



## DIABETES MELLITUS AND PREGNANCY

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### ABSTRACT

High rates of maternal and perinatal death, birth traumas, and long-term effects on the mother and foetus are all linked to diabetes. This article examines the classification, comparability of diagnostic standards, and treatment strategies used in various nations as well as the causes and mechanisms of pregestational and GSD development. Discussions include preconception patient care, dangers for diabetic pregnant women, and characteristics of the metabolism in pregnant women.

**Keywords:** *diabetes, pregnancy, gestational diabetes mellitus*

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### Introduction

Chronic hyperglycemia is a feature of diabetes mellitus (DM), a set of metabolic illnesses brought on by decreased insulin secretion, reduced glucose tolerance, or both of these causes [1]. The seventh-leading cause of death in the United States, according to Control and Prevention of Diseases, is diabetes. According to the International Diabetes Federation, there are 20 million people who experience hyperglycemia intermittently [3].

The fact that hyperglycemia can cause a variety of complications, including miscarriage morbidity, stillbirth, preeclampsia, complications with new births, a high proportion of caesarean sections, preterm birth, and a higher chance of developing type 2 diabetes in the future, according to M. Agarwal, is widely acknowledged [4]. The history of delivery in Scotland over a 15-year period was examined by S. Mackin et al. 813,921 women were included in the analysis, of whom 3,229 had SD Type 1 and 1,452 had Type 2. Preterm births increased by 5.3% in women with type 1 DM and by 21.8% in women with type 2 DM during the comparable period of time, all of which were statistically significant increases in the number of pregnancies complicated by diabetes (type 1) and type 2 (by 90%), respectively (p 0.0001).

The number of babies dying before or just after birth, and the rate of stillbirth, did not decrease significantly over time in women with diabetes.

These rates were 4-5 times higher compared to women who were not diabetic[5] M Hod and his colleagues. This statement explains that the number of cases of gestational diabetes mellitus (GDM) is increasing globally due to factors like obesity, problems with processing carbohydrates, and type 2 diabetes. This is particularly concerning for women who are able to have children. In addition, the age at which people start experiencing problems with how their body processes carbohydrates goes down. But, on the other hand, the age at which people have their first child goes up. This means that there are more and more women who are at risk of getting gestational hyperglycemia when they are pregnant.[6]

An important thing, as said by D. Mastrogiannis et al. found that the rise in the occurrence of diabetes mellitus has also had a detrimental impact on providing healthcare during pregnancy. To decrease these factors, it is suggested to start using telemedicine services. However, telemedicine does not provide any benefits compared to the usual care for women. [7]. L says According to Guariguata et al. , the number of people with GDM is going up all around the world. The percentage of fluctuation varies between 5.2 and 40.4% in different countries. This big difference is connected to several factors like BMI, ethnicity, social affiliation, and the country's economic progress. It is also influenced by the diagnostic criteria used. [8].

### Classification

The main way to classify diabetes is the one that the World Health Organization started using in 1999. According to this classification, there are four main types of diabetes: type 1 diabetes, type 2 diabetes, gestational diabetes mellitus (GDM), and other specific types of diabetes. According to the American Diabetes Association (2018) [9], SD American is classified in the same way but without being divided into different types. I'm sorry, but you haven't provided any text for me to rewrite in simpler words. Could you please provide the text you would like me to simplify. Pincus and P are two people. Pregnant women with diabetes are divided into 8 groups based on their symptoms, how long they have had diabetes, and the risks it poses for both the mother and the baby. These groups also take into account any complications from diabetes and how they are being treated. This classification is used to compare different groups of belts. However, in clinical practice in Russia, it is not used. [10].

### Etiology

M Agarwal suggests that the cause of GDM is linked to problems with the  $\beta$ -cells in the pancreas during pregnancy or a slow response of the  $\beta$ -cells to changes in blood sugar levels. It can also be caused by strong insulin resistance, which is a result of hormonal activity in placental tissue. [4].

There are certain things that increase the chances of developing GDM (gestational diabetes), as J explained. Plows et al. , are caused by being too heavy or obese, gaining too much weight during pregnancy, eating a diet that is high in unhealthy foods, having certain genetic traits that affect the body's processes, being older during pregnancy, being born with a low or high birth weight, having a family history of gestational diabetes or other diseases like polycystic ovary syndrome. The type of food we eat, like fatty foods, sugary foods, and certain types of meat, can increase the chances of getting GDM. [11].

