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The Relationship between *Mycoplasma hominis* and *Ureaplasma urealyticum* Bacterial Infections and Infertility in Women of Reproductive Age Couples

Lili Fitriati Rahmah[1], Elizabeth Bahar[2], Fika Tri Anggraini[3], Andani Eka Putra[2]

[1]Magister of Midwifery, [2]Department of Microbiology, [3]Department of Physiology,
Faculty of Medicine, Andalas University, Padang, Indonesia

Corresponding Author: Andani Eka Putra

ABSTRACT

Infertility is a failure to raise children after having approximately 12 months of regular marital contact without using contraception. One of the factors that influence infertility is infections including infections of *M. hominis* and *U. urealyticum* bacteria. This study aimed to determine the relation between *M. hominis* and *U. urealyticum* bacterial infections and infertility in women of reproductive age couples.

This research was analytic with case control design of endocervical swab on infertile women of reproductive age couples and 33 fertile women of reproductive age couple. This research was conducted in the Laboratory of Microbiology, Faculty of Medicine, University of Andalas from March 2019 to April 2020. Then, the sample was tested molecularly. *M. hominis* and *U. urealyticum* bacterial infections were examined by using PCR with a length of *M. hominis* product of 509 bp and *U. urealyticum* of 429 bp. Data processing was analyzed statistically by using the chi-square test.

The results showed that in infertile and fertile women of reproductive age couples, *M. hominis* was not found, but *U. urealyticum* was found in infertile and fertile women, but there was no statistical relation with the infertility in women of reproductive age couples, p = 0.091 and OR value = 0.313.

The conclusion of this study is that there is no statistical relation between *M. hominis* and *U. urealyticum* bacterial infections and infertility in women of reproductive age couples

Keywords: Infertile, *M. hominis*, *U. urealyticum*, Women of Reproductive Age Couples

INTRODUCTION

Infertility is defined as a failure to raise children after having approximately 12 months of regular marital contact without using contraception[1]. Infertility is divided into two, namely primary infertility, a husband and wife have never had children previously; and secondary infertile, a husband and wife have had a previous child or wife has been pregnant but abortion, ectopic pregnancy, and intra-uterine fetal death (IUFD) occured[2] .

Globally, in infertility cases according to WHO (2012), there were about 50-80 million couples with infertility. Of (30%) were found in developing countries and only (5-8%) in developed countries (Masoumi et al., 2013). The prevalence of infertility in Asia is (30.8%) Cambodia, (10%) Kazakhtan, (43.7%) Turkmenistan, and (21.3%) Indonesia[1].

Based on the data from the National Population and Family Planning Agency, the prevalence of reproductive age couples who do not have children is (9.2%) out of 11 Districts located in Padang, North Padang District ranks the highest in reproductive age couples who do not have children at (11, 5%), but the total infertility data was not found[3]. Factors causing infertility that occur in women include age with an age range of 20-29 years old

(64.5%) higher than age of 30-39 years old (20%) and age of 40-49 years old (11.8%), whereas over 50 years (3.7%), menstrual disorders (20%), tubal disorders (27.4%), uterine disorders (9.1%), ovarian disorders (3.6%), endometrial disease (5%) and unknown (24.5%) (Roupa et al., 2009; Sa'adah and Purnomo, 2016). In addition, there is (57%) influenced by disorders from women, (17.5%) disorders from men, (4.5%) disorders from men and women and (21%) unknown cause[4] .

Infection of the genitals increases the risk of infertility such as viral, fungal, and bacterial infections. Besides consuming alcohol, Body Mass Index (BMI), and stress also affect someone's fertility (Dechanet et al., 2010; Irene, 2010). Infertility is caused by an infection in the reproductive organs caused by bacteria *Mycoplasma hominis* (*M. hominis*), *Ureaplasma urealyticum* (*U. urealyticum*), *Neisseria gonorrhoeae* dan C*hlamydia trachomatis*[5.6]

