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ORIGINAL ARTICLE

The association between sociodemographic, hormonal, tubo-ovarian factors and bacterial count in *Chlamydia* and *Mycoplasma* infections with infertility

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Abstract *Aim:* To determine if there is an association between the *Chlamydia* and *Mycoplasma* infections with socio-demographic and clinical factors, and also with infertility. *Methods:* We conducted a study on 100 infertile married women and 100 control group, and collected data on the socio-demographic, hormonal and tubo-ovarian factors. The results of the endocervical swabs were analyzed for *Mycoplasma* and *Chlamydia* infection, the bacterial counts were also determined. *Results:* The percentage positivity to infection was significantly more among the infertile group compared to the control group, and also significantly more among the age group < 30 years old. The positivity for infection with *Chlamydia* and/or *Mycoplasma* was significantly correlated with age, history of irregular menstruation, and history of previous abortion. Further sub-analysis of the infertile group showed that positivity to *Chlamydia* and/or *Mycoplasma* infection was significantly correlated to hormonal factors, ovarian factors, irregular menstruation, and previous abortion. Regression analysis showed that hormonal, ovarian factors, and irregular menstruation were the most significant factors in the positivity to *Chlamydia* and *Mycoplasma* infection. Bacterial count was significantly correlated with age, history of irregular menstruation, and history of previous abortion. *Conclusion:* Infection to *Chlamydia* and *Mycoplasma* is associated to younger age ($\leqslant$30 years old), and occurs in the infertile women. There is an interplay between infection in younger women, irregular menstruation, hormonal, and tubo-ovarian factors with infertility. Bacterial count was significantly correlated with age, history of irregular menstruation, and history of previous abortion.

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1. Introduction

Infertility is an ecumenical health quandary with one in six couples suffering from this condition and with a major economic burden on the ecumenical health care industry (Zegers-Hochschild et al., 2009). The causes of infertility differ from population to population, and from research to research, proving the multiple factors that are associated with infertility (Bradshaw et al., 2006). In most of these studies, infertility is associated with sexually transmitted infections (STIs), and pelvic inflammatory diseases (PIDs). For this reason, STIs are a major health issue in most countries, causing as much as 40% of infertility cases among females (Simms et al., 2003; Simms and Stephenson, 2000).

In one of the studies, *Chlamydia trachomatis* and *Mycoplasma genitalium* were detected in 20% of symptomatic and in 4% of asymptomatic men (Yaqaneh et al., 2013; Hamasuna et al., 2008). Studies have shown that cervicitis among unprotected women were not correlated with age, smoking and hormonal contraception (Lusk et al., 2015). On the other hand, there were studies that have shown that intraepithelial and cytological lesions associated with *C. trachomatis* were associated with smoking and lifestyle activities (Wohlmeister et al., 2016). Furthermore, *C. trachomatis* infection was found to be associated to age ⩽24 years old, being single or having more than 5 sexual partners. On the other hand, *M. genitalium* infection was more frequent in patients ⩽24 years old or who had a history of abortion or their first sexual intercourse after 20 years old (Peuchant et al., 2015). Another study showed that black race, anal intercourse, and the number of sex partners correlated with asymptomatic urethritis implicating agents including *Mycoplasma* and *Chlamydia* (Gillespie et al., 2013). *C. trachomatis* and *M. genitalium* were also found to be associated with social demographics and sexual risks in a study conducted in Russia (Berle et al., 2012). *M. genitalium* was found to be an independent and strong risk factor for cervicitis and PID, as compared to *C. trachomatis* (Biartling et al., 2012). Another study showed that black race, black partner, use of contraceptives, smoking drug use, history of sexually transmitted disease, ⩽high school education, meeting and having intercourse the same day, anal sex, douching and hormonal contraception were all associated with *C. trachomatis* infection, but not with *M. genitalium* (Hancock et al., 2010). Short et al. suggested the association between *M. genitalium* and smoking and age under 25 years old (Short et al., 2010). One study refuted the association between cervicitis and *M. genitalium* infection, and suggested that cervicitis is of poor clinical utility as an indicator for the presence of *M. genitalium* infection (Oliphant and Azariah, 2013). This study sought to establish an association between *Chlamydia* and *Mycoplasma* infections with sociodemographic factors, hormonal factors and other variables, and infertility.

