Prevalence of symptoms and risk of obstructive sleep apnea in Saudi pregnant women

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Abstract:

BACKGROUND: This case-control study aimed to assess the prevalence of symptoms and risk of obstructive sleep apnea (OSA) among Saudi pregnant women.

METHODS: The study included consecutive Saudi pregnant women attending the antenatal service between July 2015 and December 2016. Pregnant women were compared with an age-matched group of nonpregnant women. OSA symptoms and risk were assessed using a validated Arabic version of the Berlin questionnaire (BQ).

RESULTS: The study included 742 pregnant women and 742 age-matched nonpregnant women. At the time of the survey, 8.2% were in the first trimester; 33.4% in the second trimester; and 58.4% in third trimester. Snoring was reported by 14% of pregnant women, and 5% reported breathing pauses during sleep. Based on the BQ stratification for risk of OSA, 19.3% of pregnant women and 16.6% of the control group were at high risk for OSA. A comparison between the high OSA-risk and low OSA-risk pregnant women revealed that the pregnant women in high risk group were older (30.9 ± 5.9 years vs. 29 ± 5.4 years, P = 0.001), had a higher body mass index (BMI) (34.3 ± 5.2 kg/m² vs 28.7 ± 5.8 kg/m², P < 0.001), and higher parity (1.9 ± 2 vs. 1.5 ± 1.7, P = 0.020). A multivariate logistic regression analysis revealed the following independent variables, BMI (odds ratio [OR] 1.173 [95% confidence interval [CI] 1.129–1.219], P < 0.001), pregnancy-induced hypertension (OR 7.85 [95% CI 1.691–36.447], P = 0.013), and the presence of restless legs syndrome (OR 2.209 [95% CI 1.332–3.279], P < 0.001).

CONCLUSIONS: OSA symptoms and risk were relatively common among Saudi pregnant women. Increasing the awareness among physicians about this association is essential to improve early detection of the disorder.

Keywords: Antenatal care, Berlin questionnaire, gestation, parity, pregnancy-induced hypertension, restless legs syndrome

Several physiological changes occur during pregnancy that may increase the risk of breathing disorders during sleep, mainly, obstructive sleep apnea (OSA).[1] In addition to weight gain that occurs during pregnancy, other physiological changes arise that may increase the risk of developing OSA, such as mucosal hyperemia and edema, narrowing of the oropharyngeal airway, and reduced functional residual capacity, which may predispose to desaturation during periods of apnea.[2] The risk of developing OSA during pregnancy increases in the third trimester. Cross-sectional studies among pregnant women in the third trimester have reported the prevalence of habitual

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snoring to range from 11.9% to 49%. Studies that assessed habitual snoring in all trimesters reported that snoring (three or more nights per week) increases from 7% to 11% in the first trimester to 16%–25% in the third trimester. In a previous study, Pien et al. prospectively assessed symptoms of OSA and daytime somnolence in 155 women using the apnea symptom score and demonstrated that frequency of OSA symptoms, including snoring, breathing pauses, gasping, choking, and daytime sleepiness, increased significantly from the first trimester to the month of delivery.

Several studies have demonstrated that sleep-disordered breathing (SDB) is linked with an increased risk of complications during pregnancy. OSA during pregnancy was associated with significantly increased risk of complications such as preterm birth, low birth weight, occurrence of an assisted vaginal delivery or cesarean delivery and an emergency cesarean, birth of an infant with a 5-min Apgar score <7, stillbirth or perinatal death, gestational diabetes mellitus, pregnancy-induced hypertension (PIH), and preeclampsia. It has been recently suggested that cultural, social, and ethnic factors can alter the risk and severity of OSA. Moreover, differences in genetics, craniofacial structure, upper airway anatomy, and pattern of fat deposition can influence OSA. OSA is common among Saudi nonpregnant women, however, no study has assessed OSA prevalence in Saudi or Arab pregnant women.

Therefore, we conducted this case-control study to assess the prevalence of symptoms and risk of OSA among Saudi pregnant women attending antenatal care clinics. In addition, as the prevalence of restless legs syndrome (RLS) is high in pregnant women, and both obesity and abdominal obesity have been reported to increase the risk of developing RLS and OSA in both women and men, we assessed the association between OSA and RLS in pregnant women in this study. No study has evaluated the association between OSA and RLS during pregnancy.

