MATERIALS AND METHODS

2. HSG- Mainstay in infertility imaging. Apart from the patency of tubes, also used for evaluation of uterine cavity.
3. TVS- Son day 12-13 (pre ovulatory period) - endometrial thickness, pattern and sub-endometrial blood flow.

Aims and objectives-
To study the endometrial status in infertility cases by following parameters:
1. Ultrasound and Doppler- non-invasive, accurate and safe. By 2D power Doppler ultrasound, on day 12-13 (pre ovulatory period) we have taken endometrial thickness, pattern and sub-endometrial blood flow.
2. HSG- Mainstay in infertility imaging. Apart from the patency of tubes, also used for evaluation of uterine cavity.
3. Endometrial biopsy, taken in premenstrual period, sent for histopathology and TB PCR.

ABSTRACT

BACKGROUND:: Various disorders lead to infertility in women of reproductive ages. This study was performed to describe the common endometrial causes of infertility and sonographic, hysterosalpingographic, and endometrial biopsy evaluation of these causes for midwives.

Introduction- Successful implantation depends on interaction between a blastocyst and receptive endometrium. Different strategies have been developed to evaluate endometrial receptivity, such as the histologic dating of an endometrial biopsy or more commonly a non-invasive ultrasound examination of the endometrium.

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To study the endometrial status in infertility cases by following parameters:
1. Ultrasound and Doppler- non-invasive, accurate and safe. By 2D power Doppler ultrasound, on day 12-13 (pre ovulatory period) we have taken endometrial thickness, pattern and sub-endometrial blood flow.
2. HSG- also used for evaluation of uterine cavity.
3. Histopathology and TB PCR of premenstrual endometrial biopsy.

Material and methods: It is a prospective study, carried out in the Department of Obstetrics and Gynecology, Institute of Medical Sciences in collaboration with the Department of Radiodiagnosis, Banaras Hindu University, over a period of 2 years. Hundred patients with infertility attending Female OPD (FOPD) of SSH, BHU were the subject. Patients complaining of infertility, aged 19-45 years, sexually active were subjected to detailed history & clinical examination, HSG, TB PCR and histopathology of premenstrual endometrial tissue and TVS & color Doppler study (endometrial thickness, pattern and vascularity). Measurements were analyzed relative to outcome.

Results: Maximum rate of conception was seen with endometrial thickness 10-14mm (61.54%) and with triple line pattern of endometrium. There was no concepation in zone I flow and maximum conception rate (25%) was seen when zone III flow was present. Majority of patients with genital tuberculosis had their endometrial thickness <7mm and absent triple line endometrium reflects poor receptivity of the endometrium and local endometrial factor as a cause for infertility.

Conclusion: Our results show that no single parameter is specific enough to predict conception. Further study is needed to make a definitive conclusion.

INTRODUCTION

According to World Health Organization (WHO) infertility is “a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.” Infertility varies across regions of the world and is estimated to affect 8 to 12 per cent of couples worldwide.

Different strategies have been developed to evaluate endometrial receptivity, such as the histologic dating of an endometrial biopsy or more commonly a non-invasive ultrasound examination of the endometrium.

Commonly used sonographic markers include endometrial thickness and pattern. With the advent of Doppler ultrasound, studying endometrial blood flow has emerged as an important means of evaluating endometrial receptivity. A triple layered endometrial pattern and an endometrial thickness greater than 7 mm have been proposed as markers of endometrial receptivity, but have yielded a high percentage of false-positive results. A good blood supply to endometrium is generally considered necessary for implantation.

AIMS AND OBJECTIVES OF THE STUDY

To study the endometrial status in infertility cases by -
1. Ultrasound and Doppler- non-invasive, accurate and safe. By 2D power Doppler ultrasound, on day 12-13 (pre ovulatory period) we have taken endometrial thickness, pattern and sub-endometrial blood flow.
2. HSG- Mainstay in infertility imaging. Apart from the patency of tubes, also used for evaluation of uterine cavity.
3. Endometrial biopsy, taken in premenstrual period, sent for histopathology and TB PCR.

MATERIALS AND METHODS

The present study was carried out in the Department of Obstetrics and Gynecology, Institute of Medical Sciences in collaboration with the Department of Radiodiagnosis, Banaras Hindu University.

Type of study: Prospective study
Duration of study: July 2014- June 2016
Place of patient work up- Sir Sunder Lal Hospital, BHU

Selection of the Patients:
Hundred patients with infertility attending Female OPD (FOPD) of SSH,BHU were the subject of the present study.

a) Inclusion criteria:
Patients complaining of infertility, aged 19-45 years, sexually active were subjected to -
- Detailed history & clinical examination.
- HSG
- TB PCR and histopathology of endometrial tissue
- Pelvic Ultrasound & color Doppler study

b) Exclusion criteria:
- Mullerian agenesis
- Male infertility

Consent:
Initially approval of the university’s ethical committee was obtained to conduct the present study.
Written informed consent was obtained from all the patients enrolled regarding history, abdominal, per speculum and per vaginal examination.