2. Material and methods

During the period between October 2012 and July 2013, this study was conducted in King Khalid University Hospital (KKUH) and King Abdulaziz University Hospital (KAUH) with the Ethics committee approval number E-12-672, both in Riyadh, Saudi Arabia, to determine the association between the socio-demographic variables, hormonal and tubo-ovarian factors with *Chlamydia* and *Mycoplasma* infections and infertility. The study was ethically approved by the Ethics Committee Board of King Saud University.

We included a total of 200 married women; 100 infertile married women aged between 19 and 46 years as the study group who attended the outpatient infertility clinic at KKUH and 100 women aged between 19 and 46 years as the control group, who attended the clinic for routine or annual check-up other than infertility. All participants agreed to participate in the study and have signed the consent. Women who had taken antibiotics in the previous 30 days were excluded from the study.

Two endocervical swabs by a speculum examination were collected from each participant in both the study and control groups by the attending clinician. The detection of *Mycoplasma* and *Chlamydia* was done using an automated DNA extraction method (MagNA Pure Compact Instrument Nucleic Acid Isolation Kit, Roche Diagnostics, Deutschland GmbH Sandhofer Str, 11668305 Mannheim). The DNA copy numbers per reaction of each sample were calculated automatically.

2.1. Statistical analysis

SPSS version 19.0 was used to perform the data analysis. We present mean ± SD, median and range for numerical variables. We present the frequencies and percentages for different items of nominal variables. We used the chi-square test to compare the significant differences between the two groups. We assumed there was a statistically significant difference when the p-value was less than 0.05.

3. Results

The mean age for all women was 34.7 ± 7.7 years (range: 19–46 years old). The mean age of the study group was 32.5 ± 6.4 years old, and mean age of the control group was 36.8 ± 8.3 years old. There were 67 (33.5%) women in the age group ⩽30 years old and 133 (66.5%) were more than 30 years old. Sixteen (8.0%) women were positive to *Mycoplasma* and/or *Chlamydia* infection. The percentage positivity to infection was significantly more among the study group (13/100, 13%) compared to the control group (3/100, 3.0%), $p = 0.009$. The percentage positivity to infection was significantly more among the younger age group (< 30 years old, 11/67, 16.4%) compared to the age group 30 years old and above (5/133, 3.8%), $p = 0.002$. (Fig. 1).

The positivity for infection with *Chlamydia* and/or *Mycoplasma* was significantly correlated with age ($p = 0.029$), history of irregular menstruation ($r = 0.191$, $p = 0.007$), and history of previous abortion ($r = 0.240$, $p = 0.001$). Positivity for infection was not significantly correlated with nationality, hormonal factor, ovarian factor, tubal factor, male factor, burning sensation during urination, genital bleeding, history of abnormal discharges, low-seated abdominal pain, history of pelvic inflammatory disease, signs of vaginosis and signs of cervicitis. Further sub-analysis of the infertile group showed that positivity to *Chlamydia* and/or *Mycoplasma* infection was significantly correlated to hormonal factors ($r = 0.247$, $p = 0.013$), ovarian factors ($r = 0.211$, $p = 0.035$), irregular menstruation ($r = 0.215$, $p = 0.032$), and previous abortion

