ORIGINAL ARTICLE

Evaluation of Uterine Biophysical Profile and to Assess its Role in Predicting Conception among Unexplained Primary Infertility Patients

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Abstract

Introduction: Infertility is a devastating disease which affects its victims at a very basic level the ability to reproduce. This can be divisive to the couples involved, their relatives and friends. The influence of infertility can be immense. There are a lot of medical and social consequences of infertility and the psychological sequelae are one of them. Affected patients and their families suffer from loss of esteem, disappointment and depression. Considering the immense effect of infertility on the life of not only the affected couples but also on their families and relatives the present study was conducted with following objective. **Objective:** To evaluate the Uterine Biophysical Profile and to assess its role in predicting the conception outcome in spontaneous cycles in patients with unexplained primary infertility. **Material &Methods:** A prospective observational study was conducted in the Department of Obstetrics and Gynaecology, U.P. Rural Institute of Medical Sciences & Research, Saifaion 55 women with unexplained primary infertility after standard diagnostic work up. Ultrasound (TVS) measurement of all patients was performed in their midcycle of spontaneous cycle. The Uterine Biophysical Profile (UBP) i.e. certain sonographic qualities of the uterus were noted during the normal mid-cycle of these patients. These included 7 parameters: Endometrial thickness in greatest AP dimension of 7 mm or greater (full-thickness measurement), a layered ("5 line") appearance to the endometrium, myometrial contractions causing a wave like motion of the endometrium, homogeneous myometrial echogenicity, uterine artery blood flow (as measured by PI, less than 3.0), blood flow within zone 3 using color doppler technique, myometrial blood flow seen on gray-scale examination. The Uterine Scoring System for Reproduction ("USSR") was used to evaluate the total score. **Results:** Among 55 unexplained primary infertility patients 24 i.e. 43.63% conceived by serial ultrasonographic monitoring of spontaneous menstrual cycle and timed intercourse. According to USSR, with a 'perfect score' of 20, there was 80% conception rate. While 9 /15 patients (i.e 60%) conceived with a score of 17-19. With a score of 14-16, 10/23 patients conceived i.e. 43.37%. Only 8.33% conception rate was seen with a low score of < or = 13. Highest pregnancy rate (60%) was seen with an endometrial thickness of 7-9mm while zone IV endometrial blood flow gave maximum conception rate of 66.66%. **Conclusion**: UBP can prove to be a simple, reliable, reproducible, rapid and non-invasive tool to predict uterine environment and hence conception outcome.

Key Words

Ultrasound; Uterine Scoring System for Reproduction

Introduction

Infertility is a devastating disease which affects its victims at a very basic level the ability to reproduce. This can be divisive to the couples involved, their relatives and friends. The influence of infertility can be immense. There are a lot of medical and social consequences of infertility and the psychological sequelae are one of them. Affected patients and their families suffer from loss of esteem, disappointment and depression.

There are many variables of success associated with achieving pregnancy in a spontaneous cycle, few are beyond our control but they play a direct role in implantation and successful outcome.

In the menstrual cycle, the endometrium has no adhesive qualities until the implantation window phase, during which for a very short time, the environment of endometrium becomes favorable for implantation of gestational sac. This feature is referred to as endometrial receptivity [1].

There are a number of strategies that have been developed to evaluate endometrial receptivity, like histologic dating of an endometrial biopsy [2], endometrial cytokines in uterine flushing [3], the genomic study of a timed endometrial biopsy or more commonly a non-invasive ultrasound examination of the endometrium. Ultrasound examination of the endometrium is a commonly used simple, reliable, reproducible, quick and non-invasive method to assess endometrial receptivity during the treatment of infertility patients.

Although there is no definitive method for predicting successful conception during any given menstrual cycle, some sonographic findings do appear which may be useful in predicting the outcome following treatment. These findings are compiled into Uterine Biophysical Profile ("UBP"). The findings are weighted according to the Uterine Scoring System for Reproduction ("USSR") by M Applebaum [4].

Aims & Objectives

1. To evaluate the Uterine Biophysical Profile among unexplained primary infertility patients.
2. To assess its role in predicting the conception outcome in spontaneous cycles among these patients.

Material and Methods

A prospective observational study was conducted in the Department of Obstetrics and Gynaecology, U.P. Rural Institute of Medical Sciences & Research, Saifai on 55 women with unexplained primary infertility. Cases were selected from the women attending the infertility OPD of our institute with complaint of not able to conceive even after one year of regular unprotected coitus. After standard diagnostic work up in these patients, 55 women with unexplained primary infertility in the age group of 20-35 years and a normal menstrual cycle were considered for the study. The history of male infertility was excluded from the study. The purpose of the study was explained to the study participants. Anonymity and confidentiality of the data was assured. Ethical approval was obtained from Institutional Ethical Committee of UP RIMS&R.