Consent was also obtained for doing HSG, Pelvis ultrasound & color
Doppler and TB-PCR, HPE test of endometrial sample.

After consent proper history was taken including name, age, years of marriage, type of infertility, present complaints, menstrual cycles, medical illness and its treatment or surgical intervention if any followed by through clinical examination done including local n systemic examination. Then they are gone under investigation including

1. Pelvic USG with Colour Doppler
2. Hysterosalpingogram (HSG)
3. TB-PCR and histopathology of endometrial tissue

STATISTICAL ANALYSIS
The statistical analysis was done using SPSS (Statistical Package for the Social Sciences version 16. for Windows version 16.0 software). The Chi-square and Fisher’s test was used. P<0.05 were considered to be statistically significant.

RESULTS AND DISCUSSION
Among patients evaluated, 77% cases were of primary infertility, 23% of secondary infertility.

Among patients evaluated, maximum patients (42%) had tubal factor (HSG), 22% had positive endometrial TB PCR, 17% had non-secretory endometrium in HPE of premenstrual endometrial biopsy (anovulatory cycles) and 12% had PCOS. The etiology was unexplained in 28% cases after work up.

Forty-two (42%) patients were in age group of 19-25 years, whereas 41% patients were in age group of 26-30 years, 14% in age group of 31-35 years and 3% were >35 year age group.

Maximum patients (66%) had 1-5 years duration of infertility, 25% with duration of 5.1-10 years and 9% had duration more than 10 years. Mean duration of infertility was 4.895 years.

49% of patients under study had education upto matriculation, 47% had upto graduation/ post-graduation and 4% were illiterate.

Approximately half of patients (51%) belonged to rural area and half (49%) of them belonged to urban area. In rural habitat, 47.06% patients had tubal factor, 17.65% had endometrial TB PCR, 13.73% had anovulatory cycle, 5.88% had PCOD and 23.5% had unexplained infertility. In urban habitat, 36.73% patients had tubal factor, 26.53% had endometrial TB PCR positive, 20.41% had anovulatory cycle, 5.88% had PCOD and 32.65% had unexplained infertility.

Majority of the patients (45%) belonged to lower middle class followed by 34% to middle class, 11% to upper middle class, 8% to lower class and 2% to upper class.

Maximum patients (82%) were housewife, only 18% were working. Majority of the patients (68%) had BMI between 18.5-24.99 kg/m2, 15% had <18.5, 15% had between 25-29.99 and 2% had BMI >30 kg/m2.

Among the patients presenting with symptoms/signs of pelvic inflammatory disease majority (19%) had complaints of per vaginal discharge, followed by pain abdomen (9%), dyspareunia (8%) and backache (7%). On per speculum examination, 23% had vaginal discharge. Cervical motion tenderness was present in 12%.

Majority of patients (56%) had regular menstrual cycles, 19% had dysmenorrhea, 12% had hypomenorrhea, 9% had oligomenorrhea and 4% with secondary amenorrhea.

15% patients had history of previous genital tuberculosis or ATT intake and 7% patients had history of pelvic surgery.

In 60 (77.92%) patients of primary infertility and 20 (86.96%) of secondary infertility there was normal secretory endometrium. Anovulatory endometrium seen in 15 (19.48%) cases of primary infertility and 2 (8.70%) cases of secondary infertility. 2 cases of primary infertility showed endometrial tuberculosis. 1 case of secondary infertility showed simple cystic hyperplasia.

Endometrial TB PCR test was positive in 20 (90.9%) cases of primary infertility and 2 (9.1%) cases of secondary infertility.

On hysterosalpingographic evaluation 44% cases had normal findings, whereas 42% had tubal factor, 22% had endometritis and in 8% both tubes and endometrium were involved.

In patients with tubal factor infertility, 14 patients (33.33%) were positive with endometrial TB PCR whereas only 8 (13.7%) patients without tubal factor were positive for endometrial TB PCR. The results were statistically significant (P value 0.01-0.025).

Vaginal discharge was present in 33.33% patients with tubal factor infertility but only 15.51% patients without tubal factor infertility had vaginal discharge. The results were statistically significant (P value 0.01-0.05).

Majority of patients (52%) had their endometrial thickness 7-9mm, 33% had <7mm, 13% had 10-14mm and only 2% had >14mm ET in USG.

In patients with tubal factor infertility, endometrial thickness in majority of patients (50%) was between 7-9 mm followed by endometrial thickness < 7mm in 35.71% patients and endometrial thickness was 10-14 mm in 14.29% patients.

Majority of patients (63.64%) with positive endometrial TB PCR had their endometrial thickness <7 mm, 18.18% had endometrial thickness 10-14mm, 13.64% had endometrial thickness 7-9mm and only 4.56% had endometrial thickness >14 mm.

