

Research Article

Chlamydia Trachomatis Infection and Ectopic Pregnancy

Infeksi Chlamydia Trachomatis dan Kehamilan Ektopik

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Abstract

Objective: To determine the relationship of Chlamydia trachomatis infection in patient with ruptured ectopic pregnancy through examination of endocervical swabs, tubal tissue using Polymerase chain reaction (PCR) and Enzyme linked immunoabsorb and assay (ELISA) serum IgG antibodies Specific to Chlamydia trachomatis.

Methods: This study was an observational analytic study with a cross sectional study design. In this study, there were 50 participants consisting of 25 ruptured ectopic pregnancy patients and 25 non-ruptured ectopic pregnancy patients who underwent treatment at Dr.Wahidin Sudirohusodo Hospital as well as networking hospitals at the Universitas Hasanuddin in Makassar City.

Results: The results showed that Chlamydia trachomatis infection in patients with ruptured ectopic pregnancies was found to be 84% positive in tubal tissue, 72% with endocervical swabs and 64% with serum examination. There was a significant relationship between chlamydial tracheal infection obtained through examination of tubal tissue, endocervical swab and specific serum IgG in patients with ruptured ectopic pregnancy ($p < 0.001$).

Conclusions: Based on the results of the study, it can be concluded that Chlamydia trachomatis infection can significantly affect the occurrence of ruptured ectopic pregnancy.

Keywords: Chlamydia trachomatis, endocervical swab, ruptured ectopic pregnancy, serum IgG, tubal tissue.

Abstrak

Tujuan: Untuk mengetahui hubungan infeksi Chlamydia trachomatis pada pasien penderita Kehamilan Ektopik Terganggu (KET) melalui swab endoserviks dan jaringan tuba menggunakan pemeriksaan Polymerase Chain Reaction (PCR) dan Enzyme linked immunoabsorb and assay (ELISA).

Metode: Penelitian ini merupakan studi analitik observasional dengan desain studi potong lintang. Pada penelitian ini terdapat 50 orang partisipan yang terdiri atas 25 orang pasien kehamilan ektopik terganggu dan 25 orang pasien non-kehamilan ektopik terganggu yang menjalani pengobatan di RSUP Dr.Wahidin Sudirohusodo serta RS jejaring Universitas Hasanuddin di Kota Makassar.

Hasil: Hasil penelitian menunjukkan bahwa infeksi Chlamydia trachomatis pada pasien dengan kehamilan ektopik terganggu didapatkan sebesar 84% positif di jaringan tuba, 72% dengan swab endoserviks dan 64% dengan pemeriksaan serum. Terdapat hubungan yang signifikan antara infeksi klamidia trakomatis yang didapatkan melalui pemeriksaan jaringan tuba, swab endoserviks maupun serum IgG spesifik pasien kehamilan ektopik terganggu ($p < 0,001$).

Kesimpulan: Berdasarkan hasil penelitian, dapat disimpulkan bahwa infeksi Chlamydia trachomatis secara signifikan dapat mempengaruhi terjadinya kehamilan ektopik terganggu.

Kata kunci: chlamydia trachomatis, jaringan tuba, kehamilan ektopik terganggu, swab endoserviks, serum IgG.

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INTRODUCTION

Infertility in women of reproductive age shows that prevalence is increasing every year and has experienced a shift in the trend of the number of cases from ovarian and uterine factors to tubal factors, which is 30-40% of cases. One factor in tubal disorders is an ectopic pregnancy.¹Ectopic pregnancy is a serious problem faced by women of reproductive age because it can cause infertility, by reducing the chances of subsequent pregnancy and increasing the chances of recurrent ectopic events and even being declared a major cause of maternal death during the first trimester.²

The incidence of Chlamydia Trachoma has increased dramatically in the last 10 years. Chlamydia trachomatis is one of the most common causes of sexually transmitted diseases in the world, and maybe the sexually transmitted disease with the highest prevalence in the United States.³Approximately 4 million cases of Chlamydia trachomatis infection are found every year. Chlamydia trachomatis is an obligate intracellular microorganism that has the same cell wall as gram-negative bacteria.^{4,5}