According to R, Rajput and their team found that if pregnant women don't have enough vitamin D during the second trimester, they are more likely to develop gestational diabetes.. Kautzky-Willer and her team The text is stating that in first-time pregnant women (primigravida), if the fetus is male, there is a 3-4% higher risk of developing gestational diabetes compared to if the fetus is female [12]. In

second-time pregnant women (second-parous), the risk is 7% higher than in pregnant women who are having a female fetus. [13].

AA's work is being simplified. Vasilyeva found that using certain technologies increases the risk of GDM and fetal macrosomia. [14] A study with 8,085 women showed that using hydroxyprogesterone caproate also increases the risk of developing GDM. In women who received progesterone through a vein or in their vagina, there was a small chance of getting gestational diabetes. However, these differences were not big enough to be considered important. Because the confidence interval (RR 0. 82; 95% CI 0. 50–112) was estimated incorrectly. [15].

The chances of pregnant women developing a condition called GDM (gestational diabetes mellitus) are three times higher if they also have high blood pressure. This finding was shown in a study by Popova et al. , where the risk was calculated using a number called odds ratio (OR) which was found to be 3. 04.The researchers also provided a 95% confidence interval (CI) of 1. 5 to 63 to show the range of this risk. Additionally, they compared women with and without high blood pressure and found a significant difference, indicated by a p-value of 0. 005[16]

Thanks to the widespread use of sex genome veneering, we are discovering more and more new types of DM.

So, I recently studied pregnant women in Mosul. I found some mutations in their genes called HNF4A and HNF1A that are related to a condition called DM. [17].

To date, it is known that MODY-diabetes associated with a defect in 13 genes (previously in the classification from 1999, 3 types were distinguished) [18].

### Pathogenesis

Type 1 diabetes happens when different things, like genes, viruses, and problems with the immune system, cause damage to cells in the pancreas. This makes it hard for the pancreas to make enough insulin. Genetic predisposition means that some people are more likely to develop type 1 diabetes because they have certain genes. Type 2 diabetes is caused by external factors such as obesity, age, lack of exercise, and genetic predisposition in women, which leads to problems with insulin and beta-cell function expression stump. [19].

According to the research, in the development of diabetes mellitus types 1 and 2, problems in the hormonal signaling systems of the brain and peripheral tissues play a significant role. Before, focus was given to the signal system that is controlled by insulin, insulin-like growth factor type 1, adipoknom, leptin [21]. Currently, according to Botam A. OShpakov and K. Vare two individuals. Derkach plays a major role in the adenylate cyclase signaling system (ACSS). ACSS includes G-protein-coupled receptors, which act as sensors. [22].

GDM is more similar to type 2 diabetes patients in how they develop.[23]. Plows et al. studied how insulin resistance happens in GDM at a molecular level. They found that there is a problem with the way insulin signals in the body, which causes the glucose transporter GLUT4 to not work properly. GLUT4 is responsible for bringing glucose into the cells to be used as energy. During pregnancy with gestational diabetes, there is a 54% decrease in the amount of insulin-stimulated glucose absorption compared to a normal pregnancy. When there are a lot of insulin receptors, normally they are not affected by low levels of tyrosine or high levels of phosphorylation of serine/threonine in the insulin receptor. However, this can weaken insulin signaling. Furthermore, the expression and/or phosphorylation alters. The things that control insulin levels are substances involved in signal transmission. These substances include IRS-1, PI3K, and GLUT4. Some of these changes in molecules continue even after pregnancy. It is thought that some of the things we mentioned before that increase the chance of getting Gestational Diabetes Mellitus (GDM) affect how insulin works in the body. For example, when there are too many saturated fatty acids in our muscles, it causes more diacylglycerol to build up inside our cells. This activates a protein called protein kinase C (PKC) and stops another protein called tyrosine kinase from working properly. Both of these things make it harder for insulin to do its job. Inflammatory proteins and a hormone called adiponectin also affect this process. [11].

