Toxoplasmosis and pregnancy in Mosul city Review

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Abstract

Toxoplasmosis is one of the most common diseases worldwide caused by a single-celled parasite called Toxoplasma gondii, an obligatory intracellular protozoan. Infection with this parasite occurs after eating meat contaminated with the parasite undercooked, or exposure to the parasite through the faces of a cat carrying it, or Passed from mother to child during pregnancy, toxoplasmosis may cause flu-like symptoms for some people, but most people who are infected have no signs or symptoms, while others have swollen lymph nodes, fever, malaise, and sometimes a sore throat or blurred vision. Pain in the eye and in people who suffer from a weak immune system due to AIDS or for people with weak immune systems, the infection can be dangerous, usually reaching the brain. As for pregnant women, the parasite can be transmitted to her foetus through the placenta, and the infection is more severe if the foetus is infected with it in Early pregnancy may cause slow fatal growth,

premature birth, miscarriage, stillbirth, or birth of a child with birth defects and can cause toxoplasmosis Congenital vision problems, convulsions, and intellectual disabilities later in life, but a woman infected before pregnancy does not pass the parasite to her foetus unless her immune system is weakened (for example, by infection with HIV), which leads to reactivation Her infection and transmission of the parasite to her foetus.

Key words: Congenital malformation, Pregnancy, Review, Toxoplasmosis

Introduction

One of the protozoan parasites that is common in the plurality of the world's nations is toxoplasma gondii (Omonijo et al., 2022), Intracellular parasite this parasite causes toxoplasmosis, which is a widespread illness in people and animals, as well as a it is a global opportunistic disease, particularly in immunocompromised persons (Torgerson and Mastroiacovo, 2013), and its prevalence in different regions of the world is between (0.2-100%) (Robinson et al., 2021), Toxoplasmosis is a common disease of humans and their pets that can cause infection in a large number of animals such as mammals and birds (Cong et al., 2014), It is one of the most common foodborne pathogenic parasites (CDC 2016), It is ranked third out of eleven parasitic foodborne diseases (Torgeson et al., 2015), Cats are the primary cause of this disease)Adugna et al.,2021 (and it is a major public health concern because it affects approximately one third of the world's population (Flegr and Kaňková 2020) This disease leads to serious health complications for humans, especially in cases with weakened immune systems and in Newborns in infected women (Flegr and Kaňková 2020), A parasite is an organism that can enter and attack all nucleated body cells multiply inside them and spread to different organs in the host body and its capacity to penetrate imbortant various barriers including the placenta, brain, and eye. (Randall and Hunter, 2011), Infection occurs in intermediate hosts by ingesting the egg with water or fruits and vegetables contaminated with these eggs, and it is also transmitted by eating raw meat that contains tissue bags., with the possibility of transmission through the placenta from

mother to fetus or through blood transfusions or organ transplants, and the definitive host the cat family which is infected by histological cysts (Attias et al., 2020).

Historical Background

Laveran, who noted its existence on the island of Java, found toxoplasma gondii for the first time in 1900, however some accounts claim that its discovery goes back to 1908. The parasite, Toxoplasma gondi, was discovered in 1909 by the two scientists Nicolle and Manceaux in the tissues of African rats named Ctenodactylus gundi in an animal colony at the Institute of Pasteur in Tunisia (Ajioka and Soldati, 2007), In 1908, researcher Splender was able to describe the parasite in a laboratory rabbit in São Paulo, Brazil. The parasite was named by this name based on its crescent shape. The word Toxoplasma is derived from the Greek name, where Toxo = acr, meaning arc, and plasma = form, meaning shape (Dubey. 2008), The first case of Toxoplasmosis in humans was discovered in 1923, when cysts of the parasite were observed in the retina of a child with congenital toxoplasmosis, and the child was suffering from hydrocephalus and microphthalmia (Elbez, 2009), In 1939, the two scientists, Wolf and Cowen, were able to diagnose the parasite in newborns (AL - Rubaia, 2008) and the disease's lesions were observed in the nervous system of a group of affected children (Hermes et al., 2008) , Toxoplasmosis was recognized as one of the major infectious illnesses affecting people after the early 1940s, and its transmission through the placenta in humans and animals was verified (Remington et al., 2006; Dubey, 2008), Regarding therapy, Warren and Sabin discovered that sulfonamides have an impact on the toxoplasma parasite in infected mice in 1942. Coleman and Eyles discovered in 1953 that pyrimethamine works better as a barrier against laboratory-acquired