Methods

This study is a part of a larger project to assess sleep disorders among Saudi pregnant women.

Ethics

The study was approved by the research ethics committee at King Saud University (15/0038/IRB), and the procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000. Study design: This is a cross-sectional, case-control study that was conducted at King Saud University Medical City (KSUMC) in Saudi Arabia, Riyadh, between July 2015 and December 2016. The study included consecutive Saudi pregnant women attending the antenatal service at KSUMC. The prevalence of OSA symptoms and risk among pregnant women were compared with an age-matched group of Saudi nonpregnant women working at the university campus.

Questionnaires were distributed to cases and controls (face-to-face) by coauthors who were trained in data collection. The details of the questionnaire were described to the patients after explaining the procedure of the study and obtaining informed consent.

Sample size calculation

Based on previous large, well-conducted studies that used the Berlin questionnaire (BQ), the prevalence of high risk of OSA in pregnant women was reported to be around 25%–33%. Therefore, a minimum sample size that would allow the detection of a high-risk OSA prevalence of 30% with α of 0.05 and a precision of 5% was chosen. In this manner, the minimum sample size was estimated to be 340.

Data collection

The collected data comprised demographics, parity, gestational age, comorbid conditions, and BQ. The comorbid conditions for cases were obtained from medical records. RLS was diagnosed using the International RLS Study Group questionnaire. PIH is defined as systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg.

Berlin questionnaire

The BQ is a validated questionnaire that explores known symptoms and features of OSA and allows the categorization of subjects into low or high risk for OSA. The questionnaire has been widely used in pregnancy with a sensitivity of 0.93 and specificity of 0.62. A validated Arabic version of the questionnaire was used.

The BQ comprised 11 questions and is divided into three categories: Category 1 incorporates questions about the participants' history of hypertension, as well as height,
and weight were incorporated. Subsequently, the participants were categorized into high risk and low risk according to their responses.

Positive responses to questions in category 1 about snoring and witnessing breathing cessation were defined as frequent symptoms (>3 times/week). In category 2, the presence of frequent symptoms in two or more questions about fatigue, sleepiness, and/or drowsy driving was defined as a positive response. In category 3, the presence of hypertension or obesity (a body mass index [BMI] >30 kg/m²) indicated a positive response.

Those with positive responses in two or three categories were categorized as high risk for OSA, while a positive response in only one section or none were categorized as low risk for OSA.  

The reliability of self-reporting was tested in 30 controls for the following parameters: age, height, weight, comorbidities including hypertension, and the estimate of the BMI for risk grouping. There was a strong agreement between self-reported data and data obtained from the electronic medical records. For all cases, age, height, weight, and BMI were verified from records of the clinic.

Statistics

Numerical data were expressed as the mean ± standard deviation, and categorical data were expressed as n (%). Continuous variables were compared using the independent samples t-test, and categorical variables were compared using the Chi-square test. For comparisons between trimesters, repeated measured analysis of variance was used.

To assess the predictors of high risk for OSA in pregnancy, a univariate logistic regression model was applied in a preliminary analysis where one explanatory variable was tested in the model at a time. Tested variables included demographics, parity, gestational age, medications used, medical comorbidities, and smoking. Variables with significant P values were then entered in a multivariate logistic regression (Forward Wald method) to define the independent predictors of high risk for OSA in pregnancy. Odds ratios were computed with 95% confidence intervals (95% CI).

A value of P ≤ 0.05 was significant. Standard statistical software, SPSS for Windows Inc. Version 22. Chicago, Illinois, USA, was used for data analysis.

Results

The study sample comprised 742 pregnant women and 742 age-matched nonpregnant women. The mean age of pregnant women was 29.4 ± 5.6 years. The distribution of the gestational age of pregnant women was as follows: first trimester 61 (8.2%), second trimester 248 (33.4%), and third trimester 433 (58.4%). None of the 742 pregnant women had previously been diagnosed with sleep disorders or OSA or referred to sleep medicine specialists with a clinical suspicion of OSA.