We know that reactions happen in DM when it is under oxidative stress. In a study done by scientists from Iraq in 2017, they found that pregnant women with diabetes and placenta had changes in their blood. These changes included too many harmful substances like radicals and specific proteins, as well as not enough helpful substances like

antioxidants. These problems that happen during pregnancy can cause negative effects on both the mother and the baby. They include abnormal development of the placenta and can result in birth defects in the baby. [24].

### **Diagnostics**

H Berger and his colleagues This statement means that controlling blood sugar levels during pregnancy can help decrease the chances of negative outcomes for both the mother and the baby. However, there isn't a specific blood sugar level at which this risk becomes a concern. In countries with lower and middle income levels like India, China, Nigeria, Pakistan, Indonesia, Bangladesh, Brazil, and Mexico, most women don't get checked for diabetes when they are pregnant. Even though there is a regular check-up, up to 85% of births happen in these countries. Surprisingly, 80% of these births are risky for pregnant women with diabetes and could have been prevented. [6].

In France, Norway, and the UK, they do screening tests that only look for certain risk factors. In Finland, everyone gets screened with a test that checks for blood sugar levels using 50 grams of glucose. In Austria and Hungary, everyone gets screened with a different test called an oral glucose tolerance test (OGTT) using 75 grams of glucose. In the UK, when patients at the coast are at high risk of developing GDM, they are given a glucose tolerance test (GTT) with 75 g of glucose right away when they sign up for it. If the test shows a negative result, they take it again between 24-28 weeks. During the 16-18 weeks of pregnancy, doctors use the World Health Organization's criteria to analyze the results of the Oral Glucose Tolerance Test (OGTT). [26].

Egan et al. found that there are no clinical trials that show any benefits from treating GDM (gestational diabetes) diagnosed before 24 weeks of pregnancy.[27]. In a perspective determines by Huhn et al. conducted a study to find out if early testing can help identify women who are at a low or high risk of developing gestational diabetes mellitus (GDM). This would help save money by not having to screen all pregnant women from 24 weeks onwards. It would also help identify women with GDM so that they can start treatment early and reduce the negative effects of high blood sugar on the baby before birth. [28].

In our country, doctors use a two-step approach to diagnose GDM. The first step is done before 24 weeks and the second step is done between 24 and 28 weeks [29]. Biochemical signs of pregnancy in

the early stage can be affected by diabetes, so it's important to consider this to prevent more incorrect positive test outcomes. So, the research of M. Savvidou and her team A study showed that the amount of PAPP-A hormone during the 11-13 weeks of pregnancy was 25% lower in women with type 2 diabetes and 9% lower in women with type 1 diabetes [30]. Pregnant women who have diabetes are monitored by a team of doctors including an obstetrician-gynecologist, an endocrinologist, a therapist, and possibly other specialists. If you feel unwell and your blood sugar level is above 11 mmol/l, you need to check for ketones in your blood and monitor your urine for glucose, ketones, and protein. The patient checks their blood sugar levels at least 6-7 times. They use a special device to continuously monitor their blood sugar levels for low sugar episodes. A study called the Cochrane Review looked at how hyperglycemia is monitored in clinical studies in Europe, the USA, and Canada. They compared different methods. Investigators determined that there wasn't sufficient evidence to show that one method had a clear advantage over the others. [20].

The main ways to check the health of the baby are ultrasound, dopplerometry, and cardiotocography. All these methods work together. Data is available on changes in the fetus and placenta during high blood sugar levels, and these changes can be fixed in a timely and appropriate manner. When you are doing research, it is best to use high-quality devices that are made for experts. These devices have a special sensor that can detect different frequencies, like 2-6 or 2-8 MHz. In addition to the routine triple screening done between weeks 10-14, 20-24, and 31-34, fetal ultrasound can also be done at different times during pregnancy. Yes, as stated by F. FN patients with GDM, crosomia can be suspected around 22-24 weeks and diagnosed accurately around 27-28 weeks. These patients need more studies to be done using ultrasonography between the second and third scenarios. [32].

Signs of diabetic fetopathy (DF), according to V. I, that are commonly seen. The authors, Krasnopolsky and colleagues, are studying how to detect macrosomia. They are not just looking at the baby's weight, but also considering a percentile assessment called ku. Getting a score on the G. Mtest that is higher than 90% of the other test takers. Dementia; noticeable signs (an extra layer of fat in the neck and abdomen, heart and liver enlargement, enlarged adrenal glands, pancreas glands, and scapula width

in the fetus); signs of poor blood supply to the fetus: excessive amniotic fluid, enlarged placenta, dilated spaces in the placenta, calcification, and difficulty with blood flow; measuring the maturity level of the fetus. [31].

