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The Prevalence of Chlamydial Endometritisin Women with Menorrhagia at an Egyptian Tertiary University Hospital

Wahba K (MD, MRCOG)
Department of Obstetrics and Gynecology – Ain Shams University

***Corresponding author:** Karim Wahba, Assistant professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, Abbasyia, Cairo, Egypt; E mail: karimwahbaobgyn@yahoo.com

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Abstract

Objective: The goal of this study is to evaluate the prevalence of Chlamydial endometritis in women with menorrhagia attending Ain Shams University Maternity Hospital.

Design: Cross-sectional study.

Setting: Ain Shams Maternity teaching hospital.

Patients and methods: 300 women were divided randomly into two equal arms of 150 women in each one.

Intervention: Patients admitted through the reception room or out-patient clinics (hospital department) and they scheduled for Pipelle endometrial sampling. Group I saught medical advice because of menorrhagia while group II were attending the hospital due to any other cause other than vaginal bleeding. Pipelle endometrial biopsy was taken and sent for detection of Chlamydia trachomatis by PCR.

Results: In group I, 82 specimens were positive for Chlamydia and the other 68 specimens were negative for Chlamydia while in group II only 22 specimens were PCR positive for chlamydia. There was a statistical significant correlation between positive cases of C. endometritis and abnormal uterine bleeding (AUB).

Conclusion: Screening for Chlamydia trachomatis in patients with menorrhagia is recommended.

Key words: Chlamydia trachomatis,Menorrhagia

Introduction

Menorrhagia, or excessive menstrual flow, is the most common complaint that women with menstrual disorders experience. It is defined as bleeding that lasts for more than seven days or results in the loss of more than 80 ml of blood per menstrual cycle[1]. Endometritis is one of the most common infectious complications of delivery in the mother, and it occurs more frequently after operative delivery[2]. Endometritis presents clinically by elevated temperature, uterine tenderness, vaginalbleeding, leucocytosis, or positive endometrial cultures. Clinically evident endometritis is usually presented inthe setting of acute PID or postpartum or post abortive[3]. Due to its subtle clinical picture, the true incidence of this pathology among women is unclear, with estimates ranging from 0.8% to19.0%. 72% of histologic samplesgathered from women asking care in STD clinics, were positive[4].

Chlamydia trachomatis (C. trachomatis) is the most frequent sexually transmitted bacterium[5].Lower genital tract infection by this organism is usually asymptomatic in men and women, 50-66% of such infections in women remain undiscovered and consequently untreated, and leading to undesired long-term effects, ectopic pregnancy and tubal infertility are outstanding examples[6]. Hence, screening is needed to detect and manage this infection to decrease the period of infectivity, transmissibility and future adverse effects[7].

As culture techniques are hard to standardize, technically exhausting and not cheap, other tests have been arised[8]. Nucleic acid amplification techniques (NAAT) are now being utilized to diagnose chlamydial infections. NAATs are used with noninvasively gathered samples, such as first-void urine samples (FVU) from men or women and vaginal smears leading to increased compliance of C. trachomatis screening programs among asymptomatic persons[9].

In a Cochrane review, the mean prevalence of endometritis was 7% after elective cesarean section and 30% after nonselective or emergency cesarean section[10]. CE is characterized by plasma cell infiltration in the endometrium[11]. Most of the time CEis accidentally discovered after an endometrial biopsyoradilatationandcurettage (D&C) for different indications such as abnormal vaginal bleeding, post menopausal bleeding, endometrial polyps, etc.

Accurate estimates of incidence data for Chlamydial infection of the female genital system using sensitive and specific methods like nucleic acid amplification tests are lacking in developing countries as Egypt. Few available data describe an increased incidence of infection, especially among symptomatic Egyptian women[12].

There is an ongoing debate as to whether or not screening of all women with menorrhagia and management of those diagnosed to be infected is needed or cost effective. The goal of this study is to evaluate the prevalence of Chlamydial endometritis in women with menorrhagia and answer the question to screen or not to screen.

Patients and Methods

This was a cross-sectional study performed in Ain Shams Maternity University Hospital involving 300 women; a first group of 150 cases with menorrhagia and a control group of 150 women with normal menstruation attending gynecologic outpatient clinic (hospital department), for any reason other than bleeding. Pipelle endometrial biopsies were collected and sent for detection of Chlamydia trachomatis by PCR.This study was carried out in the period from January 2015 to December 2015 and it was approved by Ethical Committee of the Faculty of Medicine, Ain Shams University. Explanation of the procedure and verbal consent was taken for every patient.