M. hominis and *U. urealyticum* bacteria are *Mycoplasma sp* bacterium found in the human genital tract and their growth increases with the onset of sexual activity. *Mycoplasma sp* is a bacterium that does not have cell walls and belongs to gram-positive bacteria. Data on the prevalence of *M. hominis* and *U. urealyticum* bacterial infections in abnormal vaginal secretions in Indonesia is tremendously limited. In particular, in *M. hominis* bacterial infection, its main risk is high-risk sexual behavior which has more than one sexual partner, initiating early sex and not using condoms (Tibaldi et al., 2009). This causes acute urethritis, vaginosis, pelvic inflammatory disease and infertility[7]. *M. hominis* bacterium is on high vaginal hydrogen (pH) potential. Normal low vaginal pH levels turn out to be high because the bacterium produces ammonia. Ammonia is a nutrient for the growth and propagation of pathogenic microbes. Ammonia production by this bacterium causes a fishy odor in the vagina[6] .

The research results reported by Seifoleslami et al (2015); Gupta et al (2009); Du and Zhang, (2010) showed that cases of *M. hominis* bacterial infections in infertile women in Iran were (3.14%), India (6%) and China (45%). Furthermore, the results of a study conducted by Michou et al (2013) reported that *M. hominis* bacterium was found in menstrual tissue (13.7%) and cervical mucus (19.5%). While the results of the study reported by Sleha et al (2019) cases of *M. hominis* bacterial infection were accompanied by *U. urealyticum* bacterial infection (5.4%)[8]. *M. hominis* bacterial infection is associated with various other urogenital infections such as bacterial vaginosis (BV) and non-specific genital infections (IGNS). Cases of *M. hominis* bacterial infection in women with BV in Portugal were (30%) and (20%) without BV, Poland were (9.1%) and (59.1%) whereas in Papua New Guinea were (7%) and (20%) (Zdrodowska-Stefanow et al., 2006; Dominingues et al., 2003; Clegg et al., 1997). In Indonesia, cases of *M. hominis* bacterial infection of 20-30% are the cause of non-gonorrhea urethritis[9]. The negative impact of *M. hominis* bacterial infection on the female reproductive tract which was firstly identified by Mardh in 1976 in Baczynska et al (2007) with organ culture in vitro revealed swelling in the epithelial cells of the tubal cilia. This resulted in ovum cells unable to reach the fallopian tubes and meet sperm[10]

The mechanism of *U. urealyticum* bacterium in infecting needs urea as the energy source. The virulence of *U. urealyticum* bacterium is mediated by IgA protease, adhesin, urease, phospholipase and hemolysin. In vitro, *U. urealyticum* bacterium is able to form biofilms. Biofilms can adhere strongly and resist friction repeatedly and can increase bacterial immunity so that the body's immune system is unable to reach the bacteria. The existence of this biofilm causes chronic infection because in addition to being difficult to be eliminated by the body, biofilm is also difficult to be penetrated by anitimicrobial[11].

U. urealyticum bacterium infects during sexual intercourse and moves towards the upper reproductive tract. This bacterium can be carried along with sperm into the uterus and fallopian tubes and then attach to the fallopian tube epithelium, causing swelling of the cilia and detachment of the cilia from the epithelium. This bacterium can avoid the flow of blood by attaching themselves to the surface of the tissue[12]

U. urealyticum bacterial infection is 25% as a cause of Non Gonococcal Uretritis (UNG) and often coincides with Chlamydia trachomatis infection. Infection by *U. urealyticum* bacterium causes symptoms in the form of flour albus (43.3%), burning and itching (18.9%), dysuria (10.8%) and no symptoms (8.1%) (Zdrodowska-Stefanow et al., 2006). Other studies also report that *U. urealyticum* bacterial infections are in infertile (42.5%) and fertile women (17.4%)[13].

Infection caused by the two bacteria has bad impact on the female reproductive tract and it needs immediate prevention and treatment; therefore, the researchers have conducted a study by examining *M. hominis* and *U. urealyticum* bacteria on a molecular basis that aims to determine the possible causes of infertility in reproductive age couples.

LITERATURE REVIEW

Infertility is defined as failure to raise children after having approximately 1 year of regular marital contact without using contraception1. A healthy husband and wife's reproductive system will be able to have children. According to Manuaba (2012), the husband will produce healthy spermatozoa and the wife produces eggs so that spermatozoa and egg cells meet and fertilize[14].

