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Risk Factors and Spatial Clustering of Primary Infertility in India

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Abstract

This study aims to (a) understand the level and risk factors of primary infertility, and (b) assess the spatial clustering of primary infertility at the district level in India. Data of currently married women aged 20-49 years married for at least 24 months (n=4,45,499) gathered through the National Family Health Survey-4 (2015-16) was used for this analysis. The NFHS-4 is a nationally representative survey of 601,509 households that provides information for wide range of indicators of health, nutrition, and women's empowerment. Only those respondents who gave consent were interviewed in the survey. Binary logistic regression was carried out to examine the adjusted effect of socio-economic and demographic characteristics on primary infertility. The univariate Local Indicator of Spatial Association (LISA) cluster maps and Moran's I statistics were applied for spatial autocorrelations at the district level. Three percent of the studied women had primary infertility, and the prevalence varies considerably by socio-economic and demographic characteristics. Women marrying at 30+ years (OR: 16.52), with thyroid problems (OR: 1.41), obese women (OR: 1.12), and those from socially backward classes (OR: 1.32) were more likely to have primary infertility. The univariate LISA cluster maps revealed hotspots of primary infertility in most parts of Karnataka, two clusters in Arunachal Pradesh and Tamil Nadu, one cluster each in southern Maharashtra, south-west Odisha, south Chhattisgarh, and north-central Uttar Pradesh. Awareness generation about the preventable risk factors and provision of infertility care services at primary health care facilities will be of use in addressing infertility in India.

Keywords: Infertility, Risk Factors, Logistic Models, Cluster Analysis, India

Introduction

Infertility is a critical component of reproductive health and a research priority owing to its implications for the socio-psychological wellbeing and status of women. The inability to have children affects men and women across the globe (1, 2) and has serious demographic, social, as well as health consequences. The conflux of personal, sociocultural, and religious expectations may bring a sense of failure, loss, and exclusion to those who are infertile (3). Infertility can lead to distress and depression, as well as discrimination and ostracism (4-7). Although male infertility contributes to more than half of all cases of global childlessness, infertility remains a woman's social burden (2). Infertility reduces the social status and psychological wellbeing of women, particularly in societies, including India, where it carries huge social stigma (3, 8). Infertile women have feelings of inadequacy and incompleteness and tend to avoid closeness with people and relationships (9). The adverse outcomes for the women further lead to long-lasting impacts such as domestic violence, marital instability, abandonment, exclusion from participation in social celebrations, and ceremonies (10-12). Social and financial adversities faced by childless women are further not limited to low income or low education strata (11).

Infertility has multiple causes and consequences depending on the sexual history, gender, societal status, lifestyle, and cultural background of the people it affects (13). Evidence on socio-economic and demographic correlates of infertility is again limited (14, 15). Preventable conditions such as infection, menstrual hygiene, lifestyle factors, advancing maternal age, age at marriage, postponement in childbearing, socio-economic status, occupational hazards, semen abnormalities, anovulation, and ovarian failure lead to infertility (16, 17, 18, 19). A considerable proportion of women in developing countries suffer from preventable causes of infertility such as sexually transmitted infections, tubal damage, polycystic ovary syndrome, pelvic inflammatory diseases (20). Endometriosis (21, 22), submucosal fibroids, reproductive system disorders (23) and other factors which are often not preventable, such as chromosomal and genetic causes also leads to infertility. Prothrombin G20210A mutation, has again been found as an unrecognized cause of recurrent pregnancy loss among women (24). Environmental pollution has also been seen as a risk factor for female fertility (25). Infertility can also occur due to unknown and unexplained factors (26). In India, the status of women in society continues to be highly dependent on the number of children she produces. Nevertheless, infertility is an under-researched condition in the country, as the general thrust of both programs and research continues to explain correlates of high fertility. Available scanty literature reveals wide interstate variation in infertility prevalence- 5% in Andhra Pradesh (27), 15% in Kashmir (16), 14% in Madhya Pradesh (28) and 9% in Central India (17).

