

Determinants of Successful Outcome in Couples Consulting Infertility Clinic—Postgraduate Institute of Medical Education and Research, Chandigarh, India: A Record-based Analysis

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ABSTRACT

Objective: To identify the factors determining the successful outcome in infertile cases reporting to infertility clinic at a tertiary hospital, Chandigarh, India.

Design: Retrospective record based analysis.

Setting and records: The records of all 2049 patients registered with infertility clinic over the period of 5 years from January 2002 to December 2006 were included for the analysis. Data regarding sociodemographic details, personal history, menstrual history of female, obstetrics history, Past medical and surgical history of couple; gynecological disorder, husband's sexual disorder, details of investigation and treatment received by couple and its outcome were retrieved from the records. Logistic regression model was used to reveal the most important determinants of successful outcome in infertile couples.

Results: The conception rate was twice among younger women (≤ 30 years) compared to older than 30 years. The couples with shorter duration of infertility (≤ 3 years) were more than twice likely to conceive compared to those with duration longer than 3 years. Normal semen analysis findings in men and absence of any demonstrable cause of infertility in women were also found to be favorable predictor of treatment outcome among infertile couples.

Conclusion: Our finding can help couples and clinicians in charting out the workup and counseling plan for individual couples. However, further studies are needed to validate the model developed in study.

Keywords: Infertility, India, Women, ART.

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INTRODUCTION

Globally around 8 to 10% of couples experience some sort of infertility in their reproductive lives.¹ World Health Organization estimates that in India the burden of primary and secondary infertility is 3 and 8% respectively.² National Family Health Survey III reported 3.5% of currently married women in India were infertile.³ The District Level Household survey reported that around 8% of women ever had infertility.

Recent advancement in assisted reproductive technology (ART) has attracted more and more infertile couples to opt for various ART options available.^{4,5} However, outcome of treatment among couples is affected by various clinical and other conditions.⁶⁻²³ The important determinants of treatment outcome are duration of infertility, causes of infertility, previous pregnancy, age of female partner and the duration of marriage. However, this knowledge of determinants of infertility outcome for any infertility centers should be identified to help couples and clinicians in charting out the workup and counseling for individual couples. Therefore we aimed to identify the factors determining the successful treatment outcome among infertile couples reporting at infertility clinic, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

METHODS

We analyzed infertility clinic records of 5 years from January 2002 to December 2006 to find out the factors determining successful treatment outcome among infertile couples. Compliance status of the cases was noted. A proforma was developed to extract the information on sociodemographic details, obstetrics history, medical history, gynecological history, physical examination findings, investigation records, complete treatment and follow-up from clinic records of each patient maintained at infertility clinic. A standard protocol for workup is followed at infertility clinic, PGIMER (Flow Chart 1). The successful treatment outcome was defined as conception following treatment.

Institute Ethical Committee approved the study. All the data were entered into excel spread sheet and SPSS (version-10.2) was used for analysis. Variables with significant p-value, Chi-square test and odds ratio were further evaluated by step wise backward logistic regression method to identify set of most significant variables having strong correlation with the favorable outcome. A model was developed using regression analysis to identify the predictors of successful outcome in infertile couples.

The ‘survival analysis’ a statistical method has been proposed to select certain clinical or historical characteristics that are predictors of pregnancy among infertile couples. It includes three steps: life table organization of follow-up data, single variable analysis by log rank test, and multiple variable analyses with the use of proportional hazard regression model.

RESULTS

A total of 2049 infertile couples visited to infertility clinic, PGIMER, Chandigarh from January 2002 to December 2006 and were included for analysis. The number of patients reporting and registering with infertility clinic

showed increasing trend since 2003 with the introduction of *in vitro* fertilization technologies in the clinic (Graph 1).

