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Factors associated with infertility among married women in Rajshahi City, Bangladesh

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ABSTRACT

Infertility has become a growing problem among reproductive aged women in both developing and developed countries. Recent statistics indicate a significant number of married couples suffering from infertility and visiting infertility centers has increased in Bangladesh. Therefore, this study aims to identify the factors associated with infertility in Bangladeshi women. This is a retrospective study and data were collected from 450 reproductive aged women purposively using a structured questionnaire from an infertility center in Rajshahi City, Bangladesh. Univariate, bivariate and multivariate analyses were used to reach the objectives. The results revealed that most respondents (58.2%) were overweight and obese by measuring Body Mass Index (BMI). Age, age at first marriage, BMI, duration of contraceptive use, husband's diabetes status, and husband's drug addiction were found significantly associated with infertility. Infertility cases were found to be higher among women aged ≥30 years (OR: 10.16; 95% CI: 2.70-38.2; p <0.001). Overweight and obese women are 2.33 times more likely to be infertile compared to underweight women (OR: 2.33; 95% CI: 0.12-0.57; p <0.008). The couple who use the contraceptive for 2 years and above are around 2 times more likely to be infertile compared to those using it for ≤ 7 months (OR: 1.99; 95% CI: 0.97-4.09; p <0.059). The women whose husbands use drugs are 5.51 times at higher risk to be infertile compared to those women whose husbands did not take drugs (OR: 5.51; 95% CI: 2.35-12.90; p <0.000). Thus, child expected couples should consider the aforesaid factors. As infertility has a complex relation with basic risk factors, the study findings may help the health policy researchers to address more underlying risk factors of infertility in their further studies. Moreover, these results could be carefully considered by the government and stakeholders to find effective interventions and solutions to the infertility problem in Bangladesh, especially in Rajshahi City, Bangladesh.

Key words:
infertility; socio-demographic factors; nutritional status; contraceptives; body mass index

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INTRODUCTION

Fertility is the capability to produce offspring through reproduction following the onset of sexual maturity. Fertility is addressed when there is a difficulty or an inability to reproduce naturally, which is referred to as infertility. Infertility is a global problem affecting people of all communities, and it has become a key determinant for lower fertility both in developing and developed countries. The inability of becoming pregnant even after having experience of one or more years unprotected intercourse is termed as infertility, which is mainly a disease of the reproductive system.[1] It is a common and severe health problem that affects one's ability to have children. It may be caused by a number of diverse factors in both couples' reproductive systems. However, it is sometimes not possible to explain the causes of infertility.[2] It can be classified as primary infertility when a couple never conceives and secondary infertility when a couple is unable to conceive again after having achieved successful one or more conceptions.[3] Infertility is widespread and affects millions of people of reproductive age having impacts on their families and communities. Estimates suggest that between 48 million couples and 186 million individuals live with infertility globally.[4-6] A far greater proportion of couples from developing countries compared to the proportion of couples from developed countries is facing infertility during their reproductive lifespan.[5,7] The highest prevalence of infertility affecting people ranging from 20.4 to 28.8% was observed in South Asia, Sub-Saharan Africa, North Africa/Middle East, and Central/Eastern Europe and Central Asia.[6] Around 186 million women were found infertile in developing countries except for China.[8] Infertility may not affect physical health but it has extremely adverse impacts on the infertile individual's psychological and social status. In contrast, females are suffering from infertility more than their counterparts[9] and they are frequently accused of infertility in developing countries.[10] Consequently, women from all communities are generally victims of physical and mental abuse, and economic deprivation and face social ostracism as well as neglect, and abandonment, and cannot spontaneously participate in social activities and traditional ceremonies.[11-12]

Infertility brings about robust negative consequences among people living in developing countries compared with those living in developed countries. A survey conducted in Southern Ghana revealed that the majority (64%) of women felt stigmatized, and that higher levels of perceived stigma were associated with increased infertility-related stress as well as lower levels of education.[13] In Bangladesh traditionally, having children is mandatory in terms of family happiness and many people still think of infertility as a "woman's problem", with this problem acquiring crucial social actuality. Being infertile, women suffer economic hardship and even abandonment.[14] The actual infertility rate in Bangladesh is still unknown but World Infertility Survey revealed that among South Asian Countries 4% was reported in Bangladesh and 15% on the basis of women at the end of their reproductive lives in the age of 45-49 years.[15-16] Findings from the qualitative analysis concerned a major difference between primary and secondary infertility in terms of its implications for the affected women.[17] Although low prevalence of infertility was documented in Bangladesh in the last decade, number of married couples visiting fertility centers has increased recently. Married couples with infertility problems come to fertility centers for explained causal factors (e.g., tubal, uterine and ovarian infections). [18-20] However, infertility is a multi-faceted