As with Gonorrhoea infection pathway, Chlamydia trachomatis transmission in the urogenital tract starts from the cervix or urethra upwards, and Chlamydia infection can cause serious "sequelae", especially in women, because the ascending Chlamydia trachomatis infection of the genital tract can cause bacterial colonization in endometrium and fallopian tube mucosa. Clinical symptoms of pelvic inflammatory disease (PID) in women are often asymptomatic. The subclinical form of Chlamydia trachomatis infection in the upper genital tract often arises with a lack of early detection and treatment, and the course of the disease results in acute and chronic infections that can lead to ectopic pregnancy and infertility.⁵⁻⁷

Lately there has been an increase in the incidence of ectopic pregnancies in several European and American countries. Over the past two decades the incidence of ectopic pregnancy has also increased in many developing countries.^{8,9} PID causes 5-8 times the risk of ectopic pregnancy. One of the germs that cause ectopic pregnancy is Chlamydia trachomatis.¹⁰

The number of ectopic pregnancies at Dr. Cipto Mangunkusumo General Hospital in July 2006 - June 2007 was 113 cases. There is no known relationship between Chlamydial tracheal infection and the incidence of ectopic pregnancy in Indonesia. As is well known, the main examination for Chlamydia trachomatis infection is using Polymerase Chain Reaction (PCR), several studies have detected Chlamydia trachomatis infection with PCR with varying results. Found that 7 out of 10 patients detected detecting chlamydial infection, and 67% of patients with ectopic pregnancies were infected with Chlamydia, both using PCR performed on tubal tissue taken surgically.^{8,11}

Based on the background above the authors feel interested to see the relationship between the incidence of disrupted ectopic pregnancy that has been shown to have Chlamydia trachomatis infection in tubal tissue with Chlamydia trachomatis in endocervical swabs and whether there are Specific Antibodies IgG Chlamydia trachomatis from serum samples with PCR and ELISA examination methods.

METHODS

This research is an observational analytic study with a cross sectional survey design. This research was conducted at Dr. Wahidin Sudirohusodo General Hospital and network of FK UNHAS. The research was conducted from September 2017 to March 2018.

The affordable population of this study was all female patients diagnosed with an ectopic pregnancy were disrupted and underwent surgery at Dr. Wahidin Sudirohusodo General Hospital and networking hospitals during the study period and were declared to meet the research inclusion criteria. Samples were taken nonrandom by consecutive sampling technique, with a sample size of 24 people.

The inclusion criteria were patients with an ectopic / ruptured ectopic pregnancy in the fallopian tubes with physical examination and ultrasonography and proved by laparotomy or laparoscopy. Exclusion criteria were patients at durante laparotomy or laparoscopy not a case of ectopic / ruptured ectopic pregnancy in the fallopian tubes.

Data analysis in this study uses the SPSS program and is presented in the form of tables and graphs. It is said that there is a significant relationship if the value of $p < 0.05$.

RESULTS

This study involved 25 patients diagnosed with a ruptured ectopic pregnancy based on history, physical examination, investigation and confirmed intraoperatively through laparotomy or laparoscopy. Sample characteristics were divided according to age, parity, sexual partner, education level, contraceptive history, vaginal discharge, and PID history.

In the most age group at the age of 21-35 years as many as 10 people (40%). On average, the highest number of samples is 1-3 children, 15 people (60%). Sexual partner group, 23 people (92%) only had 1 sexual partner. At the education level the average sample is in the low and middle education, each 10 people (40%). The history of contraceptive use, 15 people (60%) used oral contraception and 10 people (40%) used an IUD. For groups with a history of vaginal discharge, only 3 people (12%) had never experienced vaginal discharge, 22 people (88%) had experienced vaginal discharge. The group with a history of pelvic inflammatory disease on average 19 people (76%) had experienced (Table 1).