infections in mice when combined with sulphonamides. Spiramycin was first used to treat toxoplasmosis successfully in 1958. decreases the disease's ability to spread from infected pregnant mothers to their fetuses (Dubey, 2008) , However, many details about the parasite remained vague and under study until 1972, when the life cycle was discovered and the hosts in which the parasite lived was identified. Frankel had made it clear that domestic cats are the final hosts and the main cause of this disease (Daoud, 2007).

Classification of parasites

According to phenotypic characteristics like shape, structure, life cycle, and host specificity, the parasite was classified into the phylum Apicomplexa as a result of the discovery of the apical complex by electron microscopy that the parasite uses to penetrate the host tissue cells (Black and Boothroyd,2000; Omonijo et al.,2022), the following is the modern classification of Toxoplasma gondii (De Craeye, 2012)

Kingdom	Protistia
Phylum	**Protozoa**
Class	**Acnidosporea**
Family	**Sarcocystidae**
Order	**Toxoplasmida**
Genus	***Toxoplasma***
Species	***T.gondii***

Methods of Diagnosis

Because the clinical indications of toxoplasmosis are not evident, one of the most important causes for its spread is late detection. As a result,

early diagnosis is critical, particularly in pregnant women, in order to take early treatment steps to avoid fetal infection (Gagne, 2001). A diagnosis can be made in a variety of ways, including:

1 -Clinical signs: The first thing that causes concerns about the disease's presence in pregnant women is the occurrence of miscarriage. It should be mentioned that the infected baby is frail and may pass away 3–4 days after delivery, as well as having a high fever, breathing problems, dyspnea, abrupt death, and congenital deformities as a result of infection. pneumonia together with lymphadenopathy, skin rash, encephalitis, hydrocephalus, retinitis, and keratitis, Depression, lack of appetite, elevated body temperature, jaundice, shortness of breath, diarrhea, weight loss, muscular hyperesthesia, partial paralysis, uveitis and pancreatitis (Bethânia et al., 2014), pneumonia, and acute respiratory infections are all observed in infected cats. Despite being infected with ocular toxoplasmosis, the cats showed no clinical signs of chorioretinitis, aqueous flare, glaucoma, or retinal detachment (Muhannad et al., 2018).

2-Direct Detection:Direct observation of T. gondii in stained tissue, cerebrospinal fluid (CSF), blood or tissue biopsies, or amniotic fluid stained with Giemsa or Wright stains to reveal active phases (Tachyzoites) in the acute phase of infection can all be used to diagnose toxoplasmosis. 27, the parasite's appearance White blood cells are a confirmation of infection in all of its stages (Al-Kinani et al., 2007), but because of how difficult it is to use, it is one of the few diagnostic techniques (Dupont et al., 2020).

3 -Serological Test: It is the standard and reliable method for diagnosing toxoplasmosis because the most common form of infection is latent (Garnaud et al., 2020) This method is used to establish the presence of certain types of antibodies (Rostami et al., 2020), It is the primary way of diagnosis and involves using serological tests to determine the existence of particular antibodies to T. Different serological tests frequently assess different antibodies, each with a characteristic rise and fall pattern over time following infection to identify whether an individual was infected in the distant past or not. A combination of 12 serological tests is required for those who have recently been infected. After a week of illness, the first antibody that may be discovered is IgM, which is the first and most sensitive diagnostic marker in acute infection and may remain even in chronic infection (Teweldemedhin et al., 2019), In terms of the IgG antibody, it may be found one to two weeks after infection, peaks in the first and second months, and then starts to decline. As a result, it continues to be the primary criteria and the accepted test for persistent infection,There are several serological tests that are used to diagnose and detect humoral antibodies including latex agglutination test (LAT), indirect agglutination test, indirect fluorescent assays (IFA), and enzyme-linked immunosorbent assays (ELISA) which are widely used and are a simple method. sensitive, specific and inexpensive, However, this is not always the case since antibody manufacturing may fail or take too long. The reactivation of latent infection causes the majority of active toxoplasmosis infections, Another serological test is the Sabin-Feldmann stain test, sometimes known as the DT test, which was the first to identify