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Analysis of the second National Family Health Survey found that 1.9% of women had primary infertility in 2005-06 (3). About 21 million women in the age group 20-49 are projected to suffer from lifetime primary infertility in 2021 (29). Childbearing status is directly associated with the socio-psychological and physical health status of Indian women, urging in-depth research on infertility. Estimates on infertility prevalence, correlate, and identification of the areas/districts of more significant concern is of use for policy and program targeting women's welfare. Moreover, although important, there is no empirical evidence on the spatial clustering of primary infertility at the district level in India. This study aims to (a) understand the level and risk factors of primary infertility, and (b) assess the spatial clustering of primary infertility at the district level in India.

Methods

Data

The study used data from the fourth round of the National Family Health Survey (NFHS), 2015-16. The NFHS-4 is a nationally representative survey of 601,509 households that provides information for a wide range of monitoring and impact evaluation indicators of health, nutrition, and women's empowerment. The sampling design of the NFHS-4 is a stratified two-stage sample with an overall response rate of 98 per cent. The Primary Sampling Unit (PSUs), i.e., the survey villages in rural areas and Census Enumeration Blocks (CEBs) in urban areas, were selected using probability proportional to size (PPS) sampling. The data was gathered using computer-assisted personal interviewing (CAPI) by trained research investigators. Only those respondents who gave consent were interviewed in the survey. A more detailed description of survey design, questionnaire, quality control measures, and survey management information can be obtained elsewhere (30). The present analysis is restricted to currently married women aged 20-49 years who are married for at least 24 months (n=4,45,499).

Outcome variable

The outcome variable considered for the analysis was primary infertility. It is defined as- currently married women in the age group 20-49, married for at least 24 months by the date of interview, not currently pregnant, never used contraceptives, have no terminated pregnancies and no children ever born. The age group below 20 years of age was excluded from the analysis so as not to include the impact of adolescent sterility. The decision to use the information of women with at least 24 months of marital duration was based on a literature review (31). For each woman, CMC (Century Month Code) of marriage is subtracted from CMC of the interview date, and women with CMC difference less than 24 months were excluded to maintain at least two years of marital duration on the date of interview. Direct questions like, "Are you pregnant now?" "Have you ever used anything or tried in any way to delay or avoid getting pregnant?" "Did you have any pregnancies that terminated before January 2010 that did not result in a live birth?" were used to find women with no current pregnancy, never used any contraception, and not terminated pregnancy respectively. Information on the number of children ever born in the data set was used to find out women with no children ever born for estimating primary infertility.

Predictor variables

The predictor variables used in the analysis were current age of women (20-24, 25-29, 30-34, 35-49 years), age at marriage (≤19, 20-24, 25-29, 30+ years), consanguineous marriage (no, yes), currently have any thyroid disorder (no, yes), body mass index (BMI)- (underweight: <18.5 kg/m2, normal weight: 18.5-25.0 kg/m2, and overweight/obese: >25.0 kg/m2), completed years of schooling (no schooling, <10 years, 10+ years), religion (Hindu, Muslim, others), social groups (scheduled caste-SC, scheduled tribe-ST, other backward classes-OBC, Non-SC/ST/OBC), wealth index (poorest, poorer, middle, richer, richest), place of residence (urban, rural), and geographical regions (north, central, east, north-east, west and south). The wealth index is a measure of a household's living standard and was calculated using data on household's ownership of selected assets, materials used for housing construction, and types of water access and sanitation facilities.

Statistical analysis

Bivariate analysis was used to understand the socio-economic and demographic differentials in primary infertility. Binary logistic regression was carried out to examine the adjusted effect of socio-economic and demographic characteristics on primary infertility. Sample weights were used to adjust the non-response. STATA (V 15) was used for analyses, and the results were reported at a five per cent level of significance. To accomplish the spatial analysis, the district's map was exported to GeoDa software. The contiguity matrix was generated to present the weighted analysis. Furthermore, the Moran's I and univariate Local Indicator of Spatial Association (LISA) scatterplots were applied. Moran's I was used to present the Pearson coefficient measure of spatial autocorrelation. This measure shows the degree to which data points are similar or dissimilar to their spatial neighbours (32). LISA statistics was applied to measure the local spatial autocorrelation and the significance of hotspots. The local spatial association is studied using Moran's scatterplot (33). The four different quadrants of the scatterplot correspond to the four types of local spatial association between a district and its neighbours: High-High (a district with high infertility surrounded by districts of high infertility), Low-High (a district with low infertility surrounded by districts of high infertility), Low-Low (a district with low infertility surrounded by districts of low infertility) and High-Low (a district with high infertility surrounded by districts of low infertility) cluster of districts in India.