Table 1. Characteristics Samples

Variable	Sample		Control		P-value
	Frequency (n=25)	Percent (%)	Frequency (n=25)	Percent (%)	
Married age (y.o)					
>35	8	32	15	60	0.523
21-35	10	40	10	40	
<21	7	28	-	-	
Parity					
0	4	16	-	-	0.380
1-3	15	60	18	72	
>3	6	24	7	28	
Sexual Partner					
1 men	23	92	24	96	0.763
>1 men	2	8	1	4	
Education					
Low	10	40	12	48	0.535
Intermediate	10	40	7	28	
High	5	20	6	24	
Contraception history					
Oral	10	40	12	48	0.072
IUD	15	60	13	52	
History of Leucorrhoea					
No	3	12	5	20	0.538
Yes	22	88	20	80	
PID History					
No	6	24	8	32	0.936
Yes	19	76	17	68	

Based on the results of tubal tissue examination, with a ruptured ectopic pregnancy that in the sample group, there were 21 patients (84%) with positive results of Chlamydia trachomatis infection and 4 people (16%) showed negative results. Whereas, in the control group were obtained, 3 people (12%) positive results and 22 people (88%) were negative for infection with Chlamydia trachomatis. It can be seen that there is a significant relationship between Chlamydia trachomatis infection based on the results of examination of tubal tissue for the incidence of

ruptured ectopic pregnancy in patients with the Fisher exact test and p-value < 0.001 ($p < 0.05$) and odds ratio 38.5 (Table 2).

On the results of endocervical swab examination obtained for the sample group, there were 18 people (72%) with positive results of Chlamydia trachomatis and 7 people (28%) with negative results. While in the control group were 21 people (84%) negative results and 4 people (16%) positively infected with Chlamydia trachomatis. The fisher exact test results obtained

p-value<0.001 with odd ratio 13.5. This matter that there is a significant relationship between Chlamydia trachomatis infection based on

examination of endocervical swab with incidence of ruptured ectopic pregnancy (Table 2).

Table 2. The Results of Tuba Tissue and Endocervical Swab Examination using PCR

Specimen	Sample %	Control %	P-value	Odd Ratio
Tuba tissue				
Positive	21 (84)	3 (12)	<0.001	38.5
Negative	4 (16)	22 (88)		
Total	25 (100)	25(100)		
Endocervical swab				
Positive	18 (72)	4 (16)	<0.001	13.5
Negative	7 (28)	21 (84)		
Total	25 (100)	25 (100)		

Table 3.The relationship of Examination Results from Tuba Tissue and Endocervical Swab Specimens using PCR

Variable		Result endocervical swab specimen using PCR		P-value	Odd Ratio
		Positive	Negative		
Result Tuba tissue using PCR	Positive	17 (99.5)	4 (57.2)	0.022*	12.75
	Negative	1 (0.05)	3 (42.8)		
	Total	18	7		

There is a significant relationship between the results of PCR examination of tuba tissue with PCR results of endocervical swab specimens with p value = 0.022 (p <0.05) and odds ratio 12.75. Of the 21 patients with ectopic pregnancies

disrupted by the results of positive PCR specimens of tubal specimens, 17 people were positive for endocervical swab examination and 4 samples with negative results (Table 3).

Table 4. Relationship between Results of PCR Examination of Tuba Specimens with ELISA Results of Serum Specimens of IgG Specific Antibodies

Variable		Result IgG specific Antibody from serum specimen using ELISA			P-value
		<1	1-1.25	>1.25	
Result Tuba tissue using PCR	Positive	3 (71.5)	14(89)	4	0.218*
	Negative	2 (28.5)	2 (11)	0	
	Total	5	16	4	

Of the 25 ectopic pregnancy patients affected by Chlamydia trachomatis specific IgG antibody examination, 5 people with low IgG specific, 16 people with interdemiate results and 4 high results were found. There was no significant relationship between the results of PCR examination of Tuba specimens and ELISA results of specific IgG antibody Chlamydia trachomatis serum specimens with p value = 0.218 (p > 0.05) (Table 4).