According to WHO, in Hestiantoro in Anwar et al (2011), the classification of infertility namely primary infertility in which a woman of reproductive agehas never been pregnant even though sexual intercourse is performed regularly without contraceptive protection in less than 12 months[15]. Secondary infertility is a woman who has previously been pregnant but abortion or ectopic pregnancy occurs and cannot get pregnant anymore despite having tried for 1 year or more having sexual intercourse regularly without contraceptive protection[16].

Etiology of Infertility

Causes of infertility in women can be classified into three groups, namely: ovulation disorders, hormonal disorders, blockages, local factors[17]. Risk factors for infertility in women include ovulation disorders, polycystic ovary syndrome, tubal problems, uterine problems, cervical factors, vaginal problems, reproductive organ infections, sexually transmitted diseases (STDs), hormones, unexplained infertility, and factors risk of infertility due to lifestyle[18]. For infertile factors in men, infertility can also be caused by male, so that examinations in men are important as the part of an infertile examination. Male fertility can decrease due to congenital or acquired urogenital abnormalities, urogenital tract infections, increased scrotal temperatures (for example due to varicoceles), endocrine abnormalities, genetic disorders and immunological factors. In the UK, 20% of the main causes of infertility are low sperm count or poor sperm quality. Impaired semen quality, azoospermia and incorrect intercourse are the factors that contribute to 50% of infertile couples (RCOG, 2003). Idiopathic male infertility can be explained by several factors, including endocrine disruption caused by environmental pollution, free radicals, or genetic disorders.[19]

The handling of infertility is based on two things, namely overcoming the causes of etiology and increasing the chances of pregnancy, ovulation disorders, sperm factors, Endomentriosis, Tubal factors, Fertilization in vitro (FIV)[4]. Mycoplasma bacterium is in the class of Mollicutes. There are 7 types of *Mycoplasma* that have been isolated from

human genitalia, namely *Mycoplasma hominis, Mycoplasma genitalium, Ureaplasma urealyticum, Mycoplasma fermentans, Mycoplasma penetrans, Mycoplasma primatum* dan *Mycoplasma spermatophilum. Mycoplasma* is commonly on organs or tissues specifically. *Mycoplasma sp* is a bacterium that does not have cell walls and is gram-positive[20]

M. hominis and *U. urealyticum* bacteria are bacteria that can be found in the women urogenital tract in the presence of drastically increased sexual activity[21]. Both of these bacteria can be found in sexually active women[22]. Infection can occur when colonization is more than 104 CFU/ml[23]. *M. hominis* and *U. urealyticum* bacteria are found more frequently in women with BV than women without BV[24].

In a study conducted in Guinea-Bissau, Portugal[22], it found the prevalence of *M. hominis* bacterial infection in women with BV who had high-risk sexual behavior was of 30% and *U. urealyticum* was of (20%). The prevalence of *U. urealyticum* bacterial infections in high-risk women without BV in Poland was (59.1%) and *M. hominis* was of (9.1%). In developing countries like Papua New Guinea, the prevalence of *M. hominis* bacterial infections in high-risk women was (7%), *U. urealyticum* was (20%) and mixed infection was (65%)[23]. *Mycoplasma sp* bacteria are distinguished from other types of bacteria because of their smallest size (0.2-0.3 μm), the absence of cell walls and cell membranes containing sterols. In its growth, *Mycoplasma sp* needs cholesterol taken from epithelial cells. The absence of cell walls makes *Mycoplasma sp* resistant to antimicrobials that work by interfering with the synthesis of bacterial walls, such as penicillin, cephalosporins and vancomycin[25]. *Mycoplasma sp.* bacteria have the ability to adhere to mucosal epithelium. This plays an important role for colonization and causes disease. This attachment ability is due to the presence of variable adherence-associated (Vaa) antigens, specific attachment proteins present on the surface of M. hominis bacterium. The nature of the diversity of antigens is important for adaptation and attachment to the host. Meanwhile, the antigen in the *U. urealyticum* bacterium is called the Multiple-Banded (MB) antigen. *U. urealyticum* bacterium can be attached to erythrocytes, sperm and urethral epithelium[26].

