International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Study of Ovarian Reserve Parameters among Women Suffering from Secondary Subfertility Presenting in Infertility Clinic in a Tertiary Health Care Centre in Eastern India: A Prospective Observational Study

Dr. Shreeja Singh[1], Dr. Ankit Kumar[2]

[1]Post Graduate Resident, Department of Obstetrics & Gynaecology, Darbhanga Medical College, and Hospital, Laheriasarai, Darbhanga
Email: *shreejasingh90[at]gmail.com*

[2]Attending Consultant, Infertility Clinic, Yatharth Multispeciality Hospital, Noida Extension
Email: *ankitmaximus[at]hotmail.com*

Abstract: ***Background and Aim: Unexplained subfertility is diagnosed when standard tests for ovulation, tubal patency and semen analysis are all normal. overall incidence is 30%. We aimed to assess the availability of a test capable of providing reliable information regarding a woman's individual ovarian reserve within a certain age category. Methods: from January 2018 till June 2018, 100 females in OPD underage group between 20-35 years, suffering from secondary subfertility were selected. The collected data was analyzed using descriptive (mean, median, & standard deviation) and inferential statistics and results are presented using diagrams, graphs, and tables. The relationship between parameters i.e., AGE, BMI, Menstrual abnormality, Ovarian reserve parameters like D2 FSH, LH, AMH & antral follicular count were tested using Kruskal-Wallis's test (non-parametric test). Results: Out of 100 females in OPD, mean age was the mean age of the female partner was 32±2.7 years and that of male partner was 39±4.2 years. The variable Age (Years) was normally distributed in the 2 subgroups (Primary and secondary infertility). The mean age being highest in the secondary infertility group (t = -4.817, p = < 0.001). In terms of BMI, 54% were overweight and 37% of overweight group had primary subfertility and 67% had secondary subfertility. The following variables were significantly associated (p<0.005) with the variable 'Age (Years)': Complain, Obstetric History, Age Group, Period of Infertility (Years), Menstrual History, Day 2 AFC (Right Ovary), Day 2 AFC (Left Ovary), Peripherally Arranged Follicles, D2 FSH, AMH. Among the 100 couples suffering from secondary subfertility, 26% cases were tubal, 51% PCOD, 15% were ovulatory and 8% cases had endometriosis and that among women with PCOD more incidence is seen in women with secondary subfertility vs primary subfertility (54% vs 46%). Conclusion: We concluded that Overall FSH is most used screening tool for DOR, AFC and AMH exhibit less variability and are therefore promising tools. Currently there is no uniformly accepted definition of DOR.***

Keywords: subfertility, ovarian reserve, age, BMI, infertility

1. Background

In clinical medicine, secondary infertility is usually defined as the inability to conceive despite exposure to pregnancy for one year (2 years in some epidemiological studies), after having conceived at least once before. [1] This implies that women with secondary infertility do not necessarily have a living child.

Infertility is defined as a failure to conceive after one year of unprotected regular sexual intercourse. It is usually investigated after a year, although for some couples it may be appropriate to start investigations sooner. Some prefer the term subfertility to describe women or couple who are not sterile, but exhibit decreased reproductive efficacy. Epidemiological data indicate that conception occurs in 84% of women within 12 months and 92% by second year of ceasing contraception. [2]

The likelihood of spontaneous conception is affected by age, previous pregnancy, duration of subfertility, timing of intercourse during the natural cycle, extremes of body mass, and pathology present. A reasonably high spontaneous pregnancy rate still occurs even after the first year of trying. The estimates of the Census of India (1981, 1991, 2001) show that infertility in India has increased among reproductive-age couples.

It has risen from 13 per cent in 1981 to 16 per cent in 2001 among ever-married women [3]. It was observed that the infertility rate has declined between 1998–99 and 2005–06 [4]. Furthermore, another study from India found that about eight per cent of currently married women suffered from primary and secondary infertility, of which 5.8% per cent were secondary infertile [5]. This study also suggested that primary fertility decreases with age and was higher among younger women, while secondary infertility was higher among older women [5] infertility, of which 5.8% per cent were secondary infertile [5]. This study also suggested that primary fertility decreases with age and was higher among younger women, while secondary infertility was higher among older women [5].