Written informed consent was taken and a baseline TVS Ultrasound was performed on these patients on Day 2/3 of their spontaneous cycles. A regular follicular monitoring was done and a 3D power Doppler Ultrasound (TVS) measurement of all these patients was performed in their midcycle after they completely emptied their bladders. The Uterine Biophysical Profile (UBP) i.e. certain sonographic qualities of the uterus were noted during the normal mid-cycle of these patients. These included 7 parameters:

1. Endometrial thickness in greatest AP dimension of 7 mm or greater (full-thickness measurement)
2. A layered ("5 line") appearance to the endometrium
3. Blood flow within Zone 3 using color Doppler technique
4. Myometrial contractions causing a wave like motion of the endometrium
5. Uterine artery blood flow, as measured by PI, less than 3.0
6. Homogeneous myometrial echogenicity
7. Myometrial blood flow seen on gray-scale examination (internal to the arcuate vessels)

On basis of UBP, the Uterine Scoring System for Reproduction ("USSR") was done and total score as per Applebaum creiteria [4] was calculated. This comprised of evaluation of the following parameters:

1. Endometrial thickness (full-thickness measured from the myometrial-endometrial junction to the endometrial- myometrial junction)
2. Endometrial layering (i.e., a 5-line appearance)
3. Myometrial contractions (seen as endometrial motion)
4. Myometrial echogenicity
5. Uterine artery Doppler flow evaluation

6. Endometrial blood flow
7. Gray-scale Myometrial blood flow

Each parameter was scored as follows:

1. Endometrial thickness:
   a. < 7 mm = 0,
   b. 7 - 9 mm = 2,
   c. 10 - 14 mm = 3,
   d. > 14 mm = 1
2. Endometrial layering:
   a. no layering = 0,
   b. hazy 5-line/ tri laminar appearance = 1,
   c. distinct 5-line / tri laminar appearance = 3
3. Myometrial contractions (seen as wave-like endometrial motion):
   a. < 3 contractions in 2 minutes (real-time) = 0,
   b. > 3 contractions in 2 minutes (real-time) = 3
4. Myometrial echogenicity:
   a. coarse/inhomogeneous echogenicity = 1,
   b. relatively homogeneous echogenicity = 2
5. Uterine artery Doppler flow evaluation [Pulsatility Index – PI]:
   a. PI > 3.0 = 0,
   b. PI< 2.5 - 2.99 = 0,
   c. PI < 2.2 - 2.49 = 1,
   d. PI < 2.19 = 2
6. Endometrial blood flow within Zone 3:
   a. absent = 0,
   b. present, but sparse = 2,
   c. present multifocally = 5
7. Myometrial blood flow internal to the arcuate vessels seen on gray-scale examination:
   a. absent = 0,
   b. present = 2

Total USSR of all the patients were calculated using above parameters and timed intercourse was advised accordingly.

According to Applebaum4, the endometrial and peri-endometrial areas are divided in terms of endometrial vascularity into the following four

Zones:

Zone 1 -- a 2 mm thick area surrounding the hyperechoic outer layer of the endometrium

Zone 2 -- the hyperechoic outer layer of the endometrium

Zone 3 -- the hypoechoic inner layer of the endometrium

Zone 4 -- the endometrial cavity

Results

In the present study total 55 women with unexplained primary infertility were studied in their spontaneous cycle. When USSR scoring was calculated, 05 patients (9.1%) got a 'perfect score' of 20. While 15 patients (27.3%) landed up with a score of 17-19. Approximately 42% patients got a score of 14-16 and 21.8% (12 patients) got a score of ≤13. [Table-I]. As far as endometrial thickness is concerned maximum patients (45.5%) were in the group 7-9 mm, followed by those having 10-14 mm (34.5%) while, least had endometrial thickness >14 mm. Looking at the distribution of the peri-ovulatory endometrial blood flow of study subjects maximum were in zone III (40.0) followed by zone II (32.7%), zone I (16.4%) while only 10.9% were in zone IV.

Out of total 55 study subjects 24 patients (43.6%) conceived. With a 'perfect score' of 20, 80% conception rate was seen. While 9 /15 patients (i.e. 60%) conceived with a score of 17-19. With a score of 14-16, 10/23 patients conceived i.e. 43.4%. Only 8.3% conception rate was seen with a low score of ≤13mm. Endometrial thickness of <7mm gave only 22.2% of pregnancies. Maximum conception rate i.e. 60% was seen with endometrial thickness of 7-9mm. There was no conception i.e. 0% (0/02 patients) with endometrial thickness of >14mm while 36.8% patients conceived in the range of 10-14mm. Endometrial blood flow of zone IV gave highest conception rate of 66.6% followed by zone III (54.5%). While patients with endometrial blood flow only till zone I gave lowest i.e. 11.1% conception rate.