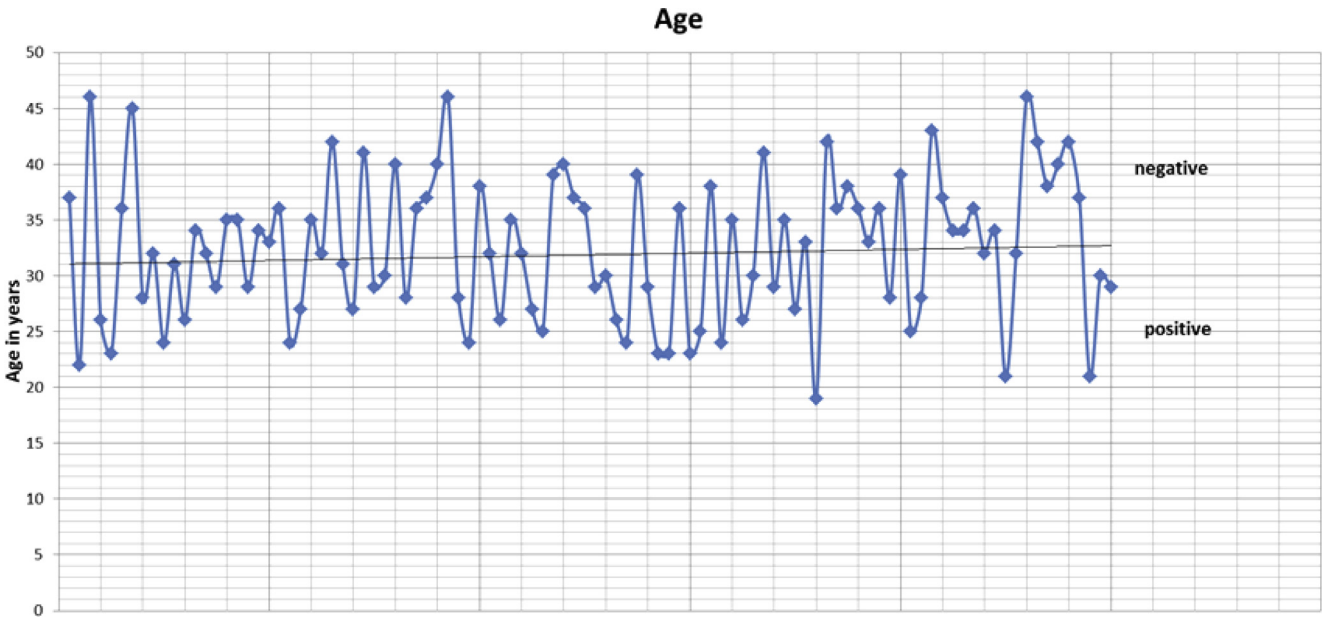

Figure 1 The association between *Chlamydia* and/or *Mycoplasma* infections with age.

Table 1 Correlates of *Chlamydia* and/or *Mycoplasma* in infertile women.

Correlates of infection to *Chlamydia* and/or *Mycoplasma*	Pearson correlation coefficient (r)	*p* values
Younger age	0.155	0.029
Hormonal factor	0.247	0.013
Ovarian factor	0.211	0.035
Tubal factor	0.126	0.076
Male factor	0.081	0.256
History of STI's	0.014	0.457
Burning sensations	0.009	0.897
Genital bleeding	0.098	0.166
Irregular menstruation	0.191	0.007
Abnormal discharges	0.049	0.488
Low-seated abdominal pain	0.123	0.082
Previous abortion	0.240	0.001
Ectopic pregnancy	0.021	0.769
Premature delivery	0.071	0.317
Signs of vaginosis	0.021	0.769
Signs of cervicitis	0.056	0.429
Pelvic inflammatory disease	0.021	0.769

($r = 0.260$, $p = 0.009$). On the other hand, sub-analysis of the control group showed that positivity to *Chlamydia* and/or *Mycoplasma* infection was significantly correlated with age ($r = 0.216$, $p = 0.031$) and irregular menstruation ($r = 0.267$, $p = 0.007$). (Table 1) Regression analysis showed that hormonal (Beta -0.457, $t = -3.514$, $p = 0.001$) ovarian factors (Beta -0.449, $t = -3.766$, $p < 0.001$), and irregular menstruation (Beta 0.206, $t = 2.021$, $p = 0.046$) were the significant factors in the positivity to *Chlamydia* and *Mycoplasma* infection. Bacterial count was significantly correlated with age ($r = 0.167$, $p = 0.022$), history of irregular menstruation ($r = 0.234$, $p = 0.005$), and history of previous abortion ($r = 0.344$, $p = 0.001$).