Inclusion criteria

1. Patients of reproductive age.
2. Complain of dysfunctional uterine bleeding.
3. No gross uterine lesions were detected by vaginal US.
4. Women who live in Cairo

Exclusion criteria

Patientswhoareimmediately post-partumorpost abortion or known cases of sexually transmitted diseases

1. Patients with any uterine abnormality detected by transvaginal sonar or hysterosalpingogram.

2. Patients with suspicion of pregnancy.

3. Women who live outside Cairo

All patients were subjected to

1. Full history taking, complete physical examination.
2. Counseling and verbal consent was taken for every patient.
3. Pipelle endometrial biopsies were taken and sent to confirm Chlamydia trachomatis endometritis by PCR.

Materials of PCR

Endometrial biopsy: Transport medium: 2-sucrose phosphate buffer (PH 7.0) supplemented with 5% fetal bovine serum, 50 ug of streptomycin / ml, 100 ug of vancomycin per ml and 12.5 ug of amphotericin B (Fungizone) per ml (Phosphate Buffer Saline).

Real Time PCR involved three main steps (Roche, Germany):

DNA extraction

DNA amplification

Detection of specific amplified product using melting curve analysis

DNA extraction:

- DNA was extracted from the samples using MagNA Pure Compact Nucleic Acid Isolation Kit I (Cat.No.o3730964001) supplied by (Roche. Germany).
- Test Principle: MagNA Pure Compact Instrument (with integrated personal computer, touch screen monitor and bar-code reader) is a small benchtop instrument intended for automated nucleic acid purification.
- All isolation kits contain optimized reagents that are prefilled in sealed cartridges, eliminating reagent mix-up or contamination. The nucleic acid isolation procedure is based on the proven MagNA Pure Magnetic Glass Particle Tech.
- Principle steps of a MagNA Pure Compact nucleic acid isolation procedure are: cells were lysed by incubation with proteinase K and a special lysis buffer containing a chaotropic salt. Magnetic Glass Particles (MGPs) were added and nucleic acids were immobilized on the MGPs surfaces. Unbound substances (e.g., proteins, cell debris, PCR inhibitors etc) were removed by several washing steps, purified nucleic acids were eluted from the MGPs.
- Nucleic acid isolation protocol: The following procedure was designed to process 8 samples at the same time. The instrument can handle all numbers of samples between 1 and 8. The Reagent Cartridge was adapted to room temperature (+15 to +25°C) before use.

1. The instrument was turned on. The Cartridge Rack and Tube Rack (with Elution Tube Rack) were removed from the instrument. The Run button on the Main Menu Screen was clicked to access Sample Ordering Screen. The software-guided workflow was followed.
2. A pre-filled Reagent Cartridge was removed from its bag.
3. All the wells on the Reagent Cartridge were inserted into the holes in the Cartridge Rack. The steps above were repeated for the desired numbers of samples.
4. Sample ordering appropriate purification protocol (Total – NA-Plasma-100-400) was selected from Protocol menu. The elution volume 200 ul was selected.
5. The appropriate number of Tip Trays (one per purification) was inserted into the assigned position in the instrument Tip Rack.
6. Sample Ordering Screen 3. The Sample Tubes were arranged in row 1 of the Tube Rack. The samples were pipetted into their respective Sample Tubes.
7. Sample Ordering Screen 5. The Tube Rack is reinserted into the instrument.
8. The Elution Tubes were placed into the Elution Tube Rack then the Elution Tube Rack was reinserted into the instrument.
9. On the Confirmation Screen, the information display was checked. If the information is correct, confirmation was done by touching the "Confirm Data" button, the front cover was closed, and the run started.
10. After the purification run had ended, the Elution Tubes were closed with the supplied tube caps and the Elution Tube Rack was removed immediately.

Amplification by Real Time – PCR: This was done by Light Cycler-DNA Amplification Kit SYBR Green I (Cat.No.2015137), using the Light Cycler 2.0 System (Roche, Germany).