antibodies against toxoplasmosis infection, among other things. It is currently considered a standard (Rostami et al.,2018), Serotyping for T. gondii is the last serological approach used to diagnose T. gondii. It is a rapid and costly procedure that does not need isolating T. gondii from the sample and there are reliable peptide tests (Xiao et al.,2009; Sousa et al.,2010) Regarding the serological examinations of the expectant woman, the Westernplot method as well as conventional laboratory procedures were utilized to differentiate between maternal antibodies and those carried by the infant during the first six months of life (Carlo et al.,2007; Tridapalli et al.,2008) .

4 -microscopic diagnosis: Examining tissues and body fluids can be done using the microscopic inspection approach (Al-Khanaq and Jasim, 2015). One of the most essential approaches for detecting tissue alterations and pathological lesions associated with the disease is to examine tissue slides (Al-Dulaimi et al., 2018).

5 -Molecular Diagnostics: Real-time polymerase chain reaction (RT-PCR) is a sensitive and promising technique that can produce a positive result when conventional diagnostics are ineffective (Hou et al.,2018) are used to find T. gondii in biological samples. Based on array size and iteration, three types of repetitive DNA sequences can be classified as follows: There are 35 copies of the B1 gene, Repeat element 300 copies 529bp and internal transcription spacer 110 copies (ITS-1) (Bastien et al.,2007) , for the detection of toxoplasmosis Several PCR methods have been developed that employ a wide range of clinical samples such as

amniotic fluid, blood, cerebral fluid, and others (Calderaro et al.,2006) Because there are three human species, conventional PCR and RT-PCR are commonly employed to identify the genotypes of T. gondii strains (Fuentes et al.,2001) Toxoplasma DNA has been detected in human fluids and tissues using polymerase chain reaction (PCR) amplification. Diagnosis of congenital, ocular, and cerebral toxoplasmosis Early identification of intrauterine T. gondii DNA by PCR method is critical to avoiding the necessity for more invasive fetal procedures.

Parasite transmission methods

Toxoplasmosis is one of the most common diseases that affect both humans and animals, and the methods of transmission vary depending on the culture and eating habits of the respective countries. factors) to a variety of factors, including:

1 -Contaminated foods: By consuming raw, undercooked meat that contains oocytes, the parasite is spread (Flegr et al., 2014). Some women contract the disease by eating contaminated meat, and other women misuse kitchen tools and knives when cutting meat, which is a source of sources. infection with the disease (Dias et al., 2005), as well as through contaminated water and soil containing egg sacks that persist for a long time and are resistant to environmental conditions (Mahjoub 2014), and in unheated milk and unpasteurized milk, which are sources of transmission of the disease. Fruits and vegetables are the main sources of egg sac infection for humans (Powell et al. 2001; Maksimov et al., 2010). fruits and vegetables are the important sources of infection with egg sacs

of the parasite, which is a dangerous factor for infection in pregnant women.

2 -Direct contact with cats or their feces: If cats are the final host of the Toxoplasma parasite's life cycle, and sexual reproduction occurs inside their intestines, producing large numbers of oocysts that are shed with their feces, which leads to contamination of hands or foods, direct contact with cats or their feces is the main factor in infection with this parasite. With egg sacks (Lass et al., 2009), Attempts by pregnant women to clean cat houses or feces without taking the necessary precautions are a major contributor to infection and transmission of the disease to the fetus (Ertug et al., 2005).

3 -Transmission of the parasite from the mother to her fetus through the placenta:This infection frequently happens during the acute phase of the disease through the transmission of the rapidly multiplying phase, and it can be passed from the pregnant mother to her fetus through the placenta (Wang, 2013). The integration of fetal growth during these last three months of pregnancy (Gilbert et al. 2003; Bouhamdan et al., 2010).

4 -Other modes of transmission: Toxoplasma gondii is also transmitted through blood transfusion and organ transplantation (Elhence et al., 2010).

Types of Toxoplasmosis

Toxoplasmosis infection can be divided into three types:

1 -Acquired Toxoplasmosis: it is caused by intaking egg sacs found in cat feces clinical symptoms include fever, malaise, sore throat, headache, and muscle pain, defect in the central nervous system (Carme et al., 2009).