4. Discussion

The problem of infertility is multifactorial; however, as suggested by several studies, most of the pathological changes related to disruption in the tubo-ovarian function are mostly brought about by an infection (Bradshaw et al., 2006; Simms et al., 2003; Simms and Stephenson, 2000; Yaqaneh et al., 2013). It is not routine for some, if not most, of the laboratories to screen for *C. trachomatis* and *M. genitalium* infections, thus the possibility of missing the diagnosis for these infections is high.

This study has shown the significant positivity to infection with *C. trachomatis* and *M. genitalium* among infertile women compared to the control group ($p = 0.009$). This highlights the role of *C. trachomatis* and *M. genitalium* in the pathology in the reproductive organs particularly among infertile women. The significance between infection and infertility suggests that infection with these organisms may cause pathological changes in the cervical, endometrial and fallopian tube lining cells that may eventually affect the capability of the woman to conceive. There is also the high possibility that these organisms cause alterations in the sperm's capability to fertilize an ovum, cause abortions even after fertilization or implantation, premature birth and even low birth weight infants.

We also found out that the percentage positivity to infection was also significantly more among the age group < 30 years old (11/67, 16.4%) compared to the age group 30 years old and above (5/133, 3.8%), $p = 0.002$. This finding is in agreement with Peuchant et al. (2015) who found higher infection rates among patients aged $\leqslant 24$ years old. However, in contrast to their study, we found the association of age and infection in patients $\leqslant 30$ years old, where most of our patients are in their prime years of their reproductive and sexual lives. This association can be attributed to a higher level of sexual activity in this age group, and that the squamo-columnar junction of the cervix was still evident in the area of the ectocervix, making them more susceptible to infection.

For this reason, various screening programs in many countries consider age as a primary determinant for selective screening.

Furthermore, apart from age, our study showed significant associations between infection and history of irregular menstruation, history of previous abortion, hormonal factors, ovarian factors, and irregular menstruation. Infection with *Chlamydia* and/or *Mycoplasma* among infertile women was significantly correlated with age and irregular menstruation. At this point, it is insufficient for us to conclude the association of these hormonal, ovarian and tubal factors to infection, except that probably, the interplay between these various hormonal, tubal and ovarian factors has something to do with the irregularities in menstruation and the causation of infertility.

Bacterial count was significantly correlated with older age, history of irregular menstruation, and history of previous abortion. One *Chlamydia* positive sample from a 34-year old infertile patient showed a count of as much as 6880 copies/reaction 1,376,000 copies/mL), and one *Chlamydia* sample registered only 8.45 copies/reaction 1690 copies/mL). The bacterial counts in our study were relatively high compared to a similar study that showed 16,760 copies/mL at their highest. (ElFeky and Baddour, 2009). However, there is a need for further studies to quantitatively determine the association between loads of bacterial count and infertility. Although there were studies that have shown the association between mixed infections and infertility, those studies concluded that the causation of infertility was more of the male factors (Al-Sweih et al., 2012).

5. Conclusion

A significantly higher percentage of infection with *Chlamydia* and *Mycoplasma* in less than 30 year old patients, and in infertile women occurs. There were significant associations between infection with younger age, irregular menstruation, and to some extent an interplay of hormonal, and tubo-ovarian factors. The interplay of these factors plus the younger age would significantly affect the fertility status of these patients.

Disclosure

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