Original Article

Risk and protective factors of miscarriage: Evidence from a nationally representative sample of women in India

Sonu H S[1], Sumit Kumar Das[2], Roshni Tony[3], Binu V S[3]

[1]Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India, [2]Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India, [3]Department of Biostatistics, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India

Abstract

Context: Miscarriage is the most distressing complication in early pregnancy, with one in every five pregnant women ending in a miscarriage, and its causes are multifactorial. Aim: This study aimed to find the risk and protective factors of miscarriage among women aged 15–49 years in India by using the National Family Health Survey (NFHS-5) data. **Methods and Material:** The data were taken from NFHS-5; 53,560 women aged 15–49 years who had reported either a miscarriage (n = 5104) or livebirth (n = 48,456) during the last 12 months preceding the survey were included in the study. **Statistical Analysis Used:** Various sociodemographic, lifestyle, comorbid, and fertility-related factors were considered in the Poisson regression analysis, and adjusted prevalence ratios were obtained. **Results:** Significant sociodemographic risk factors were age less than 20 years or more than 34 years, urban residence, primary and higher education levels, wealth index middle and above, and occupation as employed. Muslim religion, Scheduled Tribe, and Other Backward Class castes were statistically significant protective factors. Obesity, severe anemia, hypertension, and thyroid disorder were the significant comorbid risk factors, whereas tobacco chewing was the only significant lifestyle risk factor. A higher number of ever-born children was the fertility-related risk factor, whereas the use of intrauterine devices was a significant protective factor for miscarriage. **Conclusions:** To reduce the incidence of miscarriage in developing countries like India, the respective governments and healthcare providers should develop intervention programs targeting women in well-educated and high-income families.

Keywords: India, miscarriage, National Family Health Survey, prevalence ratio, risk and protective factors

Introduction

Miscarriage or spontaneous abortion refers to the expulsion or extraction of a fetus (embryo) weighing less than 500 g, equivalent to approximately 22 weeks gestation.[1] Miscarriage is a common adverse pregnancy outcome, and an estimated 30% of all pregnancies end with a miscarriage; the incidence is more than 50% among women aged 40–44 years.[2,3] In a cohort study conducted in a southern state of India, the miscarriage rate was respectively 115.3 and 60.3 per 1000 pregnancies between 6 and 8 weeks and between 12 and 20 weeks of ongoing pregnancies.[4] After the miscarriage, the woman and her family experience stigma and emotional stress, and the majority of women become socially isolated and live with major mental health issues such as anxiety and depression, which may lead to the development of cardiovascular disease.[5-11] The risk factors for miscarriages vary across populations, with demographic, lifestyle, and environmental risk factors that are modifiable in addition to clinical risk factors.

Address for correspondence: Dr. Binu V S, Department of Biostatistics, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India.
E-mail: binuvstvm@gmail.com

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In India, the miscarriage rate is increasing; the National Family Health Survey-5 (NFHS-5) conducted during 2019–21 in India reported that 7% of all pregnancies among women of reproductive age resulted in a miscarriage during the 5 years preceding the survey.[12,13] There have been only a few studies that investigated the risk factors of miscarriage in India. Considering that India is the most populous nation, the absolute number of miscarriages would be a large one. To bring down the magnitude of miscarriages in India, it is pertinent to have a multipronged approach whereby strategies of prevention can be complemented by the involvement of family physicians and primary care providers, who have the trust of the people. Thus, the identification of the risk factors would be beneficial at all levels. As the majority of risk factors associated with miscarriage are modifiable, it would be a good way to prevent this problem, which has many long-term psychological and other health consequences for the woman and her family members. Hence, this study aimed to find the risk and protective factors of miscarriage among women aged 15–49 years in India by using the NFHS-5 data.

Materials and Methods

Study population

The data for the present study were taken from NFHS-5, a nationally representative survey conducted during 2019–21 covering 707 districts from all states and union territories of India. The survey used a stratified two-stage sampling design in each district, which was stratified into urban and rural areas.[13] All women aged 15–49 years in the selected households were eligible for interview, whereas only a subsample of men aged 15–54 years were interviewed. Detailed information was obtained from 724,115 women and 101,839 men in the survey. Women aged 15–49 years who had a miscarriage or live birth during the last 12 months preceding their interview were included in the present study, whereas women who had an abortion or stillbirth were excluded. From those houses where multiple pregnancies were reported during the last 12 months preceding the survey, only one record was selected randomly. Thus, the sample for the study was n = 53,560 women aged 15–49 years who had reported either a miscarriage (n = 5104) or livebirth (n = 48,456) during the last 12 months preceding the survey.