To measure how developed the fetus is, we need to evaluate its functional maturity. Lysenko and his colleagues We want to measure a few things: the size of the cerebellum (part of the brain), the size of a specific part of the femur bone, and the ratio between two parts of the kidneys, depending on how far along a pregnancy is. From the 35th week of pregnancy onwards, the width of the fetal adrenal gland is not affected by the length of time the pregnancy has been going on. Instead, it is influenced by the ratio of thickness changes between the cortex and medulla of the gland. The adrenal ratio should be no more than 0.99 for ripe fruits. This means that there are changes happening in the adrenal gland of a developing baby, where the medulla is becoming more pronounced and the cortex is starting to shrink. A fully grown baby with a healthy brain has a cerebellum that measures 53 mm or greater in size. The dot size hardening of the bottom part of the femur bone in a developing baby can be a sign that the baby is mature inside the womb. [33].

MA is a two-year postgraduate degree that focuses on a specific field of study. Lebedev and Ch. G both did something together. Gagayev (2019) discovered that the average size of the umbilical cord can also be used as a sign of possible macrosomia. The study found that there were noticeable differences in the size of the umbilical cord in pregnant women with diabetes compared to those without diabetes. It also found that there was a connection between the babies' body weight and the size of their umbilical cord based on ultrasound measurements.[34] When a pregnant woman has high blood sugar levels, it puts more strain on the fetus's pancreas, specifically on the part that helps with digestion. This can cause the pancreas to become enlarged. Carried out by S. N Lysenko and his group. The researchers found that in fetuses with mothers who had diabetes, there were 5 times more cases of pancreatic hyperplasia compared to fetuses from mothers with a normal pregnancy. The enlargement of the pancreas in a developing baby, specifically the thickening of the pancreas, can help identify a condition called DF and show how severe it is.

These authors found a strong connection between pancreatic growth in unborn babies and low blood

sugar levels on the first day after birth [35]. Dopplerometry helps check the blood flow in the uterus and placenta which is important for diagnosing and treating pregnant women with high blood sugar levels. Prognosis - the measurement of how bad DF Hall's work is in terms of blood flow in the umbilical artery during the 34-37 week period of pregnancy. Lysenko and other researchers. Fruits can cause fetopathy, where some health issues are seen more often in fetuses compared to the control group. This difference is statistically significant ( $p < 0.05$ ) [36]

Cardiotocography is a way to study and understand how the heart and the uterus of a baby work. The result is checked using the Fisher scale score.

### **Clinic**

Type 1 diabetes is more common in young people. As the disease progresses, it can cause problems in different organs and tissues of the body, including the reproductive system. Researchers EV have found Siberian and others. Researchers found that there is a direct connection between menstrual cycle problems and how long someone has had type 1 diabetes, when they first got the disease, how serious it is, and the amount of insulin they take. 60% of children aged 11 to 17 with type 1 diabetes had problems with their menstrual cycle. These patients have three times higher chance of having short and light periods compared to healthy individuals. Among the girls, 63% had menstrual cycles without ovulation, and only 10% of the patients had no gynecological issues. [37].

One of the causes for women having trouble getting pregnant is chin with SD, according to V. M Guryeva and others. Cheny has problems with how their hypothalamic-pituitary system works. It leads to a decrease in the release of luteinizing hormone when the level of gonadotropin-releasing hormone gets lower. It also affects the basal levels of luteinizing hormone, follicle-stimulating hormone, and thyroid-stimulating hormone. This causes a decrease in the production of thyroxine and problems making prolactin. Furthermore, in diabetes, the insulin-reliant actions in the egg cells are affected because the ovaries receive lesser signals from gonadotropins. However, the way these processes work has not been fully studied. [38].

