with diet compliance significant negative correlation was found with depressive but not with anxiety scores(Table 6).

Table (1):Sociodemographic characteristics of studied groups

Groups/ Variables	Group 1 (n=140)	Group 2 (n=60)	Total (n =200)	Test	*P* value
Age(years) Mean ±SD	 50.81 7.66	 49.45 6.93	 50.41 7.46	t=1.187	0.24 •

Gender No (%)					
Male	49(35%)	20(33.3%)	69(34.5%)	X2=0.052	0.87 •
Female	91(65%)	40(66.7%)	131(65.5%)		
Education No (%)					
Basic	76(54.3%)	34(56.7%)	110(55%)	. X2=0.99	0.95 •
Secondary	25(17.9%)	10(16.7%)	35(17.5%)		
University graduate	39(27.9%)	16(26.7%)	55(27.5%)		
Occupation No (%)					0.68
Active remunerated	84(60%)	32(53.3%)	116(58%)		
Active non remunerated	26(18.6%)	13(21.7%)	39(19.5%)		
Inactive	30(21.4%)	15(25%)	45(22.5%)	X2=0.766	
Marital Status					
Married	79(56.4%)	31(51.7%)	110(55%)		
Divorced	33(23.6%)	15(25%)	48(24%)		0.51 •
Widow	28(20%)	14(23%)	42(21%)	X2=0.431	

Active non-remunerated: student & housewife, Inactive: retired & unemployed, Non significant (p> (0.05).

Table (2): Clinical characteristics of studied patients

Groups/ Variables	Group 1 (n=140)	Group 2 (n=60)	Total (n =200)	Test	*P* value
Duration of diabetes (years)					
> 1 year	29(20.7%)	15(25%)	44(22%)		
From 1-5 years	47(33.6%)	28(46.7%)	75(37.5%)	X2 =5.46	0.13 *
From6-10 years	43(30.7%)	12(20%)	55(27.5%)		
<10 years	21(15%)	5(8.3%)	26(13%)		
Body mass index					
Mean	1.429	1.483	1.445		
±SD	0.497	0.504	0.498	t=-0.711	*0.4
Diabetic therapy					
Diet only	14(10%)	7(11.7%)	21(10.5%)	X2=0.454	
Insulin only	18(12.9%)	9(15%)	27(13.5%)		*0.93
Insulin+oral	30(21.4%)	11(18.3%)	41(20.5%)		
Oral only	78(55.7%)	33(55%)	111(55.5%)		
Diet compliance					
Smoking	64(45.7%)	39(65%)	103 (51.5%)	X2=6.254.	0.01**
Never	68(48.6%)	24(40%)	92(46%)		
Formerly	48(34.3%)	24(40%)	72(36%)		
Current	24(17.1%)	12(20%)	36(18%)	X2=1.242	0.55*
Complications:					
Neuropathy	1(57.9%)	25(41.7%)	106(54%)	X2=2.420	**0.04
Nephropathy	83 (59.3%)	27(45%)	110(55%)	X2=3.463	0.09
Retinopathy	43(30.7%)	11(18.3%)		X2=3.266	0.04 **
Maculopathy	11(7.9%)	6(10%)	54(27%)	X2=0.248	0.59*
Diabetic foot	11(7.9%)	5(8.3%)	17(8.5%)	X2=0.013	0.57
Coronary artery disease	21(15%)	6(10%)	16(8%)	X2=0.899	0.49 *
Cerebrovascular accident	13(9.3%)	11(8.3%)	27(13.5%)	X2=3.256	0.09 *
Peripheral arterial	11(7.9%)	6(10%)	24(12%)	X2=0248	059 *
History of psychiatric treatment	6(4.3)	4(6.7	17(8.5%)	X2=0.827	0.35 *
Current psychiatric Treatment	20(14.3%)	12(20%)	10(5%) 32(16%)	1.02	0.4 *

** Significant (p< 0.05) *Non significant (p> 0.05)

Table (3): Hospital Anxiety Depression (HAD) scores between both groups of patients

Groups/ Variables	Group 1 (n=140)	Group 2 (n=60)	t test	*P* value
HAD depressive scores				
Mean	10.45	7.83	5.179	0.000 •
±SD	3.4	2.95		
HAD anxiety scores				
Mean	9.75	7.13	6.545	0.000 •
±SD	2.88	1.7		

Highly significant ($p<0.05$) •

Table (4) :Frequency of current DSMIV depressive and anxiety disorders between both groups of patients