uncertain but the possibility is that women aged 21-31 years are sexually active so the incidence of PID is higher. As reported PID is a major risk of ectopic pregnancy.¹² The risk of ectopic pregnancy increased progressively with age during pregnancy. The hypothesis is that sexually reproductive age involves major changes in tubal function in this case damage to the ciliary structure which indirectly predisposes women to pregnancies outside the womb, so the risk of high ectopic pregnancies is highest in the sample ages 21-35.¹³

DISSCUSSION

In this study, the age of 21-35 years was the age of the sample who had the most ectopic pregnancies. Showed the same results as this study where the most vulnerable ages were those between 25-30 years. The mechanism is

In women with parity one and sexual partners one, they experienced the most ectopic pregnancies in this study. Based on research conducted 23 of the 72 patients studied were the first pregnancies. This is related to changes in

sexual life that can cause PID and tubal damage so that ectopic pregnancies are more common in young women, and lower parity. In the most recent study, the highest incidence of ectopic pregnancy occurred between parity 1-3. The higher the parity rate in this case the age above 35 years correlates with a decrease in sexual activity which will result in the lower incidence of ectopic pregnancy.¹⁴

Based on the level of education, there are as many as 80% of the sample with ectopic pregnancy having a lower secondary education background. Based on research conducted in Nigeria those who had a lower secondary education level were more susceptible to UTI which predisposed them to an increased risk of ectopic pregnancy. Previous research shows that those with low levels of education are more likely to seek alternative and less effective treatments. So they are more likely to have a sequel to chronic UTI that increases the risk of an ectopic pregnancy.¹³

In this study, it was also shown that there were more samples who had a history of vaginal discharge, UTI and using oral contraception. Itchy and smelly vaginal discharge accompanied by PID symptoms and a history of IUD contraceptive use in this study have a relationship with the incidence of disrupted ectopic pregnancy. This is similar to Derrick's study in which the previous PID history was significantly higher in patients with ectopic pregnancies when compared with women with normal pregnancy control.¹⁵

The number of samples using oral contraception and having an ectopic pregnancy were disrupted by 40% while the rest used an IUD. The use of all types of contraception, both hormonal and mechanical, can effectively protect women from unwanted pregnancies. However, all types of contraception can have a failure, one of which is an ectopic pregnancy. One study suggests that contraceptives may not be very effective for ectopic pregnancies compared to intrauterine pregnancies, which can mean that contraceptive failure is more likely to be ectopic. In other words, if the contraception used fails to prevent pregnancy, the risk of an ectopic pregnancy can increase again. In the case of disrupted ectopic pregnancy showed similar results with this study where samples with IUDs

accompanied by PID and itchy and smelly vaginal discharge in endocervical swabs and vaginal swabs had a significant association with PCR. This explains both the sample using both oral contraception and IUD can experience an ectopic pregnancy.^{12,14}

The results of examination of tubal specimens using the PCR method, it is known that there was a significant relationship between Chlamydia trachomatis infection and patients with ruptured ectopic pregnancies based on examination of tubal specimens. Conventional laboratory diagnosis for Chlamydia trachomatis infection is done by detecting the presence of antigens or by cell culture. Now a nucleic acid amplification test (NAATS) method has been developed which is used to diagnose Chlamydia trachomatis infection. The most commonly used NAATS method is PCR and LCR, which is currently the gold standard for detecting Chlamydia trachomatis infection. The PCR method is reported to have sensitivity (100%) and specificity (99.3%) that is good for endocervical samples.¹⁶

The finding of meaningful results in this study is in line with the theory that Chlamydia trachomatis infection is a major cause of fallopian tube damage which predisposes to ectopic pregnancy. Chlamydia trachomatis has a protein on its body surface that resembles MOMP and has a membrane protein that is polymorphic with caspase 9 which prevents detection by antibodies and inhibits the apoptosis process. This is responded by the body in the form of an immune system activation. Activation of immune cells is expected to reduce elementary numbers and inhibit intracellular replication. The process then continues to replicate microorganisms and release extracellular elementary bodies. However, the number of elementary levels does not decrease even though there is an immune system. In this persistent form, Chlamydia trachomatis releases the CHSP60 protein which causes the formation of scar tissue and creates stiffness in cilia which can damage the patency of the fallopian tubes and become a predisposing factor for the occurrence of an ectopic pregnancy.¹²