EV's work is being rewritten in simpler words. Siberian and others. This study shows that self-harm and inflammation of the ovaries contribute to problems with the reproductive organs in girls with type 1 diabetes. These problems can lead to low

hormone levels and difficulties getting pregnant. The levels of antibodies against ovarian tissue are higher in girls with more severe diabetes compared to those with less severe diabetes and girls without diabetes. When studying the periods of girls with severe DM type, it was found that 166. 6% had periods that were not regular, 50% did not release eggs during their periods, and only 33. 33% had regular periods. [39].

Ovarian problems linked to diabetes not only make it harder to get pregnant, but also increase the risk of miscarriage. In a study using mice, Y. Su and his colleagues Insulin can harm the ovaries when embryos are being implanted because it disrupts the normal processes of ovarian autophagy. In the group of mice who got injected with a type of insulin, there was a decrease in certain hormones and proteins that are involved in reproduction and the production of new proteins. More growing eggs were found in the tissue, and there was a decrease in the process of egg maturation. [40].

When a woman is pregnant, certain changes can make her more likely to develop ketosis, especially if she already has LED type 1. Starting in the second trimester of pregnancy, the body becomes less responsive to insulin because of the hormones lactogen, prolactin, and cortisol, which have opposite effects on insulin. Progesterone slows down the movement of the digestive system, which helps in absorbing more carbohydrates and leads to high blood sugar levels. Most of the glucose from the mother enters the fetus and placenta easily because of the difference in concentration.

When the mother's body lacks insulin, it turns fatty acids in the liver into ketones. However, we do not know exactly how maternal diabetic ketoacidosis affects the fetus. The child is getting less oxygen because there is less of a substance called 2,3-diphosphoglycerate being made. [41].

Diabetic ketoacidosis can cause symptoms like a fast heartbeat, low blood pressure, smelling acetone from the mouth, dry skin, and in severe cases, feeling confused and falling into a coma. Provo can develop due to various factors like infections in the urinary system, dehydration, and vomiting. Not following the advice of the endocrinologist for insulin therapy and diet can have a bad impact. Ketoacidosis can cause preterm birth and it is difficult to use  $\beta$ -agonists to prevent it. Glucocorticoids can also help prevent fetal distress syndrome, but these drugs can increase blood sugar levels and lead to hyperglycemia. [41].

When pregnant patients with diabetes develop high blood pressure complications, problems with how the body processes fats and the complement system are involved. "Job ME Yablokov and his colleagues. Compare the overall level. In 102 patients, including some with GDM, there were 27 patients with high cholesterol, 28 with type 1 diabetes, and 18 with type 2 diabetes. The levels of cholesterol in pregnant women with different types of diabetes and high blood pressure did not differ from those without these conditions. However, the levels of urotriacylglyceride, found in veins, were significantly higher in all forms of diabetes and when preeclampsia was present compared to women without these conditions. Women with diabetes mellitus have the highest rate. The highest amount of triacylglycerides was found in people with type 2 diabetes ( $p=0.00001$ ) When pregnant women with diabetes also had high blood pressure, their immune system activity increased, especially in women with type 2 diabetes. [42].

The text is too short to rewrite in simpler words. Kovalev and his team This study found that there is a connection between a gene called AGT and the likelihood of developing high blood pressure disorders in women with gestational diabetes. The risk is about 3 times higher for women with this gene compared to those without it. Having the 704C allele of the AGT gene in your genes (with a combination of 704TC and CC) increases the risk of developing hypertensive disorders alongside gestational diabetes mellitus (GDM) by 3.87 times, compared to not having this allele (OR 3.87; 95% CI=160–935;  $p=0.002$ ) On the other hand, having the 704TT genotype has a protective effect against the development of this condition (OR 0.26; 95% CI 0.62–0.11;  $p=0.002$ ) [43].

Medical treatment for patients with diabetes varies depending on how far along they are in their pregnancy. The amount of insulin they need changes throughout the day: it is low at night and increases more or less in the morning, which is a symptom referred to as "dawn." This is followed by a drop in insulin levels during the day. The first trimester is the time when low blood sugar episodes happen most often. During this time, it is important to closely watch and make necessary changes to insulin treatment. From the second part of pregnancy, the body requires more insulin. After giving birth, it is important to keep a close eye on the use of drugs that lower glucose levels. This is necessary to prevent the development of low blood sugar, especially when

breastfeeding. Women who breastfeed are at risk of low blood sugar levels because carbohydrates are released in their breast milk. Before breastfeeding, it is recommended to consume more food to increase the energy value by 500 kcal. [44].