U. urealyticum bacterial infections can be found in non-specific genital infections (IGNS) and bacterial vaginosis (BV)[11]. Although *U. urealyticum* is also found more in patients with BV, there is no statistically significant difference in the prevalence of patients without BV. So far, there are still opinion differences about the role of the *U. urealyticum* bacterium in BV[27]. Infection by the *U. urealyticum* bacterium causes symptoms in the form of flour albus (43.3%), burning and itching (18.9%), and dysuria (10.8%). In 8.1% of women, no symptoms were found[23]. In addition, in women, *U. urealyticum* bacterium can cause pelvic inflammation, infertility, endometritis, chorioamnionitis, premature birth, fetal death, and so forth[23].

MATERIALS & METHODS

This is an observational analytic study with a case control research design that aims to find the relation of risk factors affecting the occurrence of a disease. This research has been carried out at the Laboratory of Microbiology, Faculty of Medicine, University Andalas, from March 2019 to April 2020. Endocervial Swab was done on Infertile and Fertile Women in Reproductive Age Couples who went to the Laboratory of Microbiology, Faculty of Medicine, University of Andalas. The sample in this study was divided into two groups: Case and Control. The technique used in taking research samples was consecutive sampling. This Univariate analysis was carried out to see the proportion of *M. hominis* and *U. urealyticum* bacterial infections. Bivariate analysis was performed by using the Chi-Square test and then was continued by using

the Odds Ratio (OR) value with a confidence level of 95% (p = 0.05). Thus, if the results showed a p value <0.05, the two variables are related. If p value is > 0.05, the two variables are not related.

RESULTS

Table 1 Characteristics of Research Subjects of Reproducive Age Couples

Respondent's Characteristics		Infertile		Fertile	
		f	%	f	%
Age	20-30 Years Old	14	42,4	20	60,6
	31-40 Years Old	19	57,6	13	39,4
	Total	33	100	33	100
Education	Elementary/Junior School	7	21,2	5	15,2
	Senior High School	13	39,4	11	33,3
	Tertiary Education	13	39,4	17	51,5
	Total	33	100	33	100
Occupation	Unemployment	14	42,4	17	51,5
	Employment	19	57,6	16	48,5
	Total	33	100	33	100
Length of Marriage	≤ 5 Years	18	54,5	10	30,3
	6-10 Years	11	33,3	14	42,4
	≥ 11 Years	4	12,1	9	27,3
	Total	33	100	33	100

Based on the research results (table 1), it was found that the age of 31-40 years old was 57.6% in infertile and 20-30 years old was mostly 60.6% in fertile. From the education level, it obtained that tertiary education (PT) was both 39.4% in infertile and 51.5% in fertile. Furthermore, there were 57.6% of employed women in infertile and 51.5% of unemployed in fertile. Then, the longest marital status was in <5 years which was of 54.5% in infertile and 6-10 years which was of 42.4% in fertile.

Table 2 Proportion of *M. hominis* Bacterial Infection with Infertile and Fertile Events in Women of Reproductive Age Couples

M. hominis bacterial infection	Infertility in women of reproductive age couples			
	Infertile		Fertile	
	f	%	f	%
Positive	0	0	0	0
Negative	33	100	33	100
Total	33	100	33	100

The isolation of *M. hominis* and *U. urealyticum* bacteria from endocervical swabs with molecular scrutiny obtained the following results: Based on the research results (table 2), *M. hominis* bacterial infection (0%) both infertile and fertile women was not found.

Table 3 Proportion of *U. urealyticum* Bacterial Infection with Infertile and Fertile Events in Women of Reproductive Age Couples

U. urealyticum bacterial infection	Infertility in women of reproductive age couples			
	Infertile		Fertile	
	f	%	f	%
Positive	21	63,6	28	84,8
Negative	12	36,4	5	15,2
Total	33	100	33	100

Based on the research results (table 3), *U. urealyticum* bacterium in infertile was found of 63.6% and fertile was of 84.8%.

Table 4 Relation between *U. urealyticum* Bacterial Infection and Infertile and Fertile Events in Women of Reproductive Age Couples

U. urealyticum bacterial infection	Infertility in women of reproductive age couples				OR (95%CI)		p *Value*
	Infertile		Fertile				
	f	%	f	%			
Positive	21	63,6	28	84,8		0,313 (0,095-1,024)	0,091
Negative	12	36,4	5	15,2			
Total	33	100	33	100			

The research subjects obtained the relations between *U. Urealyticum* bacterium in infertile and fertile namely: Based on the research results (table 4), statistical test results obtained p value > 0.05, namely p = 0.091, then statistically, there was no significant relation between *U. urealyticum* bacterial infection and infertility in women of reproductive age couples and it obtained values (OR= 0,313; CI 95%= 0,095-1,024).