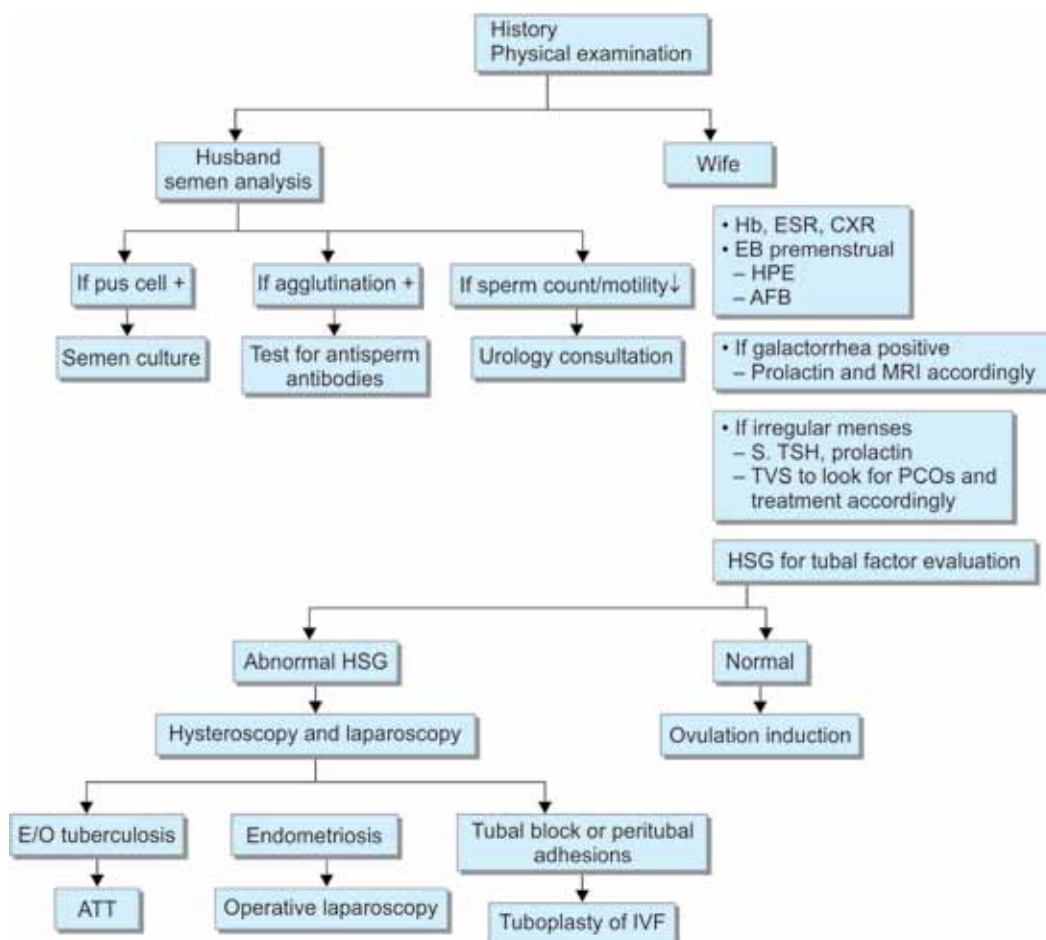
Around 958 (49%) male partners and 922 (46.7%) female partners were educated up to graduation or above. By occupation majority (66.4%) of male partners were teachers, managers, businessmen while majority (76%) of female partners were homemakers.

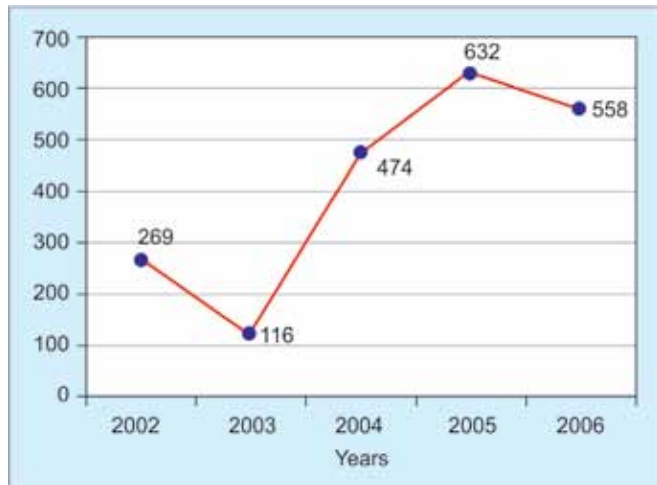
Of all 2049 couples, primary infertility and secondary infertility was diagnosed in two third and one third couples respectively. Among couples with secondary infertility, 143 (21.1%) had one or more living child, where as 330 (48.27%) had one or more abortions and 65 (9.5%) had prior ectopic pregnancy. Around 37.7 % (772) couples had duration of infertility less than 3 years while 46.8% (942) and 15.0% (307) had longer duration of infertility, i.e. 4 to 9 years and more than 10 years respectively.