Results

Prevalence of primary infertility

Three per cent of the currently married women aged 20-49 years had primary infertility (Table 1). The bivariate analysis revealed that the prevalence of primary infertility decreased with increased age. For example- 6% of those aged 20-24 years had primary infertility as against 2% of those aged 35-49 years. Fourteen out of every 100 women married in 30+ years were having primary infertility. The corresponding figure was six out of every 100 for those married between 25-29 years, three out of every 100 for those married between 20-24 years, and two out of every 100 for those married before 20 years. Four per cent of the women with thyroid disorder had primary infertility compared with three per cent of those without thyroid problems. There is no variation in primary infertility prevalence among women in consanguineous

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relationships and those in non-consanguineous marriage. Three per cent of the women with 10+years of schooling had primary infertility as against two per cent of those without any schooling. Primary infertility was relatively higher in southern and western regions compared to the other part of India. For example- three out of every 100 women from the southern and western regions had primary infertility. The corresponding figure was two out of every 100 for women from the north/east/north-east region.

Correlates of primary infertility

The logistic regression revealed that after adjusting the effect of predictors used in the model, current age, age at marriage, thyroid problem, BMI, education, social group, wealth index, place of residence, and region found to be the significant correlates of primary infertility (Table 2). The likelihood of primary infertility decreased with the increased age of women. For example- the chances of primary infertility were significantly low (OR: 0.17, 95% CI: 0.16-0.18) among women aged 35-49 years compared with those aged 20-24 years. Education and prevalence of primary infertility were inversely associated- women with 10+ years of schooling had significantly lower odds (OR: 0.84, 95% CI: 0.79-0.90) of primary infertility than those women without schooling.

Table 1: Prevalence of primary infertility among currently married women aged 20-49 years married for more than 2 years by socio-economic and demographic characteristics, India, 2015-16

Characteristics	Primary infertility	Total surveyed sample
Total	**2.6**	**4,45,499**
Current age of women		
20 - 24	5.9	59,774
25 - 29	3.1	94,133
30 - 34	2.2	86,983
35 - 49	1.6	2,04,609
Age at marriage		
19 and below years	2.0	3,01,447
20 - 24	3.3	1,16,596
25 - 29	5.6	23,698
30 and above years	13.5	3,757
Consanguineous marriage		
No	2.6	3,93,948
Yes	3.0	51,551
Currently have thyroid disorder		
No	2.6	4,33,334
Yes	3.5	12,165
Body Mass Index		
Underweight	2.7	75,846
Normal	2.7	2,56,887
Overweight/Obese	2.4	1,12,765
Completed years of schooling		
No schooling	2.2	1,50,662
Less than 10 years	2.5	1,67,702
10 and above years	3.2	1,27,135
Religion		
Hindu	2.7	3,63,337
Muslim	2.5	57,535
Others	2.3	24,626
Social group		
Non-SC/ST/OBC	2.5	1,22,163
Scheduled caste (SC)	2.7	89,589
Scheduled tribes (ST)	3.0	39,152
Other Backward Class (OBC)	2.6	1,94,594
Wealth Index		
Poorest	2.8	80,794
Poorer	2.5	85,774
Middle	2.6	89,524
Richer	2.8	94,527
Richest	2.4	94,879
Place of residence		
Rural	2.6	2,93,253
Urban	2.7	1,52,246
Region		
North	2.0	61,201
Central	2.5	1,02,804
East	2.3	1,04,064
North-east	2.2	14,328
West	2.9	64,722
South	3.4	98,381

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Table 2: Adjusted odds ratio result of primary infertility among currently married women aged 20-49 years married for more than 2 years by socio-economic and demographic characteristics, India 2015-16