DISCUSSION

Characteristics of Research Subjects

Age

Based on the research results, it was found that the age of 31-40 years old was more infertile, namely 19 (57.6%) and 20-30 years old of 20 fertile (60.6%). The results of this study obtained an average age of infertile and fertile namely 30-35 years old. Age affects the fertility of a woman where the fertile age range is 15-49 years old but the peak of fertility is at the age of 20-30 years old. At this age, the woman is in the reproductive period that still experiences regular menstruation where the possibility of getting pregnant is higher than the increased age. Then, the ability of the ovaries to produce ova has decreased. The results of this study indicate that there are women in 31-40 years old experiencing infertility; this is in line with the results of the study conducted by Shetty et al (2013), from 50 infertile women (18%), among of them were < 25 years old, (70%) aged 26-35 years old, and (12%) above 35 years old. Meanwhile, the results of the study done by Muslimin et al (2016), it obtained age <35 years old of (48%) and age > 35 years old of (51.4%). There is a relation between age and infertility in women of reproductive age. According to Marettih (2012), an increase in age will decrease the number of ovum in the ovary so that the ovary is unable to stimulate the estrogen and progesterone hormones which affect the menstrual cycle[28].

Education

Based on the research results on the education level of women, it obtained that the women with high education in infertility were 13 respondents (39.4%), and in fertility were 17 respondents (51.5%). There is a relation between education level and infertility because education can influence the process of forming attitudes. In this case, it is explained that education influences a person's attitude in dealing with a problem in her life including her reproductive health problems. A woman who is highly educated is certainly easy to accept information relating to maintaining reproductive health so that this change in attitude makes respondents more concerned with reproductive health and avoid various diseases in the female reproductive organs[29].

Occupation

Based on the research results, more than half of infertile women were employed, namely 19 respondents (57.6%); meanwhile, fertile women who were unemployed were only 17 respondents (51.5%). There is a relation between occupation and infertility which can be seen from fatigue and stress caused by the impact of work. Stress experienced by women and stress is related to hormonal balance. This statement is in accordance with the theory put forward by Mark Saver on Psychomatic Medicine which explained that women who have high stress levels are less likely to get pregnant compared to women who are not stressed. The cause is an imbalance of hormones including hormones related to the reproductive system that can affect the process of ovulation[30]

Several studies have shown that one's occupation plays an important role in infertility. It was found that (54.4%) infertile women are women who work full time, (33.3%) women who work part time and (3.5%) are women as housewives (Hammerli et al., 2010). The results of research by Oktarina et al (2014) showed that of 62 infertile women, it found 41 people (66.1%) career women and 21 people (33.9%) housewives. The same

research results also prove that working women exposed to infertile risk are of 3.91 times greater than women as housewives and it is statistically significant (OR = 3.91; p = 0.043)[31]

Length of Marriage

Based on the research results, more than half of infertile women who have got married for <5 years are (54.5%) and fertile women who have got married for 6-10 years are (42.4%).

For reproductive age couples who get married within the first year of marriage, 84% of women will easily get pregnant if they have regular marital relations without using contraception. The pregnancy rate will increase to 92% when the marriage age is two years. The longer the marriage is, the more increasing the chances of women of reproductive age couples to get pregnant[32].

The results of this study are supported by the research by Shetty et al (2013), showing that 64% of women experience infertility for 1-5 years, 32% for 6-10 years and 4% xperience infertility for 11-15 years. The longer the duration of infertility experienced by a woman, the more increasing the chance of getting pregnant. Couples of less than three years of marriage experiencing infertility have a greater chance of getting pregnant[33].

Relation between *M. hominis* Bacterial Infection and Infertility in Women of Reproductive Age Couples

Based on the research results on the relation between *M. hominis* bacterial infection and infertility, it showed that infertile women did not have *M. hominis* bacterial infection as well as in fertile women. It cannot be concluded because the chi-square test cannot be performed because the result obtained is (0%) meaning that the result of this study was not statistically significant.