In majority (62.2%) of the infertile couples female factor was responsible for it whereas male factor contributed in 5.2% cases. Around 13% of infertility resulted due to both female and male factors. The cause for infertility could not be ascertained in 19.5% couples despite detailed workup.

Less than half (576; 47.8%) of the females, had body mass Index (BMI) of <24; 537 (44.6%) had BMI between

Flow Chart 1: Infertility workup of infertile couples





Graph 1: Registration status of infertile couples over the study period

24.1-32 and 90 (7.5%) had a BMI \geq 33. Menstrual cycle was regular among majority (75%) of infertile women while few (22%) had oligomenorrhea. The proportion of women who reported history of tuberculosis, thyroid dysfunction and diabetes mellitus were 9.2, 5.2 and 0.7% respectively. In addition, 148 (7.2%) women had hirsutism, 154 (7.5%) had galactorrhea and 172 (8.4%) had abnormal pelvic examination findings. Some (14.29%; 292) of females had undergone tubal correction surgery or laparoscopy/laparotomy for tubal assessment, few (4.1%; 85) had undergone ovarian cyst removal or ovarian drilling/puncture for polycystic ovarian diseases. Hormonal analysis among females revealed abnormal Prolactin level and abnormal TSH/T3/T4 level in 218 (14.3%) and 61 (4%) respectively.

Ultrasonography revealed PCOD in one fifth females (415) and fibroids in 69 (3.4%), hysterosalpingography detected 696 (41.06) females had tubal block/Genital TB findings. In 77 (3.8%) females abnormal endometrial biopsy findings consistent with inflammatory granulomatous infection (Tuberculosis) was found. Tubal disorder was confirmed among one third of women by laparoscopy. In addition, laparoscopy detected 128 (6.2%) endometriosis cases and 79 (6.43%) multi organ involvement.

Regarding male factors, few (30; 5.9%) were found to be suffering from some illnesses; (17; 0.8% urinary tract infection). Among males, very few (1.1%; 22) had undergone varicocele/hydrocele repair. Overall, around 80% of infertile women and 94% men had no past history of significant illness.

Semen analysis (n = 1866) revealed normal finding among 1446 (70.6%), 278 (14.8%) males had oligo/asthenospermia, 127 (6.8%) had abnormal pus cells in semen (infection) and 15 (1.7%) had azoospermia.

One fourth of all couples (512) had received infertility treatment in past before consulting PGI infertility clinic. One third (31.1%; 635) couples were counseled about

fertile days of the menstrual cycles, one fourth (496) received ovulation induction with clomiphene and one fifth (406) females received ovarian stimulation with IUI (with husband's sperms).

Overall 796 (38.8%) women conceived out of 2049 registered infertile cases during the reference period. One fifth (158) women reported spontaneous conceptions either before complete investigation or after leaving the treatment (Flow Chart 2). More than one third of spontaneous conceptions were seen among females after endometrial biopsy procedure (62); 24 (15.2%) couples conceived before any workup on advice on fertility periods only.