problem caused by various determinants in the health dimension as well as socio-economic dimensions. Evidence indicated some socio-economic and demographic factors viz., residence, education, family types, income, etc. are significantly associated with infertility and these are explained as risk factors.[21-24] Health parameters (e.g., infection in reproductive organs, diabetics, menstruation, obstetrical history, body mass index [BMI]), social parameters (e.g., smoking and alcohol consumption habit, lifestyle) and environmental factors are studied as risk factors of infertility in some earlier literature.[3, 25-29] Moreover, age at first marriage and duration of contraceptive use have a robust impact on fertility. [30-32] Adequate literature focused on the explained causal factors of infertility e.g. Sexually Transmitted Diseases (STDs), Fallopian Tubal, Uterine and Ovarian Infection, etc. are available but only very few literature focused on the underlying risk factors of infertility can be found in Bangladesh.[33-35] Despite infertility being a public health concern, this important issue still is ignored in Bangladesh and attention sufficiently has not been given to it. There is needed to carry out adequate research on infertility for better understanding and identifying its underlying unexplained risk factors. Moreover, studies on infertility prevalence and identifying the underlying risk factors are scarce at the regional level in Bangladesh. Thus, the above discussion leads this study to investigate a specific research question that can be stated as- "Which underlying risk factors are influencing infertility among married women, particularly in Rajshahi City of Bangladesh?". Therefore, this study focuses on determining the prevalence of infertility and specifying the risk factors among 15-44 years aged married women from Rajshahi City, Bangladesh.

METHODS

Study Design

As this study is cross-sectional in nature, we aimed to use the survey method for collecting primary data from married women who were visiting infertility centers. This study used Z-score formula to determine the sample population and participatory approach was followed to conduct the face-to-face interview. To attain the objective of this study, a well-structured questionnaire was designed and a pre-test was conducted in a pilot study. After removing all discrepancies from the questionnaire, a well-developed final questionnaire was used in face-to-face interviews with the participants of this study. Fertility status stated as fertile and infertile was identified as the dependent variable and other variables *e.g.*, socio-economic and demographic characteristics were selected as independent variables. Infertility was the outcome variable which was expected to be influenced by independent variables. Those independent variables that influenced infertility among married women were identified as associated factors of infertility.

Study Population

As this study aimed to explore the associated factors of infertility among married women aged 15-44 years who attended the Motherland Infertility Centre (MIC) in Rajshahi City from January to March 2020, was chosen for collecting relevant primary data. This area has an area of 18,174.4 square kilometers and around 48.47% of women are living here, the literacy rate is 42.99% and most of the people are laborers (60.36%), involved in agriculture.[36]

Sample size: The total sample size is determined by using the following formula:[37]

$n = \frac{Z^2 p(1-p)}{\epsilon^2} = \frac{Z^2 pq}{\epsilon^2}$, assuming that $p = 0.5$ and $q = 0.5$.

In above equation n= sample size, Z = tabulated value = 1.96 (at 5% level of significance, p = portion of success, q = portion of failure = $1 - p$, and ϵ= margin of error = 0.05. Based on this formula the study is supposed to select 384 respondents from the selected study areas with 95% confidence level and 5% margin of error. But, for the betterment of research, 450 respondents were considered for this study. Initially, 480 respondents were interviewed, but due to incomplete information, 30 data were rejected.

Dependent and independent variables

To determine the infertile state of women, this study used "infertile or fertile" as the main dependent variable in the binary logistic regression model. "Did you have an intention to have a child during the past 2 years" with yes Vs no responses stating the fertility status of the respondents. Participants who had intention but failed to have a child during the past 2 years were coded "o" as infertile and otherwise were coded "1" as fertile.