The study of ruptured ectopic pregnancy in the tube has the same results as this study where it was reported that the incidence of Chlamydia trachomatis infection in the tube was the result of

asenderens infection from Chlamydia trachomatis infection in the cervix which can cause scar tissue to form and predispose occurrence of ectopic pregnancy.^{8,11}

There were 4 samples with ruptured ectopic pregnancies but different results were found in tubal tissue specimens that showed negative results, 2 of which showed Chlamydia trachomatis specific antibody tests and endocervical swabs with negative results. This is possible because the ruptured ectopic pregnancy is not only due to Chlamydia trachomatis infection, but can be caused by other pathogens, E. coli and Nesseria gonorrhoea. The other two samples on the specific antibody examination Chlamydia trachomatis show intermediate results, this is probably due to infections other than in the tube. While there were 3 controls that gave positive results for Chlamydia trachomatis infection in the fallopian tissue, but did not continue to interfere with an ectopic pregnancy. This was confirmed by a serum Chlamydia trachomatis specific IgG antibody examination with a negative result. This indicates that the infection in the tube does not last chronic so it does not manifest to a disrupted ectopic pregnancy.

This study found a significant association between Chlamydia trachomatis infection based on endocervical examination. Research conducted showed that of 103 samples carried out swab, only one sample was positively infected with Chlamydia trachomatis from endocervical swabs and 14 (13.6%) samples of higher vaginal swabs. This can occur because Chlamydia trachomatis is an intracellular obligate bacterium that is highly dependent on other organisms for its life process because it cannot synthesize ATP. This pathogen infects the urethral epithelial cells and column epithelial cells of the cervical fluid. Inflammation of the endocervical gland is the place most often infected by Chlamydia trachomatis germs.¹⁷

Seventy samples were examined for endocervical swab specimens with negative PCR results of Chlamydia trachomatis infection but continued to be disrupted ectopic pregnancy. This can be caused by 4 of the 7 samples showing the results of PCR examination of positive tubal specimens so that a ruptured ectopic pregnancy can occur. The other three samples showed negative results of Chlamydia trachomatis infection in both the

endocervical and tubal tissue, this was confirmed by Chlamydia trachomatis specific IgG antibody examination which showed negative results. This is attributed because the cause of ruptured ectopic pregnancy is not only due to Chlamydia trachomatis infection, but can be caused by other pathogens such as E. coli and Neisseria gonorrhoea. There are 4 controls with positive endocervical swab PCR results but no ruptured ectopic pregnancy. This is attributed to the four controls that Chlamydia trachomatis specific IgG antibody examination showed negative results. Therefore the infection that occurs in the endocervical does not chronically take place, so it does not have an impact on the incidence of ruptured ectopic pregnancy.

The results of a serum Chlamydia trachomatis specific IgG antibody examination using the ELISA method. Based on the results of this study, there was an association between Chlamydia trachomatis infection and the incidence of ruptured ectopic pregnancy. Several studies have examined antibody responses induced by Chlamydia trachomatis infection and in general have found a significant relationship between serum antibodies, Chlamydia trachomatis, and ectopic pregnancy. In addition, research in China found a significant association with the use of IUDs with rupture ectopic pregnancy and its association with Chlamydia trachomatis infection, namely Chlamydia trachomatis-specific IgG antibodies in serum.¹⁴ High titers on examination of Chlamydia trachomatis specific IgG antibody serum are associated with damage to the tube both inflammation, pelvic adhesion, which causes an increased risk of ectopic pregnancy.