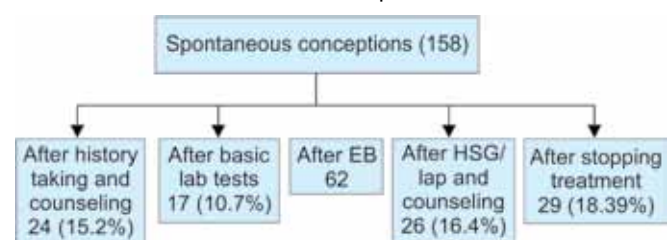
There were eight twin pregnancies and two triplets born among the recorded live births. Among socio-demographic factors, age of both wife and husband and education level of both husband and wife were found to be significant predictor of treatment outcome. Conception rate was higher among women of \leq 30 years age as compared to women aged $>$ 30 years, i.e. (45.5%; 628 compared to (25.1%; 168) and this association between age and treatment outcome was statistically significant ($p < 0.05$). Conception rate was significantly higher in females with education \geq matriculation (40.5%; 626). All infertility history variables like type of infertility (0.038), type of partner infertility (0.000) and duration of infertility (0.000) had significant relation with outcome among couples.

Among couples with primary infertility 37.3% (512) conceived as compared to 42.1% (284) in secondary infertility cases. More than half of couples with duration of infertility \leq 3 years conceived (55.6%; 429) compared to $>$ 3 years duration (28.3%).

More than one third of couples with normal semen analysis of male partners (39.5%; 571) and normal hormonal findings of female partner (35.1%; 410) conceived. Higher conceptions rate was observed among females with normal endometrial biopsy findings (39.3%; 592) and normal HSG findings (40.3%; 381) and one third of females with normal laparoscopy findings conceived (151; 31.1%).

Significantly higher proportions of couples with no demonstrable cause of infertility conceived (46.3%; 185) as compared to male partner infertility (29%; 31). One-third

Flow Chart 2: Details of spontaneous conceptions among infertile couples



of the couples with both partner infertility conceived (30.3%; 81).

Half of females with no demonstrable gynecological disorder conceived (50.5%; 293), while comparable conceptions were seen among females with PCOD (110; 41.2%) and anovulation disorders (97; 44.9%). Only one fourth of those with tubal disorders (141; 27.8%) and endometriosis (44 ; 29.1%) conceived.

Significantly higher conception rate was seen among couples with no demonstrable cause of infertility in male partners (41.1%; 686), while one third (34.7%; 17) of conceptions were seen among male partners with accessory gland infection after treatment with suitable antibiotics. Only one fourth of male partners with oligo/asthenospermia conceived (26.8%; 66).

The type of infertility treatment received by couples was found to be significantly (p = 0.000) related to the outcome. The number of treatment sessions attended by couples did not affect the outcome (p = 0.373). About half of couples who received ovulation induction (48.8%; 242) conceived and 37.3% (237) who received counseling and advise on fertility periods with minimal stimulation conceived.

Of all infertile couples who conceived, 40.70% (324) conceived within 1 year of follow-up, 35.92% (286) conceived in second year of follow-up and 14.32% (114) conceived in third year of follow-up (Table 1).

Ten variables were found to be statistically significant on univariate analysis (Table 2). However, in seven steps we got a set of only four significant variables as predictors of treatment outcome in infertility viz age of wife, duration of infertility, semen analysis, and gynecological disorders. The younger woman (≤ 30 years) and couples with shorter duration (≤ 3 years) of infertility were more likely to experience successful treatment outcome compared to older women (> 30 years) and those with longer duration (3 years) of infertility. The conception rate was higher if the male partner had normal semen analysis findings compared to those with abnormal semen results. Among female factors of infertility, the chances of conception were more if females had no demonstrable cause

of infertility and females with anovulatory disorders compared to other gynecological disorders (Table 3).

DISCUSSION

The success rate of infertility treatment has been a matter of research in many countries. The knowledge about predictors of successful treatment outcome can help in ameliorate the apprehension of couples undergoing treatment.

Our study supported the findings of other studies that the chances of better treatment outcome are influenced of age of the female partner.^{6,8,9} We observed that the chances of conception increased with education level of couple especially that of female. The possible reason could be better level of awareness about the disease as well as treatment modalities among educated couples. This would have resulted into early seeking for the treatment which indirectly influenced the treatment outcome.