Table 1 presents a comparison between pregnant women and age-matched nonpregnant women. BMI was higher among pregnant women. In addition, diabetes mellitus was more common in pregnant women than in the control group. Based on the BQ stratification for risk of OSA, 19.3% (n = 143) of pregnant women were considered as high-risk patients for OSA, compared with 16.6% (n = 123) in the control group.

Snoring was reported by 14% of pregnant women and 5% reported breathing pauses during sleep. BMI was >30 kg/m² in 43% of pregnant women. Table 2 presents a comparison between pregnant women with high and low risk for OSA. Pregnant women with high risk for OSA were older (30.9 ± 5.9 years vs. 29 ± 5.4 years, P = 0.001), had a higher BMI (34.3 ± 5.2 kg/m² vs 28.7 ± 5.8 kg/m², P < 0.001), and higher parity (1.9 ± 2 vs. 1.5 ± 1.7, P = 0.020). In addition, the prevalence of PIH, hypothyroidism, and RLS was more common among pregnant women with high-risk for OSA.

Table 3 presents the distribution of responses to the BQ at different trimesters. BMI >30 kg/m² was present in 36.8%, 32.3%, and 50.5% in the first, second and third trimesters, respectively (P < 0.001). Snoring was reported by 17.5%, 9.9%, and 14.8% in the first, second, and third trimesters, respectively. Falling asleep while in the car was reported by 45.6% of pregnant women in the first trimester, compared with 30.6% and 27.1% in the second and third trimesters (P = 0.016). The percentage of high risk for OSA in the first, second, and third trimesters were 19.3%, 16.4%, and 21.2%, respectively (P = 0.3).

Table 1: Comparison between pregnant women (cases) and nonpregnant women (controls)

| Variable Total (n=1484) | Cases (n=742) | Controls (n=742) | P  |
|-------------------------|--------------|------------------|----|
| Age (years)             |              |                  |    |
| <20                     | 29.4±5.6     | 29.2±5.7         | 0.7|
| 20-35                   | 16 (2.1)     | 21 (2.8)         |    |
| >35                     | 605 (81.5)   | 607 (81.8)       |    |
| BMI (kg/m²)             | 121 (16.3)   | 114 (15.4)       |    |
| Diabetes mellitus       | 29.8±6.1     | 26.3±10.2        | <0.001|
| Vitamin D deficiency    | 104 (14)     | 21 (2.8)         | <0.001|
| Anemia (Hb <110 g/L)    | 113 (15.2)   | 444 (59.9)       | <0.001|
| High risk for OSA       | 243 (32.7)   | 186 (25.1)       | <0.001|
| BMI=Body mass index, SD=Standard deviation, OSA=Obstructive sleep apnea, Hb=Haemoglobin | | | |
Table 4 presents the results of the univariate and multivariate binary logistic regression analyses for the predictors of high risk for OSA among pregnant women. The independent predictors of high-risk for OSA were BMI (odds ratio [OR] 1.173 [95% CI 1.129–1.219], \(P < 0.001\)), PIH (OR 7.85 [95% CI 1.691–36.447], \(P = 0.013\)), and the presence of RLS (OR 2.209 [95% CI 1.332–3.279], \(P < 0.001\)).

### Discussion

This is one of the largest case-control studies and the first in Saudis and Arabs in general to assess the symptoms and risk of OSA among pregnant women. The study revealed that OSA symptoms and risk are relatively high in Saudi pregnant women. The prevalence of high risk and symptoms of OSA in the control group was also relatively high and comparable to the prevalence in the US sample of the same age group; 16.6% in the current study compared with 19% in the American study.\[27\]

Previous studies using the BQ to screen for OSA risk and symptoms have reported a variable prevalence of OSA risk in pregnant women [Table 5]. Table 5 presents a summary of the findings of the current study and previous studies in other countries that used the BQ to assess symptoms and risk of OSA.\[16–18,24,25,27–31\] This might be related to maternal age, gestational age, and BMI at the time of the survey. In addition, ethnicity and race cannot be ruled out as possible factors.