The targeted dependent variable corresponds to some predictor variables such as "age at first marriage", "whether you were using contraceptive?", "condition of Body Mass Index (BMI)" etc. Therefore, the independent variables included predictor variables along with some underlying associated factors that were being studied in this study. For measuring infertility, participants did respond to various questions pertinent to the independent variables. Participants were asked "whether you were using contraceptives?", if yes, then how long had they been using contraceptives. Then the duration of contraceptive use was categorized as (<7, 7-23, ≥24 months). Age at first marriage of woman was studied by age groups (<20, 20-29, ≥30years) and male counterparts by age groups (<25, 25-29, ≥30years).

Nutritional status is a significantly associated factor with fertility and is generally measured by BMI. The calculated value of BMI (in kg/m^2) stated the nutritional condition of the participants and BMI was categorized as underweight (under 18.5 kg/m^2), normal weight (18.5 to 24.9 kg/m^2), overweight (25 to 29.9 kg/m^2), and obese (30 kg/m^2 or more). With these predictor variables for determining the fertility status, some modifiable underlying risk factors such as the husband's health conditions (e.g., diabetics status) and health behaviors (e.g., smoking, drug addiction), and other socio-economic variables were studied as independent variables. For details the classification and coding of independent variables are presented in Table 1.

Table 1: Coding for different variables with their indicators

Selected Variables	Coding
Fertility Status	0: fertile, 1: infertile
Predictor Variables	
Age at first marriage (in years)	for female, 1: 20; 2: 20-29; 3: ≥30, and for male, 1: <25; 2: 25-29; 3: ≥30
Using contraceptives	1: yes; 0: no
Duration of contraceptive use (in months)	1: <7; 2: 7-23; 3: ≥24
Body Mass Index (BMI) (BMI=kg/m^2)	underweight (1:<18), normal weight (2:18.5-24.9), overweight (3:25-29.9); obese (4: >30)

Selected Variables	Coding
Health related variables	
Diabetics status (husband)	0: no, 1: yes;
Drug addiction (husband)	0: no, 1: yes
Socio-economic variables	
Educational qualification	1: primary; 2: secondary, 3: higher secondary
Place of residence	1: rural; 2: urban
Types of family	1: nuclear; 2: joint
Monthly family income (in Taka)	1: <10000; 2: 10000-19000; 3: ≥20000
Monthly family expenditure (in Taka)	1: <10000; 2: 10000-19000; 3: ≥20000
Food quality	1: low; 2: medium; 3: good

Statistical analysis

To attain the objectives of this study, different statistical analyzing tools were applied. Descriptive statistics and frequency distributions were used to describe participant characteristics and Chi-square test (χ^2) was used to determine the association of various factors with primary infertility. Only statistically significant factors in bivariate analysis were entered into the binary logistic regression model. Binary logistic regression analysis was performed to examine the effects of the factors. The underlying binary logistic regression model corresponding to each variable was as follows:

$$y = \log\left[\frac{p}{1-p}\right] = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \in_i$$

where $p =$ the probability of infertility (coded 1), $1 - p =$the probability of fertile (coded 0), β_0 is the intercept term, β_i are the coefficients of the factors x_i and $\in_i$ be the error term where $(i = 1, 2, \dots, k)$. The binary logistic regression model, and odds ratios (ORs) were estimated to investigate the risk factors between infertility and factors under study. All statistical analyses were performed using STATA version 12.1/MP (STATA Corp, College Station, Texas USA).

Ethical Consideration

This is a retrospective study for which it was not mandatory to get the ethics committee's approval. Since 'The National Code on Clinical Trials' has declared that ethics approval is not necessary for real retrospective studies. However, the respondents were informed that their collected data will be used only for research works and it will not be disclosed anywhere. Moreover, prior to collecting relevant data on infertility, written consent was obtained from literate participants and verbal consent from illiterate participants.

RESULTS

The background characteristics of the respondents are presented in Table 2. It is evident that most of the respondents reside in rural areas (rural 64.9% vs urban 35.1%). The results revealed that around 62% of the women were aged 20-29 years, and 28.67% were aged 30 years and above, whereas a few (10%) were aged less than 20 years. Age of the husbands of the respondents is an important factor in case of the duration of contraception in infertile women. It was observed that around 68% of husbands were 30 years and above and very few (3.11%) were less than 25 years. Women get married at earlier ages compared to their husbands. In this study, it was found that around 61% of women were married when they were less than 20 years, and 47% of respondents' husbands were married at an age lower than 25 years. It was also observed that 23.6% of women got their first marriage at age of 20-29 years, as

opposed to 36.9% of respondents' husbands whose first marriage was at the age of 25-29 years.