There are different types of insulin that work at different times, last for different durations, and come from different sources. So, in a study conducted in 2017, researchers looked at 554 women and 554 newborns to see how they differed in different ways. There are different types of insulin. One type is called human insulin, which can be either short-acting or long-acting. Another type is insulin from animals. There is also a type called ultra-short-acting insulin, which is combined with human insulin. Lastly, there is a type called long-acting insulin, which is a mix of insulin detemir and Hagedorn insulin. There were no clear differences found between the different types of insulin and how they are given. [45].

Pregnant women are advised to use certain types of insulin for their diabetes treatment. These include short and medium-acting insulins, as well as ultrashort and prolonged acting insulins. In pregnant women, insulin is given either through multiple injections or through a pump that continuously sends insulin under the skin. The type of insulin treatment is determined by how the amount of sugar in the blood might fluctuate due to illness[1]. This is important because there is a greater chance of experiencing low blood sugar and a harmful condition called ketoacidosis. Using a skin infusion of insulin along with continuous glucose monitoring is the best way to control blood sugar levels without causing low blood sugar or fluctuations in glucose levels. [46].

Pankratova and V. V. Pankratova and V. V. Rimashevsky showed that using pump-linotherapy is beneficial for pregnant women with type 1 diabetes, based on evidence from studying newborns. A total of 117 women were studied. Out of these, 21 women had a condition called SD type 1 with PPII. In children whose mothers are treated with CSII, there is a lower chance of them having neurological, respiratory, and heart problems. They also have less swelling, signs of a genetic disorder, and episodes of low blood sugar compared to children whose mothers have high levels of MIS. [47].

Kazimova and the other authors using a substance called phytotera- pii to decrease damage caused by oxidative stress in diabetes. Specifically, they are

exploring the use of a natural compound called quercetin, which is found in Hibiscus rosa-sinensis flowers. However, if herbal remedies are used to treat diabetes during pregnancy instead of traditional methods, it is necessary to conduct extensive and detailed studies beforehand.[48]. According to E. VShikh and L. Yu are the authors of this text. Using vitamin and mineral supplements early on can help reduce the chances of having a large baby that may have health risks. This is especially true if the mother has factors such as obesity, being over 35 years old, or having had multiple pregnancies. When checking for the risk of crosomia around the 23rd-24th week of pregnancy, it is better to take a combination of vitamins that includes folic acid and zinc to improve the outcome. This combination of vitamins is made considering how its different parts work together [49]. Three controlled trials were conducted with 1,099 overweight people.[49]The results showed that changing from Metformin can help prevent GDM in a small number of cases. [50].

According to A.I. Sazonova et al., chief reason for the prohibition of the use of Metformin during pregnancy in many countries of the world and Russia This is the fact that this drug almost unchanged crosses the placenta that into the blood of the fetus [51]. Based on 45 RCTs involving 20,909 pregnant women, when taking Aspirin in doses of 50-150 mg in a period of 16 weeks and previously there was a significant decrease in the risk for preeclampsia (RR 0.57; 95% CI 0.43–0.75,  $p < 0.001$ , R2 44%;  $p = 0.036$ ), severe preeclampsia these (RR 0.47; 95% CI 0.26–0.83;  $p = 0.009$ ; R2 100%;  $p = 0.008$ ) and fetal malnutrition (RR 0.56; 95% CI 0.44–0.70;  $p < 0.001$ ; R2 100%;  $p = 0.044$ ), with higher lower doses of aspirin were more effective [52]. According to the American Diabetes association, prophylactic use low doses of Aspirin (60-150 mg/day) after the 12th non- dividing pregnancy to birth will reduce morbidity, mortality and drug costs software [9].

### CONCLUSION

In the past ten years, making laboratory and research methods better has helped pregnant women with diabetes have better outcomes. Achieving stable blood sugar levels became easier thanks to the widespread use of artificial versions of insulin and checking blood glucose levels regularly every day. The topic of discussion around the world community is the use of pill-based medicines to treat low blood

sugar. However, this is not allowed in the Russian Federation. Taking vitamin mineral supplements can decrease the number of pregnant women who have big babies (macrosomia) and babies with birth defects.

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