Characteristics	Adjusted odds ratio (95% CI)
Current age of women (Ref. = 20 – 24 years)	
25 - 29	0.41***(0.39, 0.43)
30 - 34	0.24***(0.22, 0.25)
35 - 49	0.17***(0.16, 0.18)
Age at marriage (Ref. = 19 and below years)	
20 - 24	2.00***(1.91, 2.09)
25 - 29	4.73***(4.41, 5.07)
30 and above years	16.52***(15.01, 18.18)
Consanguineous marriage (Ref. = No)	
Yes	1.01(0.94, 1.07)
Currently have thyroid disorder (Ref. = No)	
Yes	1.41***(1.25, 1.59)
Body Mass Index (Ref. = Normal)	
Underweight	0.93***(0.89, 0.98)
Overweight/Obese	1.12***(1.07, 1.18)
Completed years of schooling (Ref. = No schooling)	
Less than 10 years	0.85***(0.81, 0.89)
10 and above years	0.84***(0.79, 0.90)
Religion (Ref. = Hindu)	
Muslim	0.99(0.93, 1.05)
Others	0.90***(0.84, 0.97)
Social Group (Ref. = Non-SC/ST/OBC)	
Scheduled Caste (SC)	1.07**(1.00, 1.14)
Scheduled Tribe (ST)	1.32***(1.24, 1.42)
Other Backward Class (OBC)	1.05(1.00, 1.11)
Wealth Index (Ref. = Poorest)	
Poorer	0.89***(0.84, 0.95)
Middle	0.87***(0.81, 0.93)
Richer	0.82***(0.76, 0.88)
Richest	0.70***(0.64, 0.76)
Place of residence (Ref. = Rural)	
Urban	1.08***(1.03, 1.14)
Region (Ref. = North)	
Central	1.24***(1.16, 1.32)
East	1.25***(1.16, 1.34)
North-east	0.85***(0.78, 0.93)
West	1.49***(1.38, 1.61)
South	1.77***(1.65, 1.90)

** significant at <0.05, ***significant at <0.01

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The likelihood of primary infertility decreased with increased household wealth- women from most affluent households were less likely (OR: 0.70, 95% CI: 0.64-0.76) to suffer from primary infertility compared to their counterparts from the poorest households. As compared with women who got married below 20 years, women marrying between 20-24 years had two times (OR: 2.0, 95% CI: 1.91-2.09), those marrying between 25-29 years had four times (OR: 4.73, 95% CI: 4.41-5.07), and those marrying at 30+ years had 16 times higher odds (OR: 16.52, 95% CI: 15.01-18.18) of primary infertility. The women with thyroid problems had a higher likelihood of primary infertility (OR: 1.41, 95% CI: 1.25-1.59) than those without thyroid problems. Primary infertility was associated with BMI- overweight/obese women had higher chances (OR: 1.12, 95% CI: 1.07-1.18) and underweight women had lower chances (OR: 0.93, 95% CI: 0.89-0.98) of primary infertility compared to normal-weight women. The likelihood of primary infertility was higher among women from the ST (OR: 1.32, 95% CI: 1.24-1.42), and SC category (OR: 1.07, 95% CI: 1.00-1.14) than those from Non-SC/ST/OBC category. Women residing in urban areas had higher odds of primary infertility (OR: 1.08, 95% CI: 1.03-1.14) than those from rural areas. As compared to women from North region, the odds of primary infertility were higher in the south region (OR: 1.77, 95% CI: 1.65-1.90), west region (OR: 1.49, 95% CI: 1.38-1.61), east region (OR: 1.25, 95% CI: 1.16-1.34) and central region (OR: 1.24, 95% CI: 1.16-1.32).

Spatial distribution and clustering of primary infertility

Figure 1 presents the district wise prevalence of primary infertility in India. More than 5% of women in 10 districts of Karnataka found to have primary infertility. Similarly, in five districts of Arunachal Pradesh, three districts of Telangana, two districts each of Kerala and Chhattisgarh, more than 5% of the women had primary infertility. The Moran's I value of primary infertility indicates positive 0.373 ($p<0.05$, 999 permutation) spatial autocorrelation across the districts of India (Figure 2).