Dependent and independent variables

The dependent variable was binary with either a miscarriage (coded as 1) or livebirth (coded as 0) that occurred in the last 12 months preceding the survey among women aged 15–49 years. The independent variables considered were the age of the woman at the time of the interview, place of residence, religion, caste, wealth index, family structure, woman's highest education level, occupation status, body mass index, her anemic status, diabetic or not, hypertensive or not, presence of any thyroid disorder, her alcohol use, smokes tobacco or not, tobacco chewer or not, history of contraceptive use, history of miscarriage/abortion, had a consanguineous marriage or not, and the number of children ever born to her. The description of categories of each independent variable is given in Tables 1-3. The wealth index scores were derived using principal component analysis based on the number and kinds of consumer goods each household owned.[13]

Data analysis

The data for the study was downloaded from the Demographic and Health Surveys Program after obtaining their permission for data access and analysis.[14] As NFHS is a cross-sectional survey with a multistage sampling design, we estimated the prevalence ratio (PR) and corresponding 95% confidence intervals (CI) by using Poisson regression for each independent variable incorporating the sampling weights and sampling design. Poisson regression is one of the most appropriate regression methods for obtaining an unbiased estimate of the prevalence ratio and the corresponding standard error in cross-sectional surveys.[15,16] Univariate and multiple Poisson regression models were fitted with the Taylor series linearization method of estimating standard errors in complex sample surveys.[17] The independent variables that were significant in univariate analysis were entered into the multiple regression model. Missing data in the regression models was handled using a complete case analysis method. All analysis was carried out using the *svy* command in Stata 15.1 software to account for sampling weights as well as complex survey design, and a P value of < 0.05 was considered statistically significant. The NFHS-5 was approved by the Ethics Committee at the International Institute for Population Sciences, Mumbai, India.

Results

The majority of women in the study were 20–29 years old with secondary-level education, belonged to the Hindu religion, and resided in a rural area. Univariate analysis showed that except for family structure, all other sociodemographic factors had a significant association with miscarriage [Table 1]. The sociodemographic risk factors identified were age above 29 years or below 20 years, urban residence, primary or above education level, higher wealth index levels, and employed women. The sociodemographic factors found to be protective for miscarriage were Muslim religion and belonging to SC, ST, or OBC castes.

The univariate association of various lifestyle factors and chronic disease or comorbid conditions with miscarriage showed that all comorbid conditions were found to have a significant association with miscarriage [Table 2]. The prevalence of miscarriage was higher among women with obesity, severe anemia, diabetes, hypertension, or with a thyroid disorder. Regarding lifestyle factors, both tobacco smoking and tobacco chewing were significantly associated, whereas alcohol usage was found to have no association with miscarriage. Regarding fertility-related factors, consanguineous marriage and previous miscarriage/abortion were not significantly associated with miscarriage. The number of ever-born children four and above was a risk factor, whereas intrauterine device (IUD) usage was a protective factor for miscarriage in the univariate analysis [Table 3].

Table 1: Association of various sociodemographic factors with miscarriage by using univariate Poisson regression analysis

Variables	Miscarriage *n*=5104 (%)	Live birth *n*=48,456 (%)	PR (95% CI)	*P*
Age in years				
15–19 (*n*=3480)	426 (12.2)	3054 (87.8)	1.46 (1.28, 1.68)	<0.001
20–24 (*n*=20,799)	1762 (8.5)	19,037 (91.5)	Reference	
25–29 (*n*=18,407)	1642 (8.9)	16,765 (91.1)	1.05 (0.97, 1.15)	0.230
30–34 (*n*=7572)	801 (10.6)	6771 (89.4)	1.29 (1.16, 1.43)	<0.001
≥35 (*n*=3302)	473 (14.3)	2829 (85.7)	1.73 (1.52, 1.97)	<0.001
Place of Residence				
Rural (*n*=43,007)	3864 (9.0)	39,143 (91.0)	Reference	
Urban (*n*=10,553)	1240 (11.8)	9313 (88.2)	1.23 (1.13, 1.35)	<0.001
Respondent's highest educational level				
No education (*n*=10,152)	789 (7.8)	9363 (92.2)	Reference	
Primary (*n*=6304)	589 (9.3)	5715 (90.7)	1.24 (1.08, 1.40)	0.001
Secondary (*n*=28,617)	2824 (9.9)	25,793 (90.1)	1.19 (1.08, 1.31)	<0.001
Higher (*n*=8487)	902 (10.6)	7585 (89.4)	1.23 (1.09, 1.39)	0.001
Religion				
Hindu (*n*=39,776)	3968 (10.0)	35,808 (90.0)	Reference	
Muslim (*n*=7494)	636 (8.5)	6858 (91.5)	0.85 (0.76, 0.95)	0.003
Christian (*n*=4180)	305 (7.3)	3875 (92.7)	0.91 (0.69, 1.19)	0.504
Others (*n*=2110)	195 (9.2)	1915 (90.8)	0.94 (0.77, 1.14)	0.531
Caste[#]				
SC (*n*=11,252)	1152 (10.2)	10,100 (89.8)	0.89 (0.79, 0.99)	0.045
ST (*n*=10,751)	741 (6.9)	10,010 (93.1)	0.65 (0.55, 0.75)	<0.001
OBC (*n*=20,569)	2026 (9.9)	18,543 (90.1)	0.82 (0.74, 0.91)	<0.001
None of them (*n*=8296)	974 (11.7)	7322 (88.3)	Reference	
Don't know (*n*=365)	46 (12.6)	319 (87.4)	0.79 (0.55, 1.15)	0.233
Wealth Index				
Poorest (*n*=14,136)	1067 (7.5)	13,069 (92.5)	Reference	
Poorer (*n*=12,341)	1102 (8.9)	11,239 (91.1)	1.11 (0.99, 1.23)	0.061
Middle (*n*=10,689)	1102 (10.3)	9587 (89.7)	1.31 (1.17, 1.45)	<0.001
Richer (*n*=9207)	973 (10.6)	8234 (89.4)	1.27 (1.13, 1.43)	<0.001
Richest (*n*=7187)	860 (12.0)	6327 (88.0)	1.40 (1.24, 1.56)	<0.001
Family structure				
Nuclear (*n*=17,759)	1700 (9.6)	16,059 (90.4)	Reference	
Non-nuclear (*n*=35,801)	3404 (9.5)	32,397 (90.5)	0.99 (0.92, 1.07)	0.780
Respondent employed or not				
Not Employed (*n*=51,955)	4893 (9.4)	47,062 (90.6)	Reference	
Employed (*n*=1605)	211 (13.1)	1394 (86.9)	1.56 (1.31, 1.86)	<0.001