Female factor infertility was found in majority (62.2%; 1275) of enrolled infertility patients presenting at this clinic similar to findings of other studies.⁶ In general, one fourth of infertility is contributed each by male and female factors and rest by both or no demonstrable cause. The high proportion of female factor infertility in our study could be due to the fact that male partners did not want to get examined by doctors due to fear of fault being found within him. This is one of the important reasons that men usually avoid any investigations to be done for them. The stigma attached to the infertility is one of the most important barrier for seeking treatment or advice for it. On the other, hand it is usual in Indian society to blame only woman for not bearing a child. Because, in India it considered that to give birth is duty as well as norm for woman. Therefore, they are likely to report at treatment centers to seek care and undergo all invasive investigations and treatments to have conception.

Absence of any demonstrable cause of infertility has been reported to be favorable factor for treatment outcome.⁶ Our study findings are consistent with it. An unfavorable treatment outcome (28.3 vs 55.6% among

Table 1: Year-wise conception rate among infertile couples as per their year of registration

Year of registration (cases registered)	Year-wise number of women who conceived							Total women conceived no. (%)
	2002 (%)	2003 (%)	2004 (%)	2005 (%)	2006 (%)	2007 (%)	2008 (%)	
2002 (269)	35 (33.3)	35 (33.3)	6 (5.7)	13 (12.4)	10 (9.5)	5 (4.8)	1 (1)	105 (39)
2003 (116)		11 (18)	23 (37.7)	10 (16.4)	11 (18)	5 (8.1)	2 (3.3)	62 (53.4)
2004 (474)			64 (32)	76 (39.4)	36 (18.7)	14 (7.3)	3 (1.6)	193 (42.2)
2005 (632)				95 (37.5)	101 (39.9)	49 (19.4)	8 (3.2)	253 (40)
2006 (558)					119 (65)	51 (27.9)	13 (7.1)	183 (32.8)
Total (2049)	35	46	93	194	277	124	27	796 (38.8)

Table 2: Summarized findings of univariate analysis of significant variables with outcome of couple's infertility

Variables	Conceived		χ^2 (p-value) OR (CI)
	Yes (%)	No (%)	
Age of wife (n = 2049)			
≤30 years	628 (45.5)	751 (54.5)	79.5 (0)
>30 years	168 (25.1)	502 (74.9)	2.499 (2.037-3.065)
Age of husband (n = 2017)			
≤30 years	400 (48.3)	428 (51.7)	53.253 (0)
>30 years	383 (32.2)	806 (67.8)	1.967 (1.638-2.361)
Husband's education status (n = 1954)			
< Secondary	70 (29.3)	169 (70.7)	10.897 (0.001)
≥ Secondary	693 (40.4)	1022 (59.6)	0.611 (0.455-0.820)
Wife's education status (n = 1972)			
< Secondary	143 (33.6)	283 (66.4)	6.730 (0.010)
≥ Secondary	626 (40.5)	920 (59.5)	0.743 (0.593-0.930)
Type of infertility (n = 2049)			
Primary	512 (37.3)	862 (62.7)	4.409 (0.038)
Secondary	284 (42.1)	391 (57.9)	0.818 (0.678-0.987)
Duration of infertility (n = 2021)			
≤3 years	429 (55.6)	343 (44.4)	149.029 (0)
>3 years	354 (28.3)	895 (71.7)	3.162 (2.621-3.816)
Semen analysis (n = 1866)			
Normal	571 (39.5)	875 (60.5)	10.689 (0.001)
Abnormal	129 (30.7)	291 (69.3)	1.472 (1.167-1.858)
Endometrial biopsy (n = 1846)			
Normal	592 (39.3)	916 (60.7)	12.425 (0)
Abnormal	98 (29)	240 (71)	1.583 (1.224-2.046)