In infertile patients with anovulatory cycles (HPE of premenstrual EB-Non secretory pattern), majority (41.18%) had their endometrial thickness 7-9 mm, 23.53% had <7 mm, 23.53% had 10-14mm and only 11.76% had >14mm.

In patients with PCOD, 41.67% patients had <7mm ET, 41.67% had 7-9mm ET, 8.33% had 10-14mm ET and 8.33% had >14mm ET.

In patients with unexplained infertility, majority of patients (67.86%) had 7-9 mm endometrial thickness, 17.86% had 10-14mm and 14.28% had <7mm ET.

Majority of patients with genital tuberculosis (59.09%) had thin endometrium (<7mm), whereas only 25.64% without genital TB had ET <7 mm. The results are highly significant (p value <0.005). Chi square value is 8.683.

Majority of patients (48%) had type C or triple line endometrium, 37% had type B and 13% had type A endometrial pattern. 2 patients with infertility had endometrial calcification on USG.

In patients with tubal factor infertility, 16 patients (38.09%) had triple line pattern, 16 patients (38.09%) had type B and 10 patients (23.81%) had type A endometrial pattern on USG.

In genital tuberculosis patients, 10 patients (50%) had type B, followed by 6 patients (27.27%) had type A and only 5 patients (22.73%) had triple line pattern.

In infertile patients with anovulatory cycles (HPE of premenstrual EB-Non secretory pattern), majority (58.82%) had triple line, 4 patients (23.53%) had type B and 3 patients (17.65%) had type A endometrial pattern on USG.

In PCOD patients, 5 patients (41.67%) had triple line, 5 patients (41.67%) and 2 patients (16.66%) had type B endometrial pattern.
In unexplained infertility, 15 patients (53.57%) had triple line and 13 patients (46.43%) had type B endometrial pattern.

In patients with genital tuberculosls, only 27.27% patients had triple line endometrial pattern (statistically significant, p value 0.025-0.05).

The endometrial blood flow was in Zone 1 in 16% patients, 40% patients had blood flow in Zone II and 44% had in Zone III.

In patients with genital tuberculosis, only 4 patients (18.18%) had endometrial blood flow in Zone III (statistically significant, p value <0.01, chi square value is 7.630).

SUMMARY

Our study was intended to evaluate the endometrium in different causes of infertility by TVS and Doppler, non invasive method to assess the endometrial receptivity and premenstrual endometrial tissue histopathology and TB PCR test.

- Most common cause in our study was tubal factor infertility (42%). The high prevalence of pelvic infection and the lack of an efficient programme for its prevention and treatment have led to high level of tubal infertility in India.
- The mean and mean duration of infertility in India is lower in western world.
- Genital tuberculosis is the major causative factor for severe tubal disease in developing countries like India. To confirm the diagnosis of genital tuberculosis, TB PCR of endometrium or menstrual blood should be done in all cases.
- Histopathology of endometrial biopsy in infertility studies is the simplest, quickest, cheapest and useful method of determining the occurrence of ovulation.
- Majority of patients with genital tuberculosis had their endometrial thickness <7mm and absent triple line endometrium reflects poor receptivity of the endometrium and local endometrial factor as a cause for infertility. Zone III flow was absent in 81.82% patients with genital tuberculosis. A the prevalence of genital tuberculosis in infertile patients is very high in India, so we recommend routine TB PCR in patients with such ultrasound findings, to rule out genital tuberculosis as a cause of infertility, which may otherwise remain unexplained.
- In our study, maximum rate of conception was seen with endometrial thickness 10-14mm and only one patient conceived when endometrial thickness was <7mm. Use of endometrial thickness as a parameter for prediction of conception has a low specificity and low PPV but its main advantage lies in its high NPV in cases where endometrial thickness is not reached.
- Poor endometrial development, as assessed by the presence of a hyperechogenic endometrial pattern on the day of HCG administration before ovulation, had a strong NPV of 85.7-100% for conception. Conversely, a triple layer pattern, although a more frequently with a conception cycle, proved to have a low PPV of 33.1-47.8% and a low specificity of 9.2-42.8% to predict a clinical pregnancy. High NPV is important for counseling.
- There was no conception in patients with zone 1 flow and maximum conception rate (25%), which is equivalent to normal per cycle fecundity) was seen when zone III flow was present.
- For absent Zone III flow in prediction of conception, sensitivity and Negative Predictive Value was 100%. Specificity was 19.2% and Positive Predictive Value was 20.24%.

CONCLUSION

Our results show that no single parameter is specific enough to predict conception. These parameters had low specificity and positive predictive values but sensitivity and negative predictive value are both important. The meaning of that if adverse parameters (endometrial thickness <7mm, no triple line pattern and absent zone III flow) are present on TVS Color Doppler, we can predict endometrial receptivity. However, further study is needed to make a definitive conclusion.
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