The study shows a highly significant relationship between women and their husbands' age (p <0.001) and infertility. About 33.3% of infertile women were found at an age lower than 20 years and 27.7% of infertile women were found with husbands whose ages were between 25-29 years. Age at first marriage of both women and their husbands was significantly ($p < 0.002$) associated with women's infertility. Significant proportion of respondents reported themselves as infertile who married at age less than 20 (22.7%) and between 20-29 years (18.9%). About 22.1% and 19.3% of respondents were found to be infertile whose husbands were married at the age lower than 25 and between 25-29 years, respectively. Contraceptive use is identified as a major cause of infertility, and it had a statistically significant ($p < 0.002$) association with infertility, which can be observed in this study also. The couples who were using contraceptive more than 24 months are likely to be more infertile compared to others. Around 55% of the respondents were using contraceptives for more than 24 months, and among them, 25.2% reported themselves as infertile. The condition of women's nutritional status, measured by BMI, is significantly associated with infertility, whereas no significant association was found between BMI and husband's nutritional status can be observed in this study. But there is a significant association between husband's diabetic status and infertility. The bivariate analysis of this study has identified underweight and overweight as major risk factors for infertility. It was investigated that around 58% of respondents were overweight and obese, and 12.9% of respondents were underweight. From this study, it was also observed that around 25% of husbands were suffering from diabetes and 11% of husbands were found to be drug addicts. The bivariate analysis ($\chi^2 test$) identified that the statistically significant factors were women's age, husband's age, women's age at first marriage, husband's age at first marriage, women's BMI, duration of contraceptive use, diabetes of husband, and drug addiction of husband (Table 2).

Table 2. Distribution and association between socio-demographic variables and health related factors related to infertility at Rajshahi city, Bangladesh; *(N=450)*

Characteristics	Frequency (*N*)	Percentage (95% CI)	Infertile women (%)	*p*-values
Women age (in years)				
<20	45	10.0 (7.5-13.2)	15 (33.3)	<0.001
20-29	276	61.3 (56.7-65.7)	64 (23.2)	
≥30	129	28.7 (24.7-33.0)	6 (4.7)	
Husband age (in years)				
<25	14	3.1 (1.8-5.2)	2 (14.3)	0.01
25-29	130	28.9 (24.8-3.2)	36 (27.7)	
≥30	306	68.0 (63.5-72.1)	47 (15.4)	
Women age at first marriage (in years)				
<20	273	60.7 (56.0-65.0)	62 (22.7)	0.002
20-29	106	23.6 (19.8-27.7)	20 (18.9)	
≥30	71	15.7 (12.6-19.4)	3 (4.2)	
Husband age at first marriage (in years)				
<25	208	46.2 (41.6-50.8)	46 (22.1)	0.048
25-29	166	36.9 (32.5-41.4)	32 (19.3)	