Groups/ Variables	Group 1 (n=140)	Group 2 (n=60)	Total (n=100)	Test	*P* value
Major depressive episode	43(30.7%)	11(18.3%)	54(27%)		
Dysthymic disorder	22(15.7%)	7(11.7%)	29(14.5%)		
Generalized anxiety disorder	15(10.7%)	5(8.3%)	20(10%)		
Panic disorder with or without	14(10%)	4(6.7%)	18(9. %)		
agoraphobia	14(10%)	4(6.7%)	18(9%)		
Social anxiety disorder	8(5.7%)	3 (5%)	11(5.5%)		
Obsessive compulsive disorder	5(3.6)	2(3.3%)	7(3.5)		
Post traumatic stress disorder	19(13.6%)	24(40%)	43(21.5%)	$X^2=17.8$	0.02 •
No specific anxiety or depressive disorders					

• Significant ($p< 0.05$)

Table (5): correlation between HAD anxiety & depressive scores and HbA1c levels

	R	*p*
HAD depressive scores	0.345	0.000 •
HAD anxiety scores	0.422	0.000 •

R: Pearson Correlation co efficient, Correlation is significant at the 0. 01 level (2 tailed)

Table(6): Correlation between diet compliance and HAD scores

	R	*P*
HAD depressive scores	- 0.228	*0.001
HAD anxiety scores	0.74	0.295

R: Pearson Correlation co efficient, *Correlation is significant at o.o1 level (2 tailed).

4.Discussion:

The aim of this work was to explore anxiety and depressive disorders in type 2 non obese diabetic patients and to examine the possible relationship between these disorders and glycemic control. We found high frequency of emotional problems (anxiety &depression in diabetic patients either on self-report measures or on structured psychiatric interview (MINI), where 27% of the total sample reported current major depressive episodes and 14.5% reported dysthymic disorder. These prevalence rates were found to be higher than that reported in general population[21]. Our findings are in accordance with many studies that found association of co morbid depression with diabetes. The presence of co morbid depression was significantly higher in uncontrolled (30%) than controlled studies (21%), in clinical (32%) than community samples (20%), and when assessed by self report questionnaires (31%) than by structured diagnostic interview (11%)[22].As regard the relationship to glycemic control, patients with poor glycemic control scored significantly higher on hospital anxiety depression scale than those with good glycemic control ($p<0.05$), also, major depressive disorder and dysthmic disorder were significantly more frequent in diabetic patients with poor glycemic control than those with good glycemic control after adjustment for Sociodemographic characteristics, duration, treatment and complication of diabetes except for retinopathy simplex and neuropathy that were found to be significantly higher in poor glycemic control ($p<0.05$) and the presence of co morbid illnesses and lastly, significant positive correlation was found between depressive scores of hospital anxiety depression scale (HAD) and HbA1c level indicating the negative impact of depression on glycemic control .Our findings are in agreement with studies that found association between depression and poor glycemic control[22,23,24].A meta analysis[25] reviewed 28 studies and measured associations of