Primary subfertility—a delay for a couple who have had no previous pregnancies. *Secondary subfertility*—a delay for a couple who have conceived previously, although the pregnancy may not have been successful (for example, miscarriage, ectopic pregnancy).

The causes of infertility issues are various, including social and biological factors. However, most of the studies agreed that around half of infertility among couples prevails due to anatomical, genetic, and immunological factors. Epidemiological studies identified the primary causes of infertility among women as menstrual disorders, diseases like obesity, thyroid diseases, diabetes, uterine factor, fallopian tubes, ovulation dysfunction, and cervical factor [6,7].

Infertility should be treated as a health issue, and therefore, the potential socio-demographic and lifestyle factors affecting both primary and Secondary infertility need to be examined thoroughly. The socio-demographic covariates have been well established using large-scale survey data for India [5],[8]. Even though the exact prevalence of infertility in India is difficult to ascertain, it affects 10 to 15% couples in the western world. There has not been any major increase in the prevalence of infertility in recent years, but there is a greater awareness of the problem and availability of more effective treatments like in vitro fertilization.

The purpose of this study was to assess ovarian reserve in treatment of subfertility. ovarian reserve is predictor of good quality preovulatory oocyte in ovaries. The availability of a test capable of providing reliable information regarding a woman's individual ovarian reserve within a certain age category would enable the clinician to provide an individually tailored treatment plan.

2. Methods

A prospective type of study was conducted in a selected fertility centers in Darbhanga Medical College and Hospital. The duration of the study was from January 2018 through June 2018 among the couples suffering from secondary subfertility attending this center. We include the couple who are suffering from secondary sub fertility for more than two years, had no living issues and can showed all the documentary reports of their investigation and treatment. The female partner aged above 35 years and below 20 years were excluded from the study. Data was collected by using face to face interview with the couple suffering from secondary subfertility in the study area through a semi structured questionnaire. An informed consent was ensured. Some secondary data was collected from treatment file with the patient. Instrument for data collection were semi-structured questionnaire, observational checklist (including questionnaire, weight and height measurement instrument and available investigation reports). Socio demographic and other previous documentation in terms of D&C, MRI, Chromopertubation, diagnostic laparoscopy, USG AFC, AMH, Serum Testosterone, FAI, Thyroid profile, GTT were recorded. Hormonal reports of female partner and semen analysis of male partner were collected. Treatment of infertility like ovulation induction by CC/Letroz or GnRH or any previous procedure like IUI, IVF were noted. The data from the complete Questionnaires were entered in SPSS 20 and analyzed.

The relationship between parameters i.e., Age, BMI, Menstrual abnormality, Ovarian reserve parameters like D2 FSH, LH, AMH & antral follicular count were tested using Kruskal-Wallis's test (non-parametric test).

3. Results

In this study 100 couples suffering from secondary subfertility were included. The mean age of the female partner was 32±2.7 years and that of male partner was 39±4.2 years. Minimum age of the female was 20 and that of male 27. Maximum age of the female was 35 and that of male 52. (Tab 1)

Table 1: Distribution of female respondents by age

Age of Female Respondent	Frequency	Percent
20	11	11
22	5	5
25	27	27
26	7	7
29	7	7
31	27	27
32	6	6
33	5	5
35	5	5

Table 2: Association in between age and complains

Age	Primary Infertility	Secondary Infertility	T-Test	p value
Mean	25.53 (4.50)	28.81 (3.41)	-4.817	<0.001
Median	24.5 (22-29)	29 (26-31.75)		
Range	20 - 35	20 - 35		

The variable Age (Years) was normally distributed in the 2 subgroups of the variable Complain. (Primary and secondary infertility). Parametric tests (t-test) were used to make group comparisons. There was a significant difference between the 2 groups in terms of Age (Years) ($t = -4.817$, $p = < 0.001$) with the mean age being highest in the secondary infertility group. (Tab 2)

Distribution of female respondents by BMI

Table 3.1 Shows 8% were underweight, 12% were normal, 54% was overweight, and 26% respondents were obese.

Table 3.2 shows 37% of overweight group had primary subfertility and 67% had secondary subfertility.