2 -Ocular Toxoplasmosis: Ocular toxoplasmosis infection causes eye damage related such as retina becomes inflamed and sometimes vision weakness, but in those with weak immunity, it can result in vision loss because there is no consistent treatment for it (Nicholas et al., 2012).

3 -Congenital toxoplasmosis: Fetal toxoplasmosis is one of the leading causes of birth defects and can cause abortions in women the rate of transmission from an infected mother to the fetus is approximately 45% so 30% from neoborn suffering severe congenital malformations. (Remington et al., 2000; McLeod et al., 2009).

Disease stages

It can be divided into three stages

1 -Acute stage: Meningitis symptoms include fever, swelling in the neck and inguinal area, headache, general weariness, and muscle and joint discomfort. The illness is usually misinterpreted at this stage as a bacterial or viral infection or as influenza symptoms.. (Bout et al., 2002; Carme et al., 2009).

2 -Sub-acute stage If the patient's immunity is low, the acute phase can turn into a subacute phase, with trophozoites continuing to disappear in tissues such as the heart, liver, brain, and eyes, and destroying cells, causing necrotic lesions in various organs, retina and brain. (Remington et al., 2000).

3 -Chronic stage: Tissue cysts are located in the nervous and muscle tissues and may remain alive and active for several years without the appearance of clinical symptoms. If a host's immune system to weaken, the cysts rupture and the slow-reproducing vesicles are released to infect other tissues and form new tissue cysts.

Toxoplasmosis in pregnancy

Pregnant women are especially at risk for infection during the first trimester of pregnancy, Once the parasite has passed through the placenta, the fetus may experience a variety of congenital anomalies, which may result in abortion (Yadav et al., 2014),There are still many mysteries surrounding toxoplasmosis. Seventy percent of people do not have clinical symptoms the fact that the disease's symptoms are mild clinically and resemble influenza As a result, maternal serological tests for IgG antibodies are used to determine the primary infection while IgM is an indicator a poor predictor of acute disease low percentages indicate acute infection while high percentages indicate chronic infection (Remington et al., 2000) Therefore, early testing is important to confirm the mother's primary infection in order to assess the risk of transmission of the parasite to the fetus. Prenatal screening programs in countries with

a high prevalence such as France have cut infection by more than half, according to Olaru et al., (2019) The importance of initiating treatment during pregnancy was assessed by comparing the births of affected women who were treated versus those who were not treated. Children of treated mothers were found to have significantly lower rates of eye abnormalities (38% vs. 62%) and hydrocephalus (67% vs. 92%). Thus, antiparasitic treatment is recommended for confirmed cases where continued use of the drug during pregnancy has resulted in better clinical outcomes. (Al-Sanjary and Hussein,2012; Shaapan et al.,2020; Al-Mallah et al.,2021; Aghwan et al.,2021), Many immune factors are involved in the success and continuation of pregnancy. Disorders in their regulation may lead to recurrent spontaneous abortions, such as abnormal expression of certain white blood cell antigens, imbalance between T1 and T2 helper lymphocytes, and natural killer cell abnormalities in the uterus (Kwak-Kim). et al., 2006) Cytokines, the level of expression of adhesion molecules and some cellular immune markers also play an important role in the success of pregnancy, and imbalance in these factors may lead to miscarriage (Lee et al., 2011) and one of the main factors contributing to the inactivation of the above-mentioned immune factors In pregnant women is toxoplasma infection especially in the first trimester of pregnancy, as studies have shown that cytokines such as tumor necrosis factor-alpha (TNF-), interleukemia-2 (IL-2), IL-12, IL-4, IL-10, and interleukemia-2 (IL-2) plays an important role in infection (turnout and IL-2). (Iqbal and Al-Awadhi, 2016), Important Immune cells such as helper cells I, II, and 17, regulatory T cells, macrophages,

and natural killer cells produce these substances in toxoplasmosis (Fereig and Nishikawa, 2016) and are GATA-3, FOXP3, T-bet, IL-17, CD8, and CD68 and Perforin protein are markers for these cells (Bonfá et al., 2014; Liston and Gray, 2014). These cellular markers are also expressed in the cells of the placenta tissue, (Hampton, 2015; Rico-Torres et al., 2016). This parasite also has the ability to enter different parts of the body and spread infection to a variety of cells, including the placenta (Koloren and Dubey, 2020), A serious human illness called toxoplasmosis results in miscarriages in pregnant women. The seventh pregnancy may be reached by some mothers who have had multiple abortions (Dubey, 2010). In some nations where cats are frequently raised in homes, such as Britain, where it was discovered that 21% of infertile women may carry antibodies to the parasite toxoplasmosis, toxoplasmosis also plays a role in infertility and is one of the known risks in this direction.