depression in relation to glycemi control . They concluded that depression was associated with hyperglycemia in patients with type 1 and 2 diabetes but revealed neither the mechanism nor the direction of the association. The results of the Meta analysis were rather heterogeneous, as the study designs and methods differed considerably. The author suggested that the relationship might have been stronger in patients with clinical rather than with sub clinical depression. However our findings are not in accordance with those of some other studies. Kruse et al.[26] did not find positive association between depression and A1C in a community sample. In addition they concluded that individuals with diabetes and A1Clevel<7% more often had affective disorders than those with poor glycemic control. In general population, patients with high A1C levels reported slightly but significantly higher levels of well being than patients with low A1C levels[27].One study[28] suggested that personality traits might be important in achieving glycemic control. Lower scores on neuroticism and associated personality features of anxiety, hostility, depression, self-consciousness, and vulnerability were associated with poor glycemic control. Less dysphoric emotions may lower the motivation for maintaining the self care regimen which was suggested as the explanation for the decreased metabolic control[28] in another recently community study in which the authors used only hospital anxiety depression scale in assessing depression, hyperglycemia was not associated with depression in type 1 or type 2 diabetes. They found an inverse relationship between A1C and level of depression in both types of diabetes, although the associations were not significant[29]. Both physiologic and behavioral mechanism has been hypothesized to underlie the relationship between depression and glycemic control in diabetics. Hormonal and neurological hypotheses include changes in the pituitary adrenal cortical system through the effect of cortisol[30] changes from the effect of epinephrine and nor epinephrine on sympathetic –adrenal medullary system[31]; changes due to glucagon secretion and elevated growth hormone level in response to emotional stressors[32]. However, it is likely that behavioral mechanism play the largest role in the relationship between depression and glycemic control. Indeed, adherence to diabetes regimen has been assumed to be the critical contributor to glycemic control. Diabetes require adhering to complex set of treatment regimens including medication administration, monitoring blood glucose values, adherence to specific or general dietary guidelines, routine exercise, as well as routine food inspection and care and attending regular medical exam. These self-care behaviors have been considered to be a significant component of health outcomes[32,33]. However, in our study we found that the poor glycemic group was significantly less compliant in diet regimen than those of good glycemic one, also, there was significant positive correlation between depression and diet compliance. In a study of predominantly type 2 primary care diabetics Ciechanowski et al.,[34] and Bogner et al.,[35] found that depressive symptoms were associated with significantly poorer physical and mental functioning, decreased adherence to dietary recommendations, less adherence to oral hypoglycemic medication. Also Ciechanowski et al.,[36] and others[37,38], found that among patients with type 1 and type 2 diabetes, depressive symptoms were associated poorer physical functioning and fewer adherences to exercise and diet. The importance of improving adherence to treatment of diabetes has been emphasized in the Diabetes control and Complication Trial (DCCT)[39]. Other studies have shown that depression was associated with increased risk of diabetic complications especially retinopathy and macrovascular complications[40,41]. In our study poor glycemic diabetic patients were significantly suffering from neuropathy and retinopathy simplex than those with good glycemic control ($p<0.05$). Hypotheses have advanced that underlying factors may include increased insulin resistance and reduced glucose uptake[42] the direction of the relationship between depression and behavior and glycemic control remains unclear. Depression may be the precipitant of poor glycemic control or the results of failed efforts to improve blood glucose control a cycle of effects may occur where feeling of disappointment about poor glycemic control may affect adherence to one s prescribed regimen[35], in turn worsening glycemic control. Cross sectional studies are not methodologically capable of establishing directional effects.

Longitudinal studies that track the course of disease, psychiatric co morbidity, and glycemic control at multiple points in time are needed to distinguish the trajectory of impacts among these variables.

As regard anxiety disorders, we found that 37% of all patients reported different types of anxiety disorders (generalized anxiety disorder 10%, panic disorder with or without agoraphobia 9%, social anxiety disorder 9%, obsessive compulsive disorder 5.5%, and post traumatic stress disorder 3.5%), a prevalence rate that was found to be higher than reported in general population[21], also, poor glycemic control patients scored significantly higher on anxiety scores of (HAD) scale than those of good glycemic control and significant positive correlation was found between anxiety scores and HbA1C level . our

findings are consistent with many studies that reported co morbid anxiety disorders with type 2 diabetes[13,43]. Anxiety disorders represent an exaggerated emotional response to the fears people have. People with diabetes at higher risk for these disorders because they often live with sources and levels of fear greater than those most people experience Fear of hypoglycemia, complications and the effects of diabetes on day to day life are some of the common fears reported by people who have diabetes[44].Anxiety disorders like depression often are undiagnosed and untreated in patients with diabetes. This may be a result of confusion regarding physical common symptoms of anxiety and hypoglycemia and the misidentification of anxiety disorders as poor adjustment to diabetes[45]. As regard relationship with glycemic control, the psycho physiologic effects of anxiety on glycemia have been studied; the results of this research have been inconsistent with some studies reporting hyperglycemic response to stress, while other found no such response[43].In a met analytic review[14],the author identified 12 studies 11(92%) of which satisfied the criteria for the inclusion in the Meta analysis .In this overall group anxiety was not associated with glycemic control. In studies that determine anxiety from diagnostic interview, anxiety was associated with hyperglycemia. Recently other two studies also found significant association between anxiety depression and glycemic control in type 2 diabetic patients[24,45].

The clinical implication of our findings indicate that though we discovered high prevalence rate of depressive and anxiety disorders, only small percentage was under psychiatric treatment, so the clinician treating diabetic patients showed strive to recognize depression and anxiety among these patients because of the strong possibility that diabetes symptoms, physical functioning, diabetes self care and HbA1c levels may all improve with management of these disorders.

Future longitudinal studies, on larger scale, are required to enable causal associations to be identified that will refine existing or develop new theoretical models. The efficacy of psychological interventions and antidepressants need to be investigated .In addition the impact of such interventions on physical and mental functioning in patients with diabetes warrants examination. CONCLUSIONS: This study adds to the data about the prevalence of depression among patients with type 2 diabetes mellitus. It affects over one third of patients. Co-morbid depression is significantly associated with higher HbA1c. Early diagnosis of depression and intervention in patients with type 2 diabetes mellitus makes metabolic control easier and more likely.

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