Table 3.1: Distribution by BMI

BMI	Frequency	Percent
<18	8	8%
18-24	12	12%
25-29	54	54%
>30	26	26%
TOTAL	100	100%

Table 3.2: Distribution by type of subfertility as per BMI

BMI	Primary Subfertility	Secondary Subfertility
<18	6	2
18-24	9	3
25-29	20	34
>30	12	14
TOTAL	47	53

Distribution of the female respondent on basis of history, hormonal and radiological assessment:

Table 4: Factor wise distribution of cause of subfertility

	Frequency	Percent
Tubal	23	23%
PCOD	51	51%
Ovulatory	15	15%
Endometriosis	8	8%
Total	100	100%

The factors of subfertility among the female respondents were 23% cases tubal, 51% PCOD, 15% were ovulatory, 8% cases had endometriosis. (Tab 4).

Fig 1. "(a)". Diagrammatic representation of female respondent with factors of subfertility.

Fig 1. "(b)": Distribution as per cause of subfertility for the female respondent shows that among women with PCOD more incidence is seen in women with secondary subfertility vs primary subfertility (54% vs 46%).

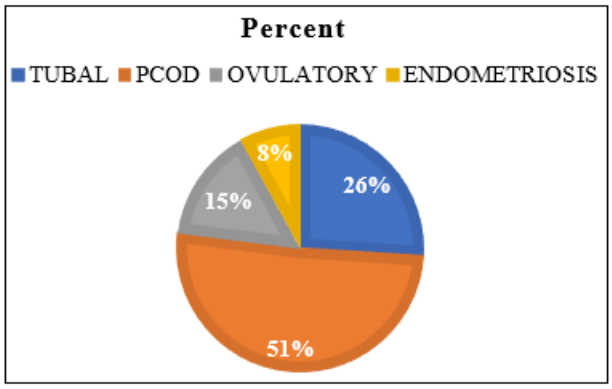

Figure 1 (a): diagrammatic representation of cause of subfertility

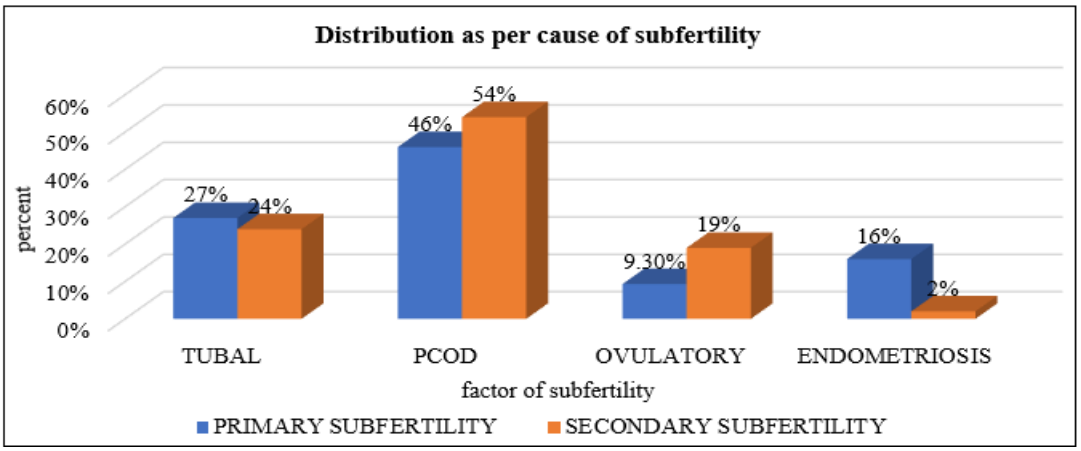

Figure 1 (b): Distribution as per cause of subfertility

Fig 2: The scatterplot depicts the correlation between Day 2 AFC (Right Ovary) and Age (Years). Individual points represent individual cases. There was a moderate negative correlation between Day 2 AFC (Right Ovary) and Age (Years), and this correlation was statistically significant (r = -0.42, p = <0.001). For every 1 unit increase in Age (Years), the Day 2 AFC (Right Ovary) decreases by 0.42 units. (Tab 5)