On the results of the examination of Chlamydia trachomatis specific IgG antibody serum using the ELISA method, it was found that 5 samples had low or negative results but there was a ruptured ectopic pregnancy. This can be caused by the specificity of Chlamydia trachomatis specific IgG antibodies compared to CHSP-60 antibodies.⁹ Whereas there were 3 intermediate and positive controls, but did not continue to ruptured ectopic pregnancy. All controls with Chlamydia trachomatis-specific serum IgG antibodies in intermediate and positive levels showed negative results on PCR examination in both tubal tissue and endocervical swabs. So the possibility that detection of serum specific IgG

antibody Chlamydia trachomatis control can be sourced outside of the tube, this is not related to the process of disrupted ectopic pregnancy. In a study conducted was shown that there were many limitations in using the Enzyme linked immunoband assay (ELISA), because previous Chlamydia trachomatis infections could produce antibodies that persisted for long periods of time and were indistinguishable from new antibodies produced by Chlamydia infection new trachomatis.¹⁸ So as the results are shown by this study, many samples showed intermediate results on ELISA examination. So the possibility of meaningful relationships obtained is another process that occurs in addition to the tube itself, for example infection with urethral epithelial cells.¹⁹

It was found a significant relationship between the results of PCR examination of Tuba specimens with the results of endocervical swab examination with p-value 0.022 ($p < 0.05$) and odds ratio 12.75. The study revealed a significant association between the incidence of ectopic pregnancy and the Chlamydia trachomatis infection in tubal tissue.²⁰ It was explained that Chlamydia trachomatis infects the cervix most often to the tube and causes adhesion resulting in damage to the tube. So the results in this study are in accordance with the theory. However, the results of this study are different from those who showed that there is not always a correlation between Chlamydia trachomatis asenderens infection in the cervix and the incidence of Chlamydia trachomatis infection in the tube through PCR examination.⁹ The results in Nigeria showed that women with ectopic pregnancies seropositive to Chlamydia trachomatis exposure through the cervical epithelial pathway had an increased prevalence of pelvic adhesion compared to those with serum Chlamydia trachomatis specific IgG antibodies. There are also reports of a significant association between tubal damage due to pelvic adhesion and increased titration of serum Chlamydia trachomatis specific IgG antibodies.¹²

Four negative samples were found for examination of tubal tissue specimens but ectopic pregnancy continued to be disrupted. Confirmed by endocervical swab examination showed results in line with 3 negative results while only 1 positive result. This is possible because of damage to the tube structure caused by other pathogenic infections previously, confirmed also by the

examination of Chlamydia trachomatis specific IgG antibody serum that 2 out of 4 negative endocervical swab samples showed intermediate levels, this is possible Chlamydia trachomatis infection other than cervix. This suggests that the increase in serum specific IgG antibodies to Chlamydia trachomatis can be well-related due to tubal damage and the severity of damage to the tube itself. This is also in accordance with the results of this study where this study showed a prevalence of 84% Chlamydia trachomatis infection in tubal PCR specimens and 72% in endocervical swab specimens which meant a higher prevalence of tubal specimens could be caused by damage to the tube itself but overall both the tube and the endocervical are found to be associated. This study supports the theory of the relationship between Chlamydia trachomatis and ectopic pregnancy and serum Chlamydia trachomatis specific IgG antibodies as a cause of tubal disease and / or ectopic pregnancy.¹²

In this study there was no significant relationship between PCR examination of tubal specimens with ELISA examination of serum Chlamydia trachomatis specific IgG antibodies. Specific Chlamydia trachomatis IgG levels detected which are intermediate or positive can be affected because replication and release of extracellular elementary bodies to invade the structure of tubal tissue is still possible by CHSP60 formation produced by Chlamydia trachomatis. Thus, the determination of Chlamydia trachomatis infection (at IgG levels > 1.25) is not significant when compared with CHSP60 examination.⁹

High titers on examination of Chlamydia trachomatis specific IgG antibody serum are associated with inflammatory tube damage, pelvic adhesion, and increased risk of ectopic pregnancy. Critical antibody sensitivity tests as well as serum titers of Chlamydia trachomatis specific IgG antibodies can decrease over time. This could explain that there was no significant relationship between the results of the examination of Chlamydia trachomatis infection in the tube with the serum examination of IgG-specific Chlamydia trachomatic antibodies.¹⁹