Toxoplasmosis and fetus

As well as causing miscarriage and stillbirth, brain calcification, ventricular hypertrophy, preterm delivery, and mortality, as well as blindness, hydrocephalus, and microcephaly, infection can have a severe impact on fetal development. (Mendez and Alvarado-Esquivel, 2011; AL-Ghezy, 2017), The infection can be passed to the fetus through the placenta during the mother's primary infection, or it can be present before pregnancy in rare cases (Bigna et al.,2020; Nori et al.,2021; Nori and Ali,2021) According to some studies, starting treatment as soon as possible reduces the chance of transmission by up to 75% (Peyron et al.,

2017), Although the toxoplasmosis parasite infection is typically asymptomatic in adults, it poses serious health risks to expectant mothers, particularly if the infection spreads to the fetus. Whether in humans or animals, this illness affects fetuses and causes many diseases (Al-Hatami et al., 2018), Such as mental retardation as studies have found toxoplasmosis to be associated with a variety of mental illnesses including autism, bipolar disorder, anxiety, and pregnancy-related depression. (Pedersen et al.,2012; Frye et al.,2016; Akaltun et al.,2018).

Toxoplasmosis has been associated with a variety of clinical symptoms in patients with schizophrenia including aggressiveness and decreased attention span. (Fernandez et al.,2011; Al Awam et al.,2015; Sagud et al.,2018).

Toxoplasmosis in Iraq

The review was based on information gathered and summarized from 60 articles written by Iraqi researchers from north to south. They were gathered from Google Scholar, academic scientific journals in Iraq, and the Iraqi Digital Repository. The goal was to determine the connection between pregnant who were infected for toxoplasmosis, As a result of Machatlie's observation of toxoplasmosis in spleen and lung swabs from stray dogs in Baghdad in 1934, the disease was first recognized in Iraq and diagnosed in 1938 (Al-Sayyidiyah, 2005). Then, in 1976, (Niazi) investigated various samples from various Toxoplasma gondii-infected regions. Rashid (1984), Al-Samani (2000), and Al-Maqdisi (2000) conducted survey and serological studies with different tests on sheep,

goats, and humans in the governorates of Baghdad and Nineveh, and the results revealed a high rate of infection of 48.16%.

eferences	Year	Type of work	Type of Sample	N	Region	Results
Razzak	2005	Research Article	Women	310	Duhok	Toxoplasmosis caused fetus loss
Alsaidi	2009	Research Article	Women	648	Wassit	31% of the women tested positive for IgM antibodies Of the women evaluated by ELISA and PCR, positive findings for IgG antibodies were found to be 4.16% and 25.83% in the ELISA tests, respectively.
Mohammed	2010	Research Article	Women	120	Baghdad	Based on one study, 43.33% of abortive women had anti-Toxoplasma antibodies, 4.16% had IgM antibodies, and 56.55% had no antibodies.
Al-Shimmery	2011	Research Article	Women	125	Diwaniyah	Toxoplasmosis most frequently affects women in the second trimester of pregnancy and is

						accompanied by IgG 43 and IgM 22 antibody positivity.
Hamad	2013	Research Article	Women	300	Erbil	The age range of 47 to 57 years indicated the greatest infection rate as well as the highest rate of infection among housewives The lowest infection rate was among non-pregnant women compared to pregnant women
Al-Barwary	2014	Research Article	Animal	496	Dohuk	It appeared that the infection rate differed according to geographical region; it was 86.7% in Aqrah, 89.5% in Dohuk, 84.3% in Zakho, and 74.3% in Sheikhan.
Ibadi	2015	Cross-sectional survey	Women	68	Al-Qadisiyah	25% of the infections were in the age range (35–39), and that the