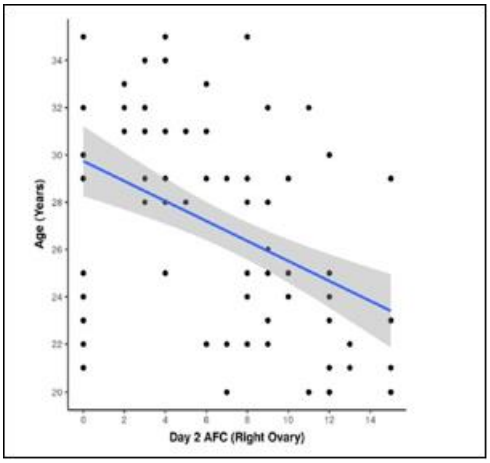

Figure 2: Scatter plot depicting correlation with D2 AFC (Right Ovary)

Table 5: Pearson correlation coefficient with D2 AFC (Right Ovary)

Correlation	Pearson's Correlation Coefficient	P Value
Day 2 AFC (Right Ovary) vs Age (Years)	-0.4	<0.001

Fig 3: The below scatterplot depicts the correlation between Day 2 AFC (Left Ovary) and Age (Years). Individual points represent individual cases. There was a weak negative correlation between Day 2 AFC (Left Ovary) and Age (Years), and this correlation was statistically significant (r = -0.26, p = 0.019).

Table 6: For every 1 unit increase in Day 2 AFC (Left Ovovary), the Age (Years) decreases by 0.35 units.

Correlation	Pearson's Correlation Coefficient	P Value
Day 2 AFC (Left Ovary) vs Age (Years)	-0.3	0.019

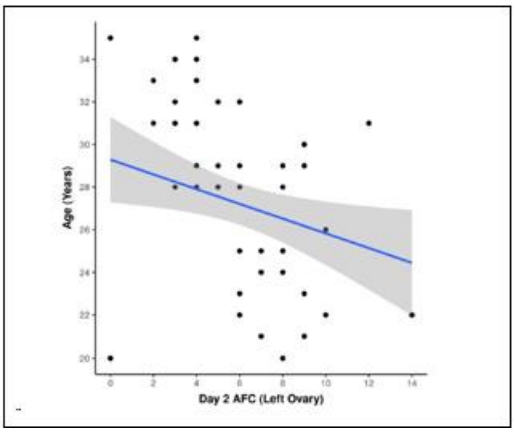

Figure 3: Scatter plot depicting correlation in between D2 AFC (Left Ovary) and Age

Fig 4: The above scatterplot depicts the correlation between D2 FSH and Age (Years). Individual points represent individual cases.

There was a moderate positive correlation between D2 FSH and Age (Years), and this correlation was statistically significant (r = 0.4, p = <0.001)

For every1 unit increase in Age (Years), the D2 FSH increases by 0.41 units. (Tab 7)

Table 7: Pearson correlation in between D2 FSH and Age

Correlation	Pearson's Correlation Coefficient	P Value
D2 FSH vs Age (Years)	0.4	<0.001

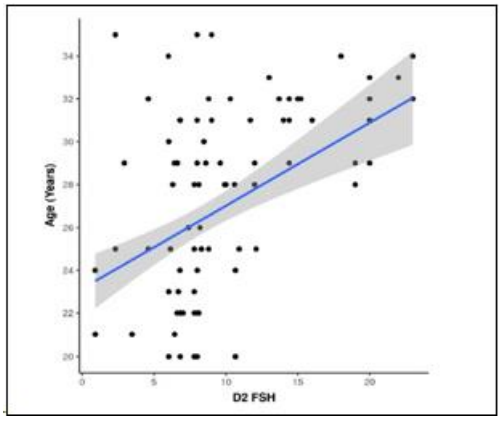

Figure 4: Scatterplot depicting correlation in between D2 FSH and Age

Fig 5: The above scatterplot depicts the correlation between AMH and Age (Years). There was a moderate negative correlation between AMH and Age (Years), and this correlation was statistically significant (r = -0.34, p = <0.001).

For every 1 unit increase in Age (Years), the AMH decreases by 0.48 units. (Tab 8)