Chlamydia trachomatis infection can be detected by various methods but none of them have a high accuracy diagnosis. So far, based on research Serum Chlamydia trachomatis specific

IgG antibodies are quite reliable even though CHSP-60 shows a 100% specification and a sensitivity of 42.9%.¹⁹ As explained Chlamydia trachomatis experienced replication of the reticulate body interruption causing Chlamydia trachomatis to remain intracellular so that it can cause a destructive immune response. In this persistent form, CHSP60 is released which can cause an inflammatory response. When elementary body numbers are below a certain critical level, activation of the immune system stops and replication of the reticulate body begins to return. So that detection of this protein is more specific for detecting Chlamydia trachomatis infection. Changes in the cycle of elementary body infections by the destruction of new and persistent epithelial cells in the intracellular release of CHSP60 cause formation of scar tissue and damage the patency of the fallopian tube.²¹

Many studies prefer using ELISA to detect Chlamydia trachomatis serum IgG and IgM antibodies specifically. In a study conducted in India, using the ELISA test also found a strong association between Chlamydia trachomatis and the incidence of ectopic pregnancy. ELISA examination is an examination of a specific genus, not specific to species so that women infected with Chlamydia pneumoniae or Chlamydia trachomatis can provide intermediate results.²²

There were 3 specimens of tubal tissue in the sample showing positive PCR results but ELISA examination of serum specific IgG antibody Chlamydia trachomatis showed negative results. This is associated with the ability of Chlamydia trachomatis to adapt the immune system to the chronic phase. In this phase, there is a change in the structure of the Chlamydia trachomatis protein in the form of CSHP-60 protein. There were 2 samples with ELISA results in serum specific IgG antibody Chlamydia trachomatis negative confirmed by tubal PCR examination with the same results. This may be caused by a pathogenic infection other than Chlamydia trachomatis. This situation makes IgG specific IgG antibodies undetectable in serum. This is similar stated that serum Chlamydia trachomatis specific IgG antibodies have lower sensitivity compared to CHSP60 antibodies. In this study, there were also 2 cases of ectopic pregnancy disrupted by the formation of serum Chlamydia trachomatis specific IgG antibodies with intermediate

levels but negative examination results in tubal tissue were found. The formation of Chlamydia trachomatis-specific serum IgG antibodies in these conditions is likely to have Chlamydia trachomatis infection other than the tube, such as urethral and rectal infections. The other two infections show negative PCR results, this may be due to other pathogenic infections.⁹

CONCLUSION

The most ruptured ectopic pregnancy events are 21-35 years old, parity 1-3 children, 1 sexual partner, lower secondary education level, history of IUD contraception, history of vaginal discharge. In this study, it was found that Chlamydia trachomatis infection in the tube plays an important role in the event of a ruptured ectopic pregnancy in the future.