M. hominis bacterium is an opportunistic pathogenic bacterium in human. The growth of this bacterium increases dramatically with the beginning of sexual activity, having more than one sexual partner and having sexual relations at an early age[34]. There are still doubts about the ability of *M. hominis* to cause a sexually transmitted infection (STI) singly. A single infection by *M. hominis* often does not cause any symptoms in infertile women and many are undiagnosed and untreated[34].

The absence of *M. hominis* bacterial infection in infertile and fertile women in this study can be caused by *M. hominis* is more often found as a co-bacterial pathogenesis in various other infectious diseases such as bacterial vaginosis, trichomonas vaginalis, Gardnerella vaginalis, Chlamydia trachomatis and Neisseria gonorrhoeae. This is due to the replacement of *lactobacillus sp* as a producer of hydrogen peroxidase (H2O2) in the vagina and is replaced by pathogenic bacteria. The replacement causes a decrease in H2O2 concentration which is generally characterized by the production of a lot of vaginal secretions, is gray to yellow, thin, homogeneous, fishy and there is an increase in pH. Damage caused by these pathogenic bacteria causes pelvic inflammatory disease, cervicitis and infertility[34]

However, women of reproductive age have a strong main body defense namely the vaginal mucosal epithelium. In the vagina of a healthy woman, there is glycogen which has purpose to supply vaginal ecosystem nutrients. Vaginal epithelial cells break down glycogen into monosaccharides which are then converted by Lactobacillus bacteria into lactic acid. In the internal female reproductive tract, there are three different surfaces for protection against infection, namely the cervix, uterine wall or endometrium, and fallopian tubes[35].

Mucosal epithelium in the reproductive organs is a component of the mucosal immune system that is connected from cells and tissues and functions as a complex immune defense mechanism on the mucosal surface. Mediators in systemic immunity also penetrate into the

reproductive tissue and secretions to protect the local immune response of the mucosa[35].

There are a large number of immune and lymphatic system cells in the female reproductive system that are able to eliminate *M. hominis* bacterium that enters the vagina because this bacterium grows and develops slowly within 1-4 days so that its growth can be inhibited by specific immunity namely B lymphocytes and T lymphocytes. B lymphocytes produce antibodies that function as a defense against extracellular infections, viruses and bacteria and neutralize the toxin; while T lymphocytes consist of helper T cells (Th) and cytotoxic T (Tc) cells. These helper (Th) T cells will release IFN cytokines γ which will activate macrophages and kill the M. hominis bacteria and stimulate the growth and development of B lymphocytes; while T cells (Tc) play a role in lysis of epithelial cells infected by M. hominis bacterium[36].

Likewise, cervix has squamous epithelium which is continuously replaced by cells in the basal layer and secretes mucus that contains various antimicrobials that protect against *M. hominis* infections which are known that the bacterium is considered pathogenic, but is asymptomatic.

Several other studies prove that the presence of *M. hominis* bacterium in infertile women is significant to the influence and damage to the reproductive organs, namely the uterus, endometrium and fallopian tubes. However, based on the results of study found by yje researchers, *M. hominis* was not found in endocervical swab examination in infertile women of reproductive age couples. This explains that women who experience infertility are not caused by this bacterium. This can be from hormonal disorders, ovarian disorders, ovulation disorders, and even factors from men.

In the results of this study, according to the researchers, the situation shows that there are many differences that occur in abroad life compared to Indonesia, especially in Padang. This is influenced by geographical, social, cultural and religious locations. In 2008, there were an estimated 498.9 million sufferers of new STIs in developing countries such as Africa, Asia, Southeast Asia[37].

The high incidence of *M. hominis* infection among fertile women in these countries proves that they are free to have sexual relations and to change partners. This is according to Menon et al (2016) stating that free sexual behavior with many sexual partners significantly increases the risk of various infections including *M. Hominis* bacterium[38].

Differences in results of this study can occur due to differences in the number of samples and in this study, clinical data collection was not performed such as women with a history of pelvic inflammatory disease, menstrual cycle regularity, weight, sexual history, obstetric history, hormone examination, follicles examination at ovulation, and husband semen analysis.