Previous studies have shown that older age, higher BMI, black race, and use of tobacco are associated with a higher risk for OSA.\[22,32,33\] The prevalence of high risk for OSA in the current study is comparable with previous studies in other countries that surveyed women at a comparable age and BMI.\[25,28,29\]

In this study, the prevalence of a positive BQ was slightly higher in the third trimester compared with the first and second trimesters, 21.2% versus 19.3% and 16.5%, respectively. Frequency of OSA symptoms, including snoring, breathing cessation, and choking increased significantly from the first trimester to the end of pregnancy.\[4\] Several factors contribute to the increasing prevalence of OSA symptoms in the third trimester, including increased blood volume (blood volume peaks at 40%–50% over baseline by the third trimester) and interstitial fluid, and a probable restoral fluid shift to the upper airway leading to upper airway narrowing.\[34,35\] Furthermore, the progressive elevation of the diaphragm secondary to the enlarging uterus, in the third trimester, results in...
a reduction in the tracheal traction and narrowing of the upper airway.\textsuperscript{[34]}

Obesity and older age are risk factors for OSA in the general population. Similarly, a higher BMI and advanced maternal age have been reported to increase the risk of OSA in pregnant women.\textsuperscript{[3]} In the current study, pregnant women with a higher risk of OSA were older and had a higher BMI. Moreover, BMI was an independent predictor of OSA in pregnant women. However, BMI is one of the criteria used in the BQ; therefore, it is expected to be a predictor. Nevertheless, increased BMI may alert treating physicians to the increased risk of OSA among pregnant women, as it is thought that pregnant women who were obese before pregnancy are at higher risk of developing OSA during pregnancy.\textsuperscript{[33,36,37]} Therefore, special attention is needed during the first visit of obese pregnant women to the antenatal clinics, as they may have a higher risk of OSA.

In addition, PIH was an independent predictor of OSA risk in pregnant women. The existing studies recognize hypertension in pregnant women to have a strong association with OSA.\textsuperscript{[38]} Moreover, studies have demonstrated a strong association between OSA and PIH.\textsuperscript{[39]} Two meta-analyses have confirmed the strong association between OSA and PIH.\textsuperscript{[38,40]}

The current study also detected the presence of RLS as an independent predictor of OSA. Previous studies that assessed OSA in pregnant women did not explore the association with RLS. However, a higher prevalence of RLS in patients with OSA has been reported in the general population.\textsuperscript{[41]} Nevertheless, no direct relationship between the severity of RLS and the severity of the OSA has been reported.\textsuperscript{[41]} The link between OSA and RLS is not known; however, obesity and abdominal obesity have been reported to increase the risk of developing RLS in both women and men.\textsuperscript{[14]}