Table 3: The summary statistics of significant variables selected in model

Variables	Adjusted Odds ratio	95%CI
Age of wife	2.1	1.6-2.7
Infertility duration	2.7	2.1-3.3
Semen analysis	1.6	1.2-2.1
Gynecological disorder		
No demonstrable cause	1.9	1.3-2.7
Tubal/GTB/PID	0.8	0.5-1.1
Anovulation	1.5	1.0-2.4
PCOD	1.4	0.9-2.0
Endometriosis	0.8	0.5-1.3
Uterine disorder	1.9	0.9-4.2

Reference variables: For age of wife, age > 30 years; for infertility duration, duration > 3 years; for semen analysis, abnormal findings and for gynecological disorders, multiorgan disorders; Figures in bold are statistically significant

couples with longer duration (>3 years) of infertility as compared to couple with shorter duration (≤3 years) could be attributed to number of psychological and etiological implications and also the fact that longer duration of infertility means that the problem is serious and it is likely that couples might had already have tried various options. Further, advancing age itself is an unfavorable factor for conception rate which is likely to be higher among couples with longer duration of infertility considering the mean age of marriage of women in India. This has been propounded in number of other studies.^{10,12,16}

Dhaliwal et al observed maximum conceptions (65.2%) in couples with <24 months duration of infertility.⁶

The effect of occupational and lifestyle factors like obesity, smoking, alcohol intake and psychosocial factors on infertility has received much attention recently.^{11,17,18} The combined effect of several negative lifestyle factors has been associated with a progressive reduction in fertility.¹¹ In our study also, 18% husbands reported smoking and alcohol consumption. However, underreporting of unhealthy lifestyle is not uncommon which could have resulted into lesser proportion of men as smoker in our study compared to general population.

Higher conception rate among women with normal HSG (40.3%; 381) compared to those with abnormal HSG reports (31.2%; 234) is expected finding as reported by others studies because infertility due to tubal factor has been reported to be an adverse factor for conception rate.²⁴ In the current study also tubal factor infertility was found to be adversely affecting the conception rate where it was only 27.8%. Similar findings were observed in other studies.⁶ The conception rate is not only influenced by the presence or absence of tubal pathology but also the severity of damage in fallopian tubes.²⁵⁻²⁷

Higher conception rate of 44.9% (97) observed among females with anovulatory menstrual cycles in current study is similar to results of other studies.^{6,28} Overall conception rate as estimated in our study, i.e. 38.8% (796)



among all infertile couples is higher than usual range of 20 to 30% reported in other studies. However, success rate of treatment should ideally be evaluated based on live birth rate rather than conception rate. Because, few proportion of conceptions are likely to end as miscarriage. Moreover, this conception rate is likely to be an underestimation. It is likely to improve further when couples are followed up for longer duration since more than half (1120) cases were followed up for only 1 to 2 years in our study. Overall trends of conceptions as per the registration year also hint toward the possibility of increase in the conception rate in coming years. For example, it increased from 39% for women registered in 2002 to 53.4% in women registered in 2003. In addition, the options for infertile couples have also increased since 2002 with the introduction of IVF procedure in PGIMER, infertility clinic.

The predictors of successful treatment outcome found in this study were consistent with other studies.^{6,7,13,19,21,24} Thus, the knowledge of age of female partner and duration of infertility after taking history of couple followed by semen analysis of male partner and ascertainment of correct cause of infertility in female partner after complete workup can help the clinicians to predict the outcome in infertile couples.

The study has its own share of limitations such as the individual cases were not followed up personally in the study. It was a record based analysis therefore variables that were recorded into registers could only be analyzed. Moreover, the reference period was 2002-2006 only therefore; follow-up duration for calculation of conception rate of 2005-2006 cases was lesser as compared to those registered in 2002-2004. So, the results should be interpreted accordingly. Other limitation is that we defined favorable treatment outcome in terms of conception rate which can overestimate the benefits of treatment as compared to live birth rate because some of the conception is likely to result in miscarriage.

To conclude, the model developed in this study can be further tested and validated to see its robustness, goodness of fit and statistical significance. The findings of present study also suggested the need for further research in this area in Indian context in different settings to validate this study findings and for individualizing the workup plan and intervention plan for infertile couples.

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