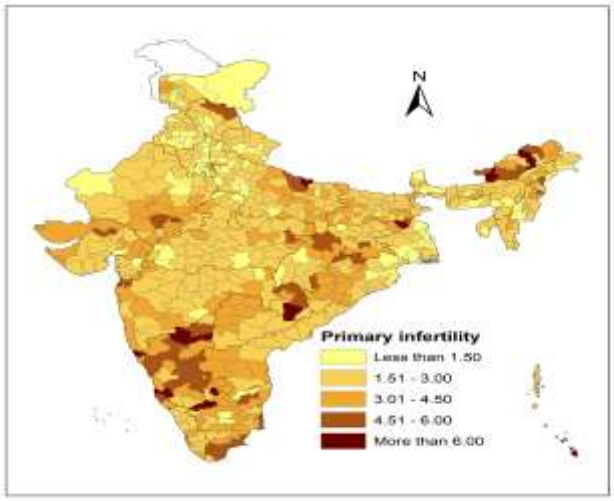

Figure 1: District wise prevalence of primary infertility among currently married women aged 20-49 years married for more than 2 years, India 2015-16 (Based on Authors' analysis)

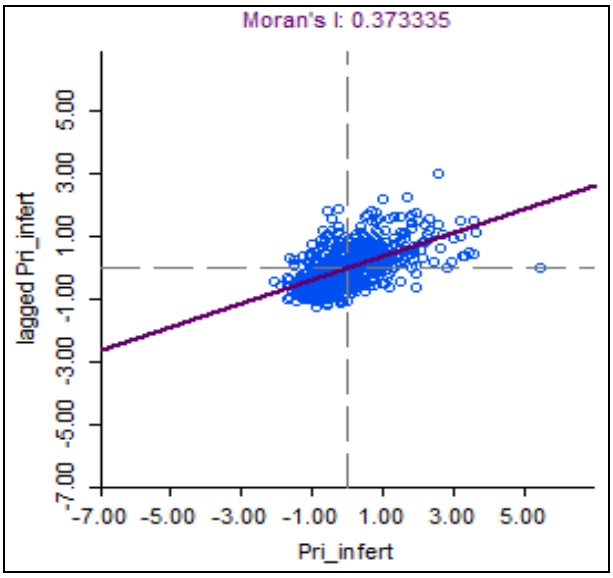

Figure 2: Moran's I plot (Based on Authors' analysis)

The univariate LISA cluster maps revealed a cluster of hotspots (high-high) of primary infertility in most parts of Karnataka, two clusters of districts in Arunachal Pradesh and Tamil Nadu, one cluster each in southern Maharashtra, south-west Odisha, southern Chhattisgarh, and north-central Uttar Pradesh (Figure 3). On the other hand, the cold spots were observed in several clusters of districts in Punjab, Haryana, Himachal Pradesh, and Jammu & Kashmir in northern India; in districts of Odisha and West Bengal in eastern India; and in districts of Assam as well as Mizoram in north-eastern India.

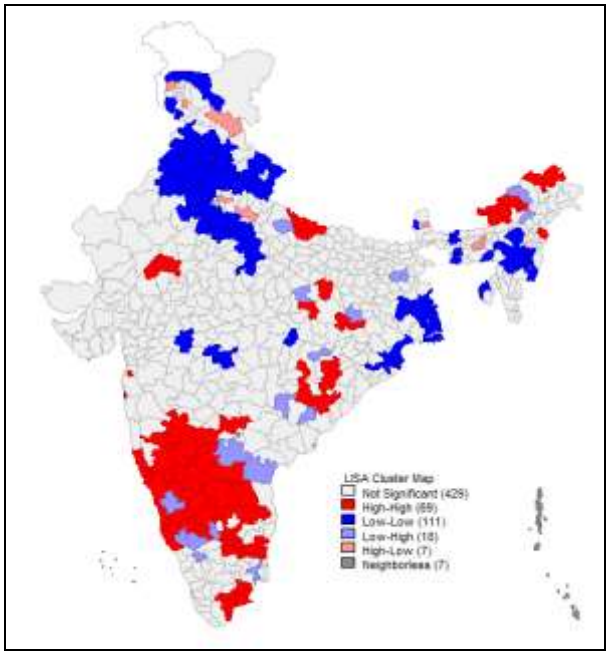

Figure 3: Univariate LISA cluster map of primary infertility, India, 2015-16 (Based on Authors' analysis)