Characteristics	Frequency (*N*)	Percentage (95% CI)	Infertile women (%)	*p*-values
≥30	76	16.9 (13.6-20.6)	7 (9.2)	
Place of Residence				
Rural	292	64.9 (60.3-69.7)	57 (19.52)	0.642
Urban	158	35.1 (30.8-39.6)	28 (17.72)	
Body mass index (Husband)				
Under weight	58	38.4 (34.0-43.0)	8 (13.8)	0.356
Normal weight	130	16.9 (13.6-20.6)	22 (16.9)	
Over weight and obese	262	44.7 (40.1-49.3)	55 (21.0)	
Body mass index (Women)				
Under weight	176	12.9 (10.0-16.3)	47 (27.2)	<0.001
Normal weight	73	28.9 (24.8-33.2)	15 (19.7)	
Over weight and obese	201	58.2 (53.5-62.7)	23 (11.4)	
Monthly family income (in taka)				
<10000	67	14.9 (11.8-18.5)	16 (23.9)	0.523
10000-19000	147	47.7 (28.4-37.1)	26 (17.7)	
≥20000	236	52.4 (47.8-57.0)	43 (18.2)	
Monthly family expenditure (in taka)				
<10000	114	25.3 (21.5-29.5)	23 (15.03)	0.315
10000-19000	183	40.7 (36.2-45.2)	39 (21.31)	
≥20000	153	34.0 (29.7-38.5)	23 (20.18)	
Education (women)				
Primary	99	22.0 (18.3-26.0)	21 (21.2)	0.739
Secondary	206	45.8 (41.2-50.4)	39 (18.9)	
Higher secondary	145	32.2 (28.0-36.6)	25 (17.4)	
Education (husband)				
Primary	78	17.3 (14.0-21.2)	16 (20.51)	0.790
Secondary	140	31.1 (26.9-35.5)	28 (20.00)	
Higher secondary	232	51.6 (46.9-56.1)	41 (17.67)	
Duration of contraceptive use (in month)				
<7	102	22.7 (19.0-26.7)	10 (9.8)	<0.001
7-23	102	22.7 (19.0-26.7)	10 (9.8)	
≥24	246	54.6 (50.0-59.2)	62 (25.2)	
Diabetes status (husbands)				
Yes	110	24.4 (20.6-28.6)	7 (6.4)	<0.001
No	340	75.6 (71.3-79.3)	78 (22.9)	
Drug addiction (husbands)				
Yes	46	10.2 (7.7-13.3)	13 (28.3)	0.087
No	404	89.8 (86.6-92.2)	72 (17.8)	
Smoking status (husbands)				
Yes	211	47.1 (49.3-44.3)	44 (18.57)	0.816
No	237	52.9 (57.1-63.4)	41 (19.43)	
Food quality				
Low	19	4.2 (2.7-6.6)	3 (15.79)	0.751
Medium	196	43.6 (39.0-48.1)	40 (20.41)	
Good	235	52.2 (47.5-56.8)	42 (17.87)	

Notes: *Percentage of infertile women was calculated in row percentage; 'CI, confidence interval', 'kg, kilogram', and 'BMI, body mass index'.*

The factors which were significantly associated with fertility status were considered for binary logistic regression model and the results are presented in Table 3. The binary logistic regression model identified that the women aged 30 years and above were 10.16 times more likely to be infertile compared to the

women aged less than 20 years (OR: 10.16; 95% CI: 2.70-38.2; p <0.001). In the case of the husband, those aged 25-29 years were 79% less likely to be infertile compared to those who were 25 and less (OR: 0.21; 95% CI: 0.04-.105; p <0.057). Overweight and obese women were found to be 2.33 times more likely to be infertile compared to underweight women (OR: 2.33; 95% CI: 0.12-0.57; p <0.008). The couple who use the contraceptive for 2 years and above were around 2 times more likely to be infertile compared to contraceptive use duration of 7 months and less (OR: 1.99; 95% CI: 0.97-4.09; p <0.059). The women whose husbands use drugs were at 5.51 times higher risk of being infertile compared to their counterparts (OR: 5.51; 95% CI: 2.35-12.90; p <0.001).

Table 3. Determination of risk factors using binary logistic regression analysis for infertility at Rajshahi City, Bangladesh.

Characteristics	Odds ratio (OR)	95% CI of OR	*p*-values
Women age (in years)			
<20$^{(r)}$	1.00	-	-
20-29	1.97	0 .81- 4.78	0.135
≥30	10.16	2.70- 38.23	< 0.001
Husband age (in years)			
<25$^{(r)}$	1.00	-	-
25-29	.21	0.04-1.05	0.057
≥30	.25	0.47-1.36	0.110
Women age at first marriage (in years)			
<20$^{(r)}$	1.00	-	-
20-29	1.37	0.69-2.71	0.362
≥30	3.25	0.75-14.20	0.116
Husband age at first marriage (in years)			
<25$^{(r)}$	1.00	-	-
25-29	.10	0.50-1.98	0.993
≥30	.97	0.31-3.05	0.961
Body mass index (women)			
Under weight$^{(r)}$	1.00	-	-
Normal weight	1.18	0.56-2.46	0.683
Over weight and obese	2.33	1.25-4.37	< 0.008
Duration of contraceptive use (in month)			
<7$^{(r)}$	1.00	-	-
7-23	3.42	1.59-7.35	< 0.002
≥24	1.99	0.97-4.09	0.059
Diabetes status (husbands)			
No$^{(r)}$	1.00	-	-
Yes	5.51	2.35-12.90	< 0.000
Drug addiction (husbands)			
No$^{(r)}$	1.00	-	-
Yes	.624	0.28-1.38	0.243