Statistical methodology: Retrieved data were recorded on an investigative report form.The data were analyzed with SPSS®

for Windows®, version 15.0 (SPSS, Inc, USA). Description of quantitative (numerical) variables was performed in form of mean, standard deviation (SD) and range. Description of qualitative (categorical) data was performed in the form of numbers and percent. Analysis of numerical variables was performed by using student's unpaired t-test (for two groups) or ANOVA (for more than two groups). Analysis of categorical data was performed by using Fischer's exact test and Chi-squared test. Significance level was set at 0.05.

Results

This cross sectional study involved 300 women consented to participate in this study; group I (test group) of 150 cases with menorrhagia and group II (control group) of 150 women with normal menstruation recruited from gynecologic outpatient clinic (hospital department), and complaining from any reason other than bleeding. Pipelle endometrial biopsies were collected and sent for detection of Chlamydia trachomatis by PCR.Both groups were comparable in terms of age, body mass index, gravidity, parity, duration of marriage, frequency of coitus per week, mode of delivery (vaginal or cesarean), level of education (≤High school or >High school), occupation (house wife or employed/business woman) and previous use of IUCD and (Table 1).

The 300 specimens were sent for detection of Chlamydia trachomatis by PCR.In group I, 82 specimens were positive for Chlamydia and the other 68 specimens were negative for Chlamydia while in group II only 22 specimens were PCR positive for chlamydia (Table 2). There was a significant difference between the two groups as regards the incidence of C. trachomatis among symptomatic Egyptian females complaining of dysfunctional uterine bleeding.

Table 1: Clinic-demographic data of the population under study

	Group I	Group II	P- value
Age	36.56 ± 5.3	36.3 ± 3.1	0.6044
Body mass index (kg/m^2)	32.3 ± 4.4	33.1 ± 3.8	0.0930
Previous gravidity	3 ± 0.8	3.1 ± 0.9	0.3099
Previous parity	2.2 ± 0.7	2.3 ± 0.3	0.1089
Duration of marriage	6.9 ± 2.1	7.1 ±1.8	0.3765
Frequency of coitus per week	2.4 ± 0.9	2.5 ± 0.8	0.3099
Mode of delivery Vaginal Cesarean	 83 67	 81 69	> 0.05
Education ≤High school >High school	 64 86	 61 89	> 0.05
Occupation House wife Employed/business Woman	 97 53	 102 48	> 0.05
Previous use of IUCD	97	101	> 0.05

Table 2: Number and percent of positive cases for C. trachomatis by PCR

	Group I	Group II	Chi square	P value
Positive cases	82 (55%)	22 (14.7%)	52.9827	< 0.05 (significant)
Negative cases	68 (45%)	128 (85.3%)		

Discussion

The goal of Chlamydia Trachomatis screening programs is to limit the morbidities from upper genital tract effects and the incidence of the infection by controlling its spread[13].Moreover, pre-existing silent disease can spread more when patients undergo uterine instrumentation for further assessment and management of their problems. So, the Royal College of Obstetricians and Gynecologists advise that all patients undergoing uterine instrumentation should be screened for Chlamydia or should receive prophylactic antibiotics[14].

In Egypt and most Arab nations, the incidence of sexually transmitted diseases in general and Chlamydial genital infection in particular is not exactly known, reflecting the deficient specific diagnosis and management protocols. Different small studies from various countries showed different prevalence of C. trachomatis infection; United Arab Emirates (2.6 %)[15], Jordan (3.9 %)[16], Qatar (5.3 %)[17], and Saudi Arabia (15 %)[18]. This difference in prevalence is linked to age of the individuals under study, as well as the different specific techniques utilized for diagnosis.

Chronic endometritis (CE) is a subtle pathology which is hard to both diagnose andmanage[19-21].Chronic endometritis is usually clinically asymptomatic, but may be associated wild mild complaints including chronic pelvic pain, abnormal uterine bleeding, painful coitus and leucorrhea[22].The presence of an inflammatory infiltration containing plasma cells is usually pathognomonic to chronic endometritis.Hence, it cannot be excluded an endometritis if, besides infiltration, there are factors such as attacking behavior against endometrial glands, the presence of an exudates inside gland lumina or the formation of granulomas[23].

The purpose of this study was to determine the prevalenceof C. trachomat is in endometrial tissues of patients with menorrhagia. The use of PCR technology is the most currently accepted method for diagnosing endometrial tissue for C. trachomatis antigen and has been validated[24,25]. Nucleic acid amplification has a high sensi¬tivity (90-97%) and specificity (99%), the samples are suitable for testing several days after collection, even if kept at room temperature [26-28]. Actually, Ain Shams University Teaching Hospital is one of the biggest referral hospitals in Egypt and manages women with any obstetric or gynecological complaint from a large geographical area so the rates were nonetheless striking.