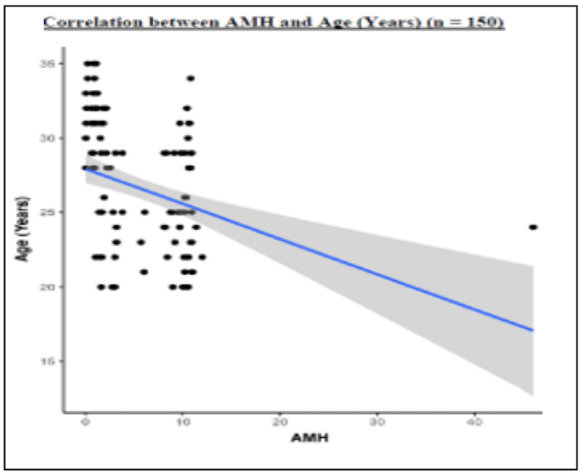

Figure 5: Correlation in between AMH and Age

Table 8: Pearson correlation coefficient in between AMH and Age

Correlation	Pearson's Correlation Coefficient	P Value
AMH vs Age (Years)	-0.3	<0.001

Fig 6: The below scatterplot depicts the correlation between D2 LH and Age (Years). Individual points represent individual cases. There was a weak positive correlation between D2 LH and Age (Years), and this correlation was not statistically significant (r = 0.12, p = 0.147) (Tab 9)

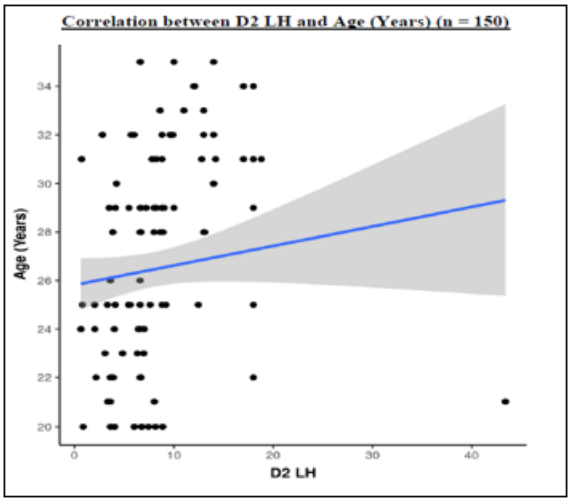

Figure 6: The above scatterplot depicts the correlation between D2 LH and Age (Years)

Table 9: Pearson correlation coefficient in between D2 LH and Age

Correlation	Pearson's Correlation Coefficient	P Value
D2 LH vs Age (Years)	0.1	0.147

4. Discussion

Infertility is a fairly common problem in our country and has got more social and clinical significance in a developing country like India. A prospective observational study was done in a selected fertility center, in Darbhanga Medical College and Hospital. This study shows that mean age of the female partner was 32 and maximum age of the female was 35.

The findings of the present study are compatible with references in medical literature that female fertility begins to decline around 30 years of age and a fall in the male fertility potential around 40 years of age. [9,10] overall fertility rates are 4-8% lower in women aged 25-29 years, 15-19% lower in those aged 30-34 years, 26-46% lower in women aged 35-9 years and as much as 95% lower for women aged 40-45 years.

In our study 54% of the women were overweight and out of this, 37% presented with primary subfertility and 63% presented with secondary subfertility. This was compatible with standard US literatures study that shows that obesity in women is associated with menstrual irregularities, decreased fertility, and increased risks of miscarriage and obstetric and neonatal complications. [11]

In this present study, the factors of subfertility among the female respondents were 26% cases tubal, 51% PCOD, 15% were ovulatory and 8% cases had endometriosis. And as per the distribution of subfertility for the female respondents with PCOS shows that among women with PCOD more incidence is seen in women with secondary subfertility vs primary subfertility (54% vs 46%). Though it is assumed that the main cause of secondary subfertility is the tubal pathology. However, in this study big percentage of female was suffering from PCOD. Another group of women had ovulatory disturbance with irregular ovulation or anovulation named as non PCO ovulatory disorder. There was hormonal imbalance, history of ovarian cyst, endometriosis and DM were found in some cases of ovulatory disorder. Women suffering from secondary subfertility present with hormonal imbalance like Hypothyroidism or Hyperprolactinemia. Although in this study, no cases of hormonal imbalance associated with subfertility were seen.

In this study, the following variables were significantly associated ($p<0.005$) with the variable Age (Years), Complain, Obstetric History, Age Group, Period of Infertility (Years), Menstrual History, Day 2 AFC (Right Ovary), Day 2 AFC (Left Ovary), Peripherally Arranged Follicles, D2 FSH, AMH.