This type of research is still rarely done in Indonesia so that the number of sufferers of *M. hominis* infection in infertile women still cannot be reported. In West Sumatra region, Padang in particular, there is no research conducted yet to find out the number of sufferers and the relation between *M. hominis* infection that can affect infertility in women of reproductive age.

There are some weaknesses that occur during the study, such as the number of samples that are too small, so it is difficult to know the prevalence of *M. hominis* infection in infertile women. Furthermore, the researchers have limited time. In addition, many other factors are not examined related to infertility in women of reproductive age couples.

Relation between of *U. urealyticum* Bacterial Infection and Infertility in Women of Reproductive Age Couples

The results of the study showed that more than half of infertile women of reproductive age had *U. urealyticum* bacterial infections with 21 respondents

(63.6%) and more than 28 respondents with fertile women (84.8%). Statistical test results obtained p value > 0.05, namely p = 0.091. It can be concluded statistically that there is no significant relation between *U. urealyticum* bacterial infection and infertility in women of reproductive age couples. The value is (OR = 0.313; 95% CI = 0.095-1.024).

Infection caused by *U. urealyticum* bacterium is found in the women urogenital tract and the prevalence of this bacterium can reach 80% in normal people, but increases because of changing sexual partners, low socioeconomic status, smoking and the use of contraceptives in the womb (AKDR[11].

U. urealyticum bacterial infection enters through the ascending pathway and moves to the upper reproductive tract. Due to the influence of hormonal changes during ovulation and menstruation, it causes non-pathogenic organisms to overgrow and move upwards. Opening of the cervix during menstruation and sexual intercourse can cause infection facilitating the ascending movement of microorganisms. Bacteria can be carried along with sperm into the uterus and fallopian and then attach to fallopian tube epithelium which causes swelling and damage to the cilia and detachment of the cilia from the epithelium[39].

Based on in vitro, *U. urealyticum* bacterium is able to form biofilms. Biofilms consist of bacterial cells that are densely arranged along with an extracellular matrix so that the body's immune system is unable to reach the bacteria. The existence of this biofilm causes chronic infections because in addition to being difficult to be removed by the body, it is also difficult to be penetrated by antimicrobials[11]. This is because biofilms can increase the tolerance of bacteria to harmful environmental conditions. These bacteria can be avoided, carried away and separated from the flow of water or blood by attaching themselves to the surface of the tissue. Biofilms can be strongly attached to and resist repetitive friction[12].

This study explains that not only *U. urealyticum* bacterial infection which can cause infertility in women, but many factors can influence it. As explained above, there are factors of age, education, occupation, length of marriage including psychological stress[40].

The results of the study conducted by the researchers found that not only infertile women (cases) who were infected by the *U. urealyticum* bacterium, but also fertile (control) women also experienced these bacterial infections. In this study, there are limited samples and many other factors that cause the spread of *U. urealyticum* bacterial infections, namely decreased body immunity, the ability of these bacteria to avoid the immune system, hot climate, vaginal douching, use of vaginal antiseptics and sexually transmitted infections.

Theories and results of other studies prove that *U. urealyticum* bacterium is a microorganism found in the urogenital tract of healthy women when sexual activity begins, having early sexual intercourse without using a condom, and habit of changing sexual partners. Thus, these bacteria are able to enter and survive in the bloodstream, countering normal defense mechanisms, including antibodies, complement, and transferrin. The results showed that living in the hot tropics makes us sweat frequently. This sweat makes our body moist, especially sexual and reproductive organs that are closed and folded. As a result, bacteria are easily breed and the ecosystem in the vagina is disturbed, causing unpleasant odors and infections[41].

CONCLUSION

Based on the research results on *M. hominis* and *U. urealyticum* bacterial infection and infertility and fertility in women of reproductive age couples, it can be concluded that in research subjects, *M. hominis bacterium* is not found on fertile and infertile women of reproductive age couples. In more than half of infertile women of reproductive age couples, *U. Urealyticum* bacterium is found. In the

event of *M. hominis* bacterial infection, there is no significant relation in infertile women of reproductive age couples (p> 0.05). Besides, in the event of *U. urealyticum* bacterial infection, there is no significant relation with infertility in women of reproductive age couples (P > 0.05).

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