Notes: *"r", reference category', 'CI, confidence interval', and 'kg, kilogram'.*

DISCUSSION

Infertility is an age-dependent disorder, possibly resulting from the ageing process of reproductive organs and endocrine function. Of the socio-demographic factors, age both for women and their husbands is the most strongly associated factor with the likelihood of infertility. Infertility has a stepwise increased relationship with age. It has been observed that the age at first marriage is also responsible for infertility especially for those women who are late married. The study results revealed that age at first marriage later than 25 years proved to be a significant risk factor for women's infertility which is comparable with the finding of the study conducted in Egypt in 2006,[38] and according to National Family Health Survey-III in India.[39] Similarly, a survey reported that about 46% of Indians in the age group of 31 to 40 years seeking medical help for conceiving a child were found to be infertile; this means they were unable to conceive even after two years of trying for a child.[40] Birth control technique especially contraceptive use plays a significant role in reaching the replacement level of fertility. Using contraceptives for a long period results in reduced fertility among couples. This study also found that women who are using contraceptives for more than 24 months are like to have a higher risk of infertility. At present, more than 60% of women in Bangladesh are using contraceptives, and they are at high risk of being unable to become pregnant. Obesity is a common problem characterized by excessive weight gain and affects approximately half of the total population worldwide. Unhealthy weight gain negatively impacts the reproductive system, particularly ovarian dysfunction could be caused by excess weight gain and/or loss.[41] Outcomes of the assisted reproductive technique and its treatment efficacy may be negatively impacted by the gain in overweight. In this present study, overweight has been proved to be significantly associated with women's infertility and the result indicates that overweight is a major risk factor for infertility, which is congruent with some national and international studies.[42-44] Diabetes is known to affect the reproductive health of both males and females. Diabetes causes menstrual disturbances among females and negatively affects the fertility prominence of the couple.[45-47] Those women whose husbands were suffering from diabetes were found as more likely to be infertile. In Bangladesh, the prevalence of diabetes among adults has increased during the last decade,[48] and according to the International Diabetes Federation (IDF), it will be 13% by 2030.[49] This substantial increase in diabetes may increase the intensity of infertility. Therefore, to sustain the replacement rate of fertility, attention should be placed on addressing underlying risk factors, and special concentration should be given to taking the necessary initiatives to respond to the infertility problem in Bangladesh. During the survey, some problems have arisen which were taken as limitations of this study. There was a tendency to hide the correct answer to some aspects like age, income, uterus problem, etc. which was noticed among the respondents. Some of the problems arise due to illiterate patients. Some female patients did not give interviews directly for the protection of religious bindings. Some of the respondents did not give accurate answers to some questions because they felt boring to give information about their personal affairs. Therefore, this study mostly focused on some predefined independent variables e.g. age at first marriage, husband age at first marriage, body mass index, duration of contraceptive use etc.

CONCLUSIONS

Infertility is a health problem addressed as a disease of the reproductive

system of both males and females during the reproductive lifespan, and requires appropriate diagnosis and identification of its socio-economic determinants. Therefore, this study concludes by addressing the underlying risk factors responsible for infertility among married women residing in Rajshahi City, Bangladesh. The major underlying risk factors were women's age, delay in marriage, being overweight and obese, using contraceptives for a long time, and husband's diabetes. Although the relationship is naturally complex, these factors significantly maintain the association with infertility. As infertility has its complex relation with underlying risk factors, the finding of this study may help the health researcher to address more underlying risk factors of infertility in their further studies. Moreover, these results could be carefully considered by the government and stakeholders to find effective interventions and solutions to the infertility problems in Bangladesh, especially in Rajshahi City, Bangladesh.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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ABBREVIATION

BMI: Body Mass Index, CI: Confidence Interval, ISAR: Indian Society for Assisted Reproduction, MIC: Motherland Infertility Centre, and OR: Odds Ratio

AUTHORS' CONTRIBUTION

NK, MNIM, and MRI created the concept; NH, MNIM, MRI, and MKH shaped the design of the study. NK, MSI, MRI, and MNIM performed the statistical analysis; NK, MSH, MSI, and MNP drafted the manuscript; MRK, MSI, MKH, MRI, and MNIM made critical revisions of the manuscript. All authors read and approved the final version of the manuscript.

CONSENT TO PARTICIPATE

Not applicable

CONSENT FOR PUBLICATION

Not applicable

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