Discussion

Endometrial receptivity is crucial to the implantation of an embryo. According to study conducted by Narendra Malhotra *et al* [5] in spontaneous cycles of 222 patients, USSR score of 20 gave 80% of pregnancy rate while score of 17-19 gave 79% of conception. While only 7.6% conceived with a score of < or = 13. Similar results were seen in our study. This signifies that a score of 20 will obviously yield high percentage of pregnancies. But it is difficult to have a 'perfect score' of 20 in infertile patients. A Score of 17-19 is the score ideally we should try to obtain to have better pregnancy rates.

It is agreed that both endometrial thickness and endometrial and sub-endometrial blood flow pattern are useful as prognostic parameters for successful pregnancy. Adequate perfusion to the endometrium is vital to implantation. No consensus has been reached with regard to the minimum endometrial thickness required for successful pregnancy. According to present study maximum conception

rate (60%) was seen with endometrial thickness of 7-9mm. Oliveira JB [6] by their study concluded that pregnancies did not occur when the endometrial thickness was less than 7 mm however, other studies found that a minimum endometrial thickness of 6 mm is acceptable for implantation [7]. According to a study conducted by Thomas S *et al* [8] revealed that inadequate endometrium can be considered as a main fertility determining factor. According to study conducted by Kevin S *et al* [9] it was found that endometrial thickness was greater in cycles resulting in pregnancy than in cycles not resulting in pregnancy and clinical pregnancy rate increased gradually with increasing endometrial lining thickness beyond 9 mm. Interestingly, Sundstrom [10] reported a successful pregnancy with an endometrial thickness as little as 4 mm. Unexplained infertility appears to be associated with impairment of endometrial perfusion. Singh N *et al* [11] in their study found a higher pregnancy rate when the blood flow to the endometrium was in Zone III (51.8%) as compared to Zone I (14.8%). As per Ari Kim *et al* [12] study, sub-endometrial flow is vital to determine pregnancy outcome. In our study also we observed a higher pregnancy rate when the blood flow to the endometrium was in Zone III (54.5%) as compared to Zone I (11.1%).

Conclusion

Infertility and its management leads to a lot of stress and depression to the couple involved and if the couple is not able to conceive with the basic treatments available, they may have to go for Assisted Reproductive Techniques which demands great amount of time, energy- mentally and physically along with good amount of money to be put in.

Low USSR demonstrated decreased endometrial receptivity in women with unexplained infertility who failed to conceive. Parameters of UBP i.e endometrial thickness and blood flow to endometrial and sub-endometrial area are useful prognostic factors for a successful pregnancy. UBP can prove to be a simple, rapid and non-invasive tool to predict uterine environment and hence pregnancy outcome.

Relevance of the study

The present study contributes to further reinforcement of the evidence regarding role of UBP, endometrial thickness and peri-ovulatory endometrial blood flow in predicting the outcome in terms of pregnancy among females suffering from primary infertility.

Authors Contribution

PG: Designed study, data collection, drafting; SC: Drafting; AK: Statistical analysis; PKJ: Drafting.

Acknowledgement

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Tables

TABLE 1 DISTRIBUTION OF STUDY SUBJECTS AS PER UTERINE CHARACTERISTICS (N=55)

S. No.	Characteristic	No.	%
1	USSR		
	20	05	9.1
	17-19	15	27.3
	14-16	23	41.8
	≥13	12	21.8
2	Endometrial Thickness		
	<7 mm	09	16.4
	7-9 mm	25	45.5
	10-14 mm	19	34.5
	>14 mm	02	3.6
3	Peri-ovulatory Endometrial Blood Flow		
	Zone I	09	16.4
	Zone II	18	32.7
	Zone III	22	40.0
	Zone IV	06	10.9

TABLE 2 ASSOCIATION OF CONCEPTION WITH UTERINE CHARACTERISTICS

S. No.	Characteristic	Conceived (24) n (%)	Not Conceived (31) n (%)	Test of Significance
1	USSR			
	20	04 (80.0)	01 (20.0)	χ^2=10.40
	17-19	09 (60.0)	06 (40.0)	df=3
	14-16	10 (43.4)	13 (56.6)	P=0.01
	≤13	01 (8.3)	11 (91.7)	
2	Endometrial Thickness			
	<7mm	02 (22.2)	07 (77.8)	χ^2=5.68
	7-9mm	15 (60.0)	10 (40.0)	df=3
	10-14mm	07 (36.8)	12 (63.2)	P=0.12
	>14mm	00 (0.0)	02 (100.0)	
3	Peri ovulatory Endometrial Blood Flow			
	Zone I	01 (11.1)	08 (88.9)	χ^2=6.39
	Zone II	07 (38.8)	11 (61.2)	df=3
	Zone III	12 (54.5)	10 (45.5)	P=0.09
	Zone IV	04 (66.6)	02 (33.4)	