						majority of them had a low level of education, 41.2% were from primary school, 76.5% were housewives, and 52.9% of urban dwellers had a limited income.
Abbas	2016	Research Article	Women	96	Babylon	The proportion of IgM, IgG and (IgM and IgG) together was (35.1%, 22.8% and 19.3%) in pregnant women while in aborted women it was 59.0%. The percentage of positive pregnancy tests in adults was (16.6%, 33.3%, 50%) according to age groups.
Aiz	2016	Research Article	Animal	508	Wasit	Serological testing was done with ELISA technology, while molecular tests were done by amplifying the B1

						gene with PCR-RFLP technology.
Khalaf	2017	Research Article	Animal		Tikrit	The mucosal layer comprises connective tissue or loose ligaments and bundles, which contain white blood cells. In the duodenum, goblet cells in the villi's pulp are penetrated by lamina propria, the primary plate of blood cells, and mucous masses of mucous cells lining those white glands..
Ali	2018	Research Article	Women	65	Muthanna	Acute infections were present in 13 of the 65 abortion cases examined in the Muthanna governorate. 52 of those who tested positive for toxo-IgM had ongoing infections. The rate of miscarriages was

						lowest in the first month and greatest in the third and fourth.
Mohammed	2019	Research Article	Women	75	Babylon	which was conducted on 75 sera samples of aborted women with toxoplasmosis, the infection rate was 42.6% using the LAT test, while using the ELISA test it was 18.6% in the age group (21-25), as for IgM and IgG, their percentage was 4% and 22.6%, respectively
Khanamir	2020	Research Article	Animal	7	Duhok	The presence of T. gondii in Giemsa-stained impression smears combined with distinctive histological alterations in various organs is a wonderful core approach for the identification of

						aborted cases in Toxoplasmosis
AL- Dorry	2021	Research Article	Women	180	Diyala	Higher levels of IFN-, TNF-, and IL-10 were found in the serum of infected pregnant aborted women

Table (1): showing the studies conducted in Iraq

References	Year	Type of work	Type of Sample	N.S	Region	Results
AL-Kanani	2007	Research Article	Animal	599	Mosul	Pathological tissue lesions were discovered in the brain, liver, heart muscle, lung, eye, pancreas, and spleen. These included encephalitis, liver necrosis, myocarditis, interstitial pneumonia in the lung, and choroiditis in the eye.
Al-Khshab	2009	Research Article	Women	77	Mosul	the infection led to a decrease in the zinc level and a

						high level of copper
Al-Dabbagh	2011	Research Article	Blood Donors	90	Mosul	The results showed that 3% seropositive and for CMV 10% seropositive
Al-Obaidi	2011	Research Article	Women	45	Mosul	They discovered a rise in the level of the two enzymes GOT and GPT, countered by a decrease in the level of the alkaline phosphatase enzyme ALP
Alshahery	2012	Research Article	Female, Male	79	Mosul	The findings revealed that antibodies using LAT were discovered in 72.2% (71.4% of females and 77.8% of males), while antibodies using 2-ME were detected in 57% (57.1% of females and 55.6% of males).
Al-Dabbagh	2017	Research Article	patients	40	Mosul	The findings revealed that six

						out of forty individuals were 15% positive for IgG, whereas two were positive for IgG. IgM at 5%
Al-Safar	2019	Research Article	Women	120	Mosul	According to the study's findings, nested PCR (36.6%) outperformed ELISA (31.6%), ELFA (26.6%), and Latex (18.3%) in terms of effectiveness in treating acute T. gondii. The results revealed no significant differences across age groups; however, the location of the residence affects the incidence rates.
Al-Marsoomy	2021	Research Article	Women	120	Nineveh	The study discovered a significant proportion of toxoplasmosis infections with a

						62% positive latex test result. Another serological approach was used to retest the results. The outcome was 44 (73.3%) The third test, which displayed the findings using the conventional molecular test PCR, had a percentage of 51.61%.
Al-Hassan	2022	Research Article	soil	50	Mosul	The difference was clear between the wet samples with a rate of (14/48) positive samples, while the number of positive dry samples was (6/52) that confirmed infected 8 of the positive samples were subjected to a molecular examination using the polymerase chain reaction (PCR).

						Furthermore, the results showed the presence of 3 positive samples for B1 gene of the Toxoplasma parasite.

Table (2): showing the studies in Mosul

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