In the current study, the C. trachomatis infection was detected in 82 cases (55%) in patients with menorrhagia and 68cases (45%) were negative for chlamydia.

In a similar study, that included 2,190 diagnostic hysteroscopies, histologic diagnosis of CE was made in 388 cases, it is found that

several bacteria can cause CE, the most common among them E. coli, Streptococci, Staphylococci, Enterococcus fecalis, and Yeast species. C. trachomatis and Ureaplasmaurealyticum were isolated in only a small proportion of the patients with a histologic diagnosis of CE in this study. Regarding the type of infectious agent, it is worthy underlining that at the endometrial level the most frequent agents found were common bacteria, accounting for about 60% of Cases; U. urealyticum was detected in 10% of cases. Unexpectedly, Chlamydia was demonstrated in only 2.7% of positive endometrial cultures. No cases of N. gonorrhea were found; this in partial agreement with the current study (13.3% of cases) [28].

Attheendometriallevel, the prevalence of C. trachomatis in our study was higher that reported in the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) study as reported that Chlamydia represents about 14% ofwomen with chronic endometritis[29].

Some studies put no set of histologic features or degree of intensity of inflammation predicted a particular clinical presentation, a response by the clinician to prescribe antibiotics or outcome[30-32].Also in another study implied that histological examination of an endometrial biopsy is a reproducible method for diagnosis and treatment of CE in asymptomatic patients prior to IVF/ICSI is substantial[33].Moreover, in patients treated with antibiotics for C. trachamatis, the histological features of endometritis promptly resolves and endometrial cultures become negative[34].

Another study found that Chlamydial endometritis increases as age and parity increase, which was explained due to exposure to infections.This is in partial agreement with our study which found that CE increases with parity while here was no relation with age[35].

It is stated that there was an associationofCE and salpingitis. Itseems that CE is a marker ofanascendinginfection, whichinyoungerpatients might impair fertility by the presence of salpingitis. A genital tract infection that remains untreated or partially treated or a subclinical ascending infection may progress to cause CE and possible salpingitis with potential impact on fertility[36,37].This was in accordance with findings from Feghali et al (2003)[38] who found in 45% of cases some pathological finding at diagnostic hysteroscopy prior to IVF most of these abnormalities were endometritis.

Bayer-garner et al[39] implied that CE was diagnosed in between 3% and 10% of women who complaining of abnormal uterine bleeding, also Thurman and Soperimplied that CE was more common in women who experiencing dysfunctional uterine bleeding.Also, Krettek et al[40] found that C. trachomatis represent 3:5 folds in patients with abnormal uterine bleeding associated CE.This was in contrast with Wiesenfeld et al[24] study who found no relation between CE and abnormal uterine bleeding but these findings were limited to sample size and association between C. trachomatis and CE.

In one of the first studies on CE, reported that the clinical presentation of patients with CE was some types of vaginal bleeding[12].Wiesenfeld et al (2005) reported that, the prevalence of CE was higher in women undergoing hysteroscopy due to abnormal uterine bleeding (14.4% vs 11.7%), furthermore, the indications related to bleeding [pre-menopausal abnormal uterine bleeding (AUB), suspected endometrial polyp, endocervical polyp, intracavitarymyoma] they were present in up to 36.3% of cases of CE[24].There was partial agreement with results of the current study and some studies[41,42], clinical reviews who using PCR to detect C. trachomatis in cases of CE. These studies proved that C. trachomatis was associated with severe CE and dysfunctional uterine bleeding is a common symptom of CE.

Conclusion & Recommendations

In view of such findings, the aim of the present work was to detect the prevalence of C. trachomatis in symptomatic Egyptian females complaining of dysfunctional uterine bleeding.

We documented higher than expected C trachomatis prevalence in these patients reflecting lack of STI-specific programs in Egypt. Review of these data led to a change of menorrhagia workup policy in our unit, with the introduction of Chlamydia serological screening and antibiotic treatment of positive cases. We hope to use the results of this study to help design and complete larger clinical trials involving the use of endometrial curetting's for the detection of Chlamydial antigen by DNA amplification. This may lead to improved identification and characterization of this subgroup of women whose menstrual abnormalities are currently unexplained.

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