REFERENCES

1. Malik A, Jain S, Hakim S, Shukla I, Rizvi M. Chlamydia trachomatis infection & female infertility. *Ind J Med Res.* 2012; 770-5.
2. WHO. Tubal infertility. Serologic relationship to past Chlamydia and gonococcal infection. WHO Task force on the prevention & management of infertility. *Sexual Trans Diseases.* 1995;22(2):71-7.
3. Gravent MG, Sampson JE. Chlamydia trachomatis. High Risk Pregnancy Management option. London : WB Saunders Co Ltd. 1996:520-21.
4. Aibinder SW, ramin SM. Sexually Trasmitted Diseases & Pelvic Infection Current Obstertric & Gynecologic Diagnosis & Treatment. New York. McGraw-Hill Co. 2003: 727-9.
5. Daily SF. Infeksi Genital Non spesifik. Ilmu Penyakit kulit dan kelamin FKUI. Balai Penerbit FKUI. Jakarta. 2001 : 340-1.
6. Wisnuwardani SD. Penyakit menular Ilmu Kebidanan. Yayasan Bina Pustaka Sarwono Prawirohardjo. Jakarta. 1991: 554-5.
7. Brocklehurst P, Rooney G. Intervention for treating genital chlamydia trachomatis Infection in pregnancy. *Cochrane Database of Systematic Reviews.* 2013;2: 1-31.
8. Barlow R, Cooke ID, Odukoya O, Heatley MK, Jenkins J, Narayansingh G, et al. The prevalence of Klamidia tracomatis in fresh Tissue spesiment from patient with ectopic pregnancy or Tubal factor infertility as determined by PCR and in situ Hybridisation.UK. *J. Med. Microbiol.* 2001;50:902-8.
9. Lan J, Brule, AJC, Hemrica DJ, et al. Klamidia tracomatis and ectopic pregnancy: retrospective analysis of Salfingectomy specimens, Endometrial Biopsies, cervical smears. *J Clin Pathol.* 1995; 48: 815-9.
10. Kinnunen, A. klamidial Heat Shock Protein 60 and cell-mediated immunity in tubal factor infertility. National Public Health Institute. Department of Microbiology. Finland 2002:13-6.

11. Gerard HC, Branigan PJ, Balsara GR, Health C, Minassian SS, Hudson AP. Viability of Chlamydia trachomatis in fallopian tube s of patients with ectopic pregnancy. USA. *Fertil Steril*. 1998;70(5):945-8.
12. Agholor K., Homoadjoba, Okonofua. Association of anti-chlamidia antibodies with ectopic pregnancy in Benin City, Nigeria. *Afr Health Scienc*. 2013;13: 430-41.
13. Kaddam LA., Mohager M.O., Adam A., Taha MA., Detection of Klamidia trakomatisinfection and it's asociation in ectopic pregnancy amog pregnant ladies attending Omderman Maternity Hosopital. In *tj Advance Pharma Chemist*. 2014;3: 388-90.
14. Li C., Zhao WH., Meng CX., Ping H.,et.al. Contraceptive use and the risk of ectopic pregnancy : a multicenter case control study. *PLOS ONE* 2015: 1-17.
15. Mpiima DP, Salongo GW, Lugobe H, Ssemujju A, Mulisya OM, Masinda A, et al. Association between Prior Chlamydia trachomatis Infection and Ectopic Pregnancy at a Tertiary Care Hospital in South Western Uganda. *Obstet Gynecol Int*. 2018:1-5.
16. Afrasiabi S., Monieri R., Samimi M., Korsidi A. The prevalency of endocervical Klamidia trakomatisinfection among young females in Gaza, Iran. *Jundisapoor Microbiol*.2013: 1-4.
17. Anom Suwardhika. Infeksi Klamidia trakomatissebagai salah satu penyebab oklusi tuba fallopi. Universitas Udayana. 2015: 1-32.
18. Ghazi, H. O., Daghestani, M. H., & Mohamed, M. F. Seropositivity of Chlamydia trakomatis among saudi pregnant women in makkah. *J Fam Comm Med*. 2006;13(2): 61-4.
19. Thomas K, Coughlin L., Manninon PT.,Haddad N.G. The value of Klamidia trakomatisantibodi testing as part of routine infertility investigation. *Hum Reprod*. 2000;15(5): 1079-82.
20. Unemo M, Seth-Smith HM, Cutcliffe LT, et al. The Swedish new variant of Chlamydia trachomatis: genome sequence, morphology, cell tropism and phenotypic characterization. *Microbiol*. 2010;156(5):1394-404.
21. Douvier S, Sainte-Barbe C, Oudot C, Habert F, Fritz MT . Chlamydia trakomatis infection: risk factors. *Contracept, Fertil, Sexual*.1996; 24(5):391-8.
22. Witkin SS, Minis E, Athanasiou A, Leizer J, Linhares IM. Chlamydia trakomatis: the Persistent Patogen. *Clin Vaccine Immunol*. 2017;24(10):e00203-17.