| Table 3: Distribution of some of the responses in pregnant women in different trimesters |
|-----------------------------------------------|----------------|----------------|----------------|
| Variable                                      | Mean±SD/n (%)  | First trimester | Second trimester | Third trimester |
| Category 1                                    |                | (1-12 weeks)   | (13-27)         | (>27 weeks)     |
| Age (years)                                   | 30.4±5.6       | 28.8±5.2       | 29.6±5.7       | 0.106           |
| Do you snore? (yes)                           | 11 (17.5)      | 25 (10)        | 64 (14.8)      |                 |
| How often do you snore?                       |                |                |                |                 |
| Never or nearly never                          | 51 (84)        | 221 (89)       | 368 (85)       | 0.779           |
| Nearly every day                              | 2 (3.5)        | 6 (2.5)        | 19 (4.4)       |                 |
| 3-4 times a week                              | 2 (3.5)        | 10 (4)         | 18 (4.2)       |                 |
| 1-2 times a week                              | 2 (3.5)        | 5 (2.1)        | 16 (3.7)       |                 |
| 1-2 times a month                             | 3 (5.3)        | 5 (2.1)        | 12 (2.7)       |                 |
| Does your snoring bother other people? (yes)  | 5 (8.7)        | 15 (6)         | 32 (7.4)       |                 |
| How often have your breathing pauses been noticed? |                |                |                |                 |
| Never or nearly never                          | 59 (96.5)      | 240 (96.6)     | 403 (93)       | 0.591           |
| Nearly every day                              | 1 (1.8)        | 2 (0.9)        | 4 (1)          |                 |
| 3-4 times a week                              | 0 (0)          | 2 (0.9)        | 6 (1.4)        |                 |
| 1-2 times a week                              | 1 (1.8)        | 1 (0.4)        | 10 (2.3)       |                 |
| 1-2 times a month                             | 0 (0)          | 3 (1.3)        | 10 (2.3)       |                 |
| Category 2                                    |                |                |                |                 |
| How often do you feel tired or fatigued after sleep? |                |                |                |                 |
| Never or nearly never                          | 18 (30)        | 129 (52)       | 214 (49.5)     | 0.082           |
| Nearly every day                              | 19 (31.6)      | 46 (18.5)      | 94 (21.7)      |                 |
| 3-4 times a week                              | 7 (11.5)       | 25 (10)        | 46 (10.6)      |                 |
| 1-2 times a week                              | 10 (16)        | 36 (14.7)      | 48 (11)        |                 |
| 1-2 times a month                             | 6 (10)         | 11 (4.3)       | 31 (7.2)       |                 |
| Are you tired during wake-time?               |                |                |                |                 |
| Never or nearly never                          | 20 (33)        | 130 (52.5)     | 221 (51)       | 0.126           |
| Nearly every day                              | 16 (28)        | 44 (17.7)      | 85 (19.7)      |                 |
| 3-4 times a week                              | 5 (8.2)        | 28 (11.2)      | 50 (12.3)      |                 |
| 1-2 times a week                              | 14 (22.8)      | 29 (11.7)      | 53 (12.1)      |                 |
| 1-2 times a month                             | 5 (8.7)        | 17 (6.9)       | 20 (5)         |                 |
| Category 3                                    |                |                |                |                 |
| BMI ≥30 kg/m\(^2\)                            | 22 (36.8)      | 80 (32.3)      | 219 (50.5)     | <0.001           |
| Do you have high blood pressure? (yes)        | 2 (3.5)        | 7 (3)          | 13 (3)         | 0.233           |
| High risk for OSA                             | 12 (19.3)      | 41 (16.5)      | 92 (21.2)      | 0.337           |

BMI=Body mass index, SD=Standard deviation, OSA=Obstructive sleep apnea
of > 30 kg/m², the odds ratio for developing RLS was 1.42, even after controlling for potential confounders. Several studies have reported a dysfunction in the dopaminergic pathway in obese subjects. This insufficiency in the dopaminergic pathway in obese people could explain the relationship between RLS and OSA. Future studies are needed to assess the link between RLS and OSA during pregnancy.

Although an association between OSA and worsened maternal and fetal outcomes had been reported, OSA remains under-recognized and undertreated in pregnant women. Felder et al. reviewed a database of approximately 3 million pregnant women in California and reported that only 0.05% of pregnant women were diagnosed with OSA based on ICD-9 codes. Two other recent studies in the US using huge databases reported an OSA prevalence of 0.12% (n = 1,577,632) and 0.087% (n = 305,001). The above findings concur with our results, where none of the pregnant women were referred to sleep medicine service. These findings suggest that OSA is significantly underrecognized and

Table 4: Univariate and multivariate binary logistic regression analyses for predicting restless legs syndrome among pregnant women (n=742)

| Variables in the equation | OR (95% CI) | P     |
|---------------------------|------------|-------|
| Univariate analysis       |            |       |
| Age (years)               | 1.062 (1.028-1.097) | <0.001 |
| BMI (kg/m²)               | 1.165 (1.125-1.206) | <0.001 |
| Parity (multiparty [>3])  | 1.146 (1.038-1.264) | 0.007 |
| Gravida                   | 1.11 (1.024-1.203) | 0.01  |
| Diabetes mellitus         | 2.357 (1.49-3.729) | <0.001 |
| Gestational diabetes      | 2.639 (1.627-4.281) | <0.001 |
| Hypertension              | 3.389 (1.455-7.895) | 0.005 |
| Pregnancy-induced hypertension | 6.609 (2.313-18.886) | <0.001 |
| Hypothyroidism            | 1.888 (1.001-3.562) | 0.048 |
| RLS                       | 2.321 (1.599-3.369) | <0.001 |
| Multivariable analysis    |            |       |
| BMI (kg/m²)               | 1.173 (1.129-1.219) | <0.001 |
| Pregnancy-induced hypertension | 7.851 (1.691-36.447) | 0.013 |
| RLS                       | 2.209 (1.332-3.3279) | <0.001 |

Multicollinearity: No, Overall accuracy: 81.3%, Sensitivity: 24%, Specificity: 95%, area under the curve (ROC): 82%, Hosmer-Lemeshow goodness of fit: P=0.007, Nagelkerke R²: 27.4%.