Ovarian reserve tests includes both biochemical and ultrasonographic measures of the size and quality of ovarian follicular pool. Biochemical tests include both basal measurements, such as FSH, estradiol, inhibin B and Anti Mullerian Hormone (AMH), and provocative tests, such as clomiphene citrate challenge test. Ultrasonographic measures of ovarian measures includes AFC (antral follicle count) and ovarian volume. [11]

Serum FSH vary significantly across cycle, the concept of obtaining FSH in between D2-D4, with repeat tests is of little value. Therefore, many authors prefer to additionally measure baseline serum estradiol. When basal FSH is normal and the estradiol concentration is elevated (>60-80 pg/ml), the likelihood of poor response to stimulation is increased and the chance of pregnancy is decreased. [11]

Anti-Mullerian Hormone (AMH) is an excellent diagnostic aid to evaluate the female fertility potential as the level in the blood indicates its optimum or borderline potentiality which helps the couple to make an early decision. [12]

AMH is a very promising screening test for Ovarian Reserve and studies shows that it is likely to be more useful in a general IVF population or in women at high risk for poor ovarian reserve.

Histologic studies have revealed that the number of small antral follicles in the ovaries is proportional to the number of primordial follicles remaining. A low AFC has high specificity for predicting poor response to ovarian stimulation and treatment failure, making it a useful test, but low sensitivity limits its overall clinical utility. [11]

Therefore, according to this study, overall FSH is most used screening tool for DOR, but a single value is very less reliable due to high inter and intracycle variability. AFC and AMH exhibit less variability and are therefore promising tools. Currently there is no uniformly accepted definition of DOR.

Studies regarding other provocative tests for ovarian reserve like exogeneous FSH stimulated estradiol, inhibin B or AMH levels, clomiphene citrate challenge test, found no evidence that that these more complex and costly tests predict response to ovarian stimulation or pregnancy better than basal FSH, AMH and AFC. [11]

In this study, female respondent's age above 35 years show decrease fertility potential or no fertility potential with the report of Anti-Mullerian Hormone (AMH). Which is important to stop the couple to take unnecessary hormone to induce or stimulate ovaries.

5. Conclusion

This study concluded that ovarian reserve tests should always be interpreted with caution. These tests results should not be used to deny treatment, but only to obtain prognostic information that may help to guide the choice of treatment and the best use of available resources. Therefore, although the probability of pregnancy may be low, many with abnormal test results will achieve pregnancy if afforded the chance.

References

[1] WHO. Challenges in reproductive health research:biennial report 1992-1993. Geneva: World Health Organization. World Health Organization. 1994:186.
[2] Bari S et al. Int J Reprod Contracept Obstet Gynecol. 2018 Mar; Secondary subfertility among the couple attending selected fertility centre of Dhaka, Bangladesh;7(3):817-823.
[3] Ram U. Childlessness in time, space and social groups and its linkages with fertility in india. 2006.
[4] Sarkar S, Gupta P. Socio-Demographic Correlates of Women's Infertility and Treatment Seeking Behavior in India. J Reprod Infertil. 2016; 17: 123–132. https://doi.org/10.1210/jcem.90.4.9997 PMID: 27141468
[5] Syamala TS. INFERTILITY IN INDIA: LEVELS, TRENDS, DETERMINANTS AND CONSEQUENCES. 25
[6] Sarkar S, Gupta P. Socio-Demographic Correlates of Women's Infertility and Treatment Seeking Behavior in

India. J Reprod Infertil. 2016; 17: 123–132. https://doi.org/10.1210/jcem.90.4.9997 PMID: 27141468.

[7] Vayena E, editor. Current practices and controversies in assisted reproduction: report of a meeting. Geneva: WHO, Department of reproductive health; 2003.

[8] Evens EM. A Global Perspective on Infertility an Under Recognized Public Health Issue. University Center North Carolina at Chapel Hill. 2004; 18: 1–40.

[9] Adetoro OO, Ebomoyi EW. The prevalence of infertility in a rural Nigerian community. Afr J Med Med Sci. 1991; 20:23-7.

[10] Shireen JJ. Infertility in India: levels, patterns and consequences: priorities for social research. J Fam Welf. 1998; 44:15-24.

[11] Speroff's Clinical Gynecologic Endocrinology and Infertility, 9TH edition, chapter 27; female infertility

[12] Bresnick ER. A holistic approach to the treatment of the crisis of infertility. J Marital Fam Therap. 1981; 7:181-8.