Discussion

The study found a considerable number of Indian women have primary infertility, and the prevalence varies considerably by socio-economic and demographic characteristics. There is again a spatial clustering of primary infertility in various parts of the country. The result reveals that higher education and economic status significantly reduce the likelihood of primary infertility. This may be because of their better awareness and access to quality reproductive health care services, thus reducing the chance of primary infertility. Age at first marriage is positively associated with primary infertility. The higher infertility rate among women marrying in 30+years indicates their reduced ability to bear children. An earlier study also revealed that the capacity of women to bear children decreases with increasing age at first marriage (3). This result suggests the need for a regular health check-up to ensure proper health conducive for pregnancy and avoid delayed marriage whenever possible. Women with thyroid problems are at higher risk of infertility. A past study too revealed that hypothyroidism and hyperthyroidism adversely affect reproductive health, especially in reducing conception, the early loss of a pregnancy, and adverse pregnancy outcome (34). The study found overweight/obese women more likely to have primary infertility. The result conforms to past research that found that obesity-induced menstrual dysfunction and hormonal imbalance affect the reproductive function of women (17). A majority of infertility cases due to ovulation disorders may be preventable through modifications of diet and lifestyle (35), suggesting the need to promote healthy food habits.

Primary infertility is higher among socially backward women. Evidence suggests these women's low awareness and utilization of reproductive health care services (30), often due to inadequate exposure to mass media and limited access to health facilities. Women from socially disadvantaged groups also found to have insufficient knowledge and awareness of menstrual hygiene and their ill-effects on health (36-38). They are further much less likely to use safer menstrual hygienic practices compared to those from the socially forward groups (39, 40), exposing them to a host of unwanted health concerns such as reproductive tract infection (41) and urogenital infection (42); which might again reduce their ability to bear a child. A past study found a higher prevalence of infertility among women who used the unhygienic method of menstrual protection (43). Earlier studies also found that knowledge about infertility is inadequate among different population groups in many parts of the world (44-46). Many women have poor awareness of the period of the month in which they are most fertile and when to seek treatment (47). Additionally, there are a number of misconceptions regarding infertility across many countries (48,49). Urban women found to be at higher risk of primary infertility, perhaps owing to their lifestyle behaviours and marriage at a later age. An earlier study revealed a similar finding (3). Primary infertility is higher among women from southern India. Some past studies also found a higher prevalence of childlessness in all the southern states (3, 50). The study found several hotspots of primary infertility, especially in the south and north-east India, suggesting the need for customized household-level studies to understand the aetiology better. Nevertheless, area-specific tailor-made interventions would benefit women with a higher risk of primary infertility.

The strengths of the study are that the results are an addition to inadequate evidence on correlates and spatial clustering of infertility at the district level in India. Findings are further based on a large sample size from a nationally representative survey with a robust sampling design. Moreover, results are deemed useful for program and policy aiming better reproductive health of women. The limitations of the study are - the cross-sectional design of the study limits the causal association of infertility with socio-economic and demographic factors drawn from this analysis. Further, the estimation of infertility is based on self-reported responses and may differ from clinical tests, especially when infertility continues to be a socially undesirable status for women. Additionally, other biological factors affecting women and husband's health condition may further lead to primary infertility, which could not be included in the analysis due to data unavailability.

Conclusion

Infertility has emerged as a significant public health challenge in India. Living as an involuntarily childless woman is challenging for the female role in the Indian context, urging urgent program and policy attention. The preventable risk factors of infertility, such as late age at marriage, thyroid disorder, and obesity, are often affected by socio-demographic and lifestyle factors, thus providing ample scope for policy and program intervention. Awareness generation about the risk factors and provision of infertility care services in primary health care facilities will be of use in addressing infertility in India.

Author's contribution

Conceptualization: MRP; Literature review: MRP, SP; Data analysis: SKP, SP, MRP; Wrote the manuscript: MRP, SKP, SP

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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