Table 5: Summary of studies that assessed the risk of obstructive sleep apnea in pregnant women using the Berlin questionnaire

| Author               | Country | Study sample and protocol | Age of the sample at survey (years) | Gestational age at survey (weeks) | BMI at survey | Conclusions |
|----------------------|---------|---------------------------|------------------------------------|----------------------------------|--------------|-------------|
| Fernandez et al.     | Spain   | 367 women at the end of pregnancy No control group | 31±7.0 | Median age 39 | 28±5.5 | High risk for OSA in 40% Higher prepregnancy BMI and higher maternal weight at survey were predictors of OSA risk |
| Ko et al.            | Korea   | 642 pregnant women 59% were in the third trimester No control group | 32.3±3.8 (range 20-45) | 28.9±8.9 | - | - |
| Rice et al.          | Peru    | 1032 pregnant women No control group | 28.6±6.2 (range 18-45) | Between 24 and 28 | - | The prevalence of high risk for OSA was 2.1%, 8.0%, and 25.7% for lean, overweight and obese study participants, respectively |
| Karaduman et al.     | Turkey  | 97 with chronic diseases and 160 healthy No control group | 30.1±5.0 | - | 25.2±3.6 | The risk of OSA was 20.6%-23.3% in the whole group 10%-12.5% in healthy pregnant women 34%-45.4% in pregnant with chronic diseases Hypertension and diabetes were predictors of OSA risk |
| Jaimchariyatam et al.| Thailand| 1345 pregnant women No control group | - | 18.1±3.29 | - | The risk for OSA was 10.1% The risk of OSA was significantly associated with prepregnancy BMI |
| Ismail et al.        | India   | 1000 pregnant women No control group | 28.12±4.07 (range 18-45) | - | 31.5±4.1 | 13.4% women were high risk for OSA |
| Higgins et al.       | USA     | 4074 women presenting for delivery, and a control nonpregnant women (n=490) | 18-45 | - | - | High risk for OSA was 33% versus 20%, in pregnant and nonpregnant women, respectively, P<0.001 |
| Antony et al.        | USA     | 1157 were available for outcomes analysis | 28.8 | 24.71 | 29.76 | 15.5% screened positive on BQ |

Contd...
undertreated in pregnant women. Therefore, focused and targeted education of physicians, who run the antenatal services, about SDB and other sleep disorders in pregnancy will allow early detection, and hence, the provision of early treatment and the prevention of complications.

The current study has strengths and limitations. Strengths include sample size calculation, including a control group, and being the first study to evaluate OSA symptoms and risk in Saudis and Arabs in general. Limitations include the fact that we only assessed subjective symptoms of OSA and did not perform an objective assessment for OSA. Nevertheless, none of the pregnant women was referred by the treating physician to a sleep medicine service to assess OSA objectively. Hence, this study is important to increase the awareness of healthcare providers looking after pregnant women to ask about symptoms of OSA and refer pregnant women if OSA is suspected. In addition, it is not practical to perform sleep study for all pregnant women. However, objective assessment of all high OSA risk pregnant women would be the next step. Moreover, as this is not a longitudinal study, assessment of the impact of OSA risk and symptoms on pregnancy outcomes was not addressed. The next step should be a prospective longitudinal study to assess the effects of OSA and its symptoms on maternal and fetal outcomes. In addition, future studies should collect socioeconomic data to see if the socioeconomic status related to the risk of OSA in pregnant women like what has been shown in the general OSA population.

In summary, this is the first case-control study to report OSA symptoms and risk in Saudi (Arab) women during pregnancy. OSA symptoms and risk are relatively common but under-recognized among Saudi pregnant women. The study revealed that OSA risk during pregnancy was related to BMI, hypertension, and RLS.

Since OSA adversely affect both maternal and fetal outcome, increasing awareness among physicians and the public about the manifestations and symptoms of this disorder is essential.

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**Conflicts of interest**

There are no conflicts of interest.

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