[#]Some values are missing

For the multiple Poisson regression analysis, family structure, alcohol consumption, history of miscarriage/abortion, and consanguineous marriage were excluded as they were not significant in the univariate analysis. The adjusted prevalence ratios were not statistically significant for diabetes as well as tobacco smoking in the multiple regression model. Among the sociodemographic variables, the risk factors identified were age less than 20 years or more than 34 years, urban residence, primary or higher education level, middle and above wealth index, and employed status. The statistically significant sociodemographic protective factors were Muslim religion and ST and OBC castes. Regarding chronic diseases, obesity, severe anemia, hypertension, and thyroid disorder were all identified as significant comorbid risk factors. Among the lifestyle factors, tobacco chewing was the only significant risk factor. The lifestyle factors found to be protective were a higher number of ever-born children and the use of IUDs [Figure 1].

Discussion

Miscarriage is the most distressing complication in early pregnancy, with one in every five pregnant women ending in a miscarriage, and its causes are multifactorial.[18,19] Most of the studies from India attempted to identify risk factors for recurrent miscarriages, and only very few studies were carried out to know the risk and protective factors of miscarriages in India.[4,20,21] To the best of our knowledge, there are no studies in the Indian context that tried to find the association of sociodemographic, lifestyle, chronic disease conditions, and fertility-related risk and protective factors with miscarriage on a nationally representative sample. Awareness of primary care physicians about these risk factors would allow them to provide preventive aspects of comprehensive care for their patients.

Multiple regression analysis of sociodemographic factors indicated that the miscarriage rate was higher among very

Table 2: Association of various lifestyle factors and comorbid conditions with miscarriage using univariate Poisson regression analysis

Variables	Miscarriage *n*=5104 (%)	Live birth *n*=48,456 (%)	PR (95% CI)	*P*
Respondent is a tobacco smoker				
No (*n*=53,413)	5081 (9.5)	48,332 (90.5)	Reference	
Yes (*n*=147)	23 (15.6)	124 (84.4)	1.91 (1.07, 3.41)	0.030
Respondent is a tobacco chewer				
No (*n*=51,043)	4808 (9.4)	46,235 (90.6)	Reference	
Yes (*n*=2517)	296 (11.8)	2221 (88.2)	1.30 (1.11, 1.53)	0.001
Respondent drink alcohol				
No (*n*=52,928)	5051 (9.5)	47,877 (90.5)	Reference	
Yes (*n*=632)	53 (8.4)	579 (91.6)	1.02 (0.71, 1.46)	0.923
Respondent's BMI				
Normal BMI (*n*=29,314)	2520 (8.6)	26,794 (91.4)	Reference	
Underweight (*n*=7452)	666 (8.9)	6786 (91.1)	1.01 (0.90, 1.12)	0.911
Overweight (*n*=6948)	704 (10.1)	6244 (89.9)	1.16 (1.04, 1.29)	0.006
Obese (*n*=9846)	1214 (12.3)	8632 (87.7)	1.38 (1.27, 1.51)	<0.001
Respondent's Anemia level[#]				
Severe (*n*=1194)	156 (13.1)	1038 (86.9)	1.43 (1.13, 1.81)	0.003
Moderate (*n*=16,314)	1501 (9.2)	14,813 (90.8)	0.95 (0.88, 1.04)	0.280
Mild (*n*=13,625)	1226 (9.0)	12,399 (91.0)	0.91 (0.84, 0.99)	0.047
Non-anemic (*n*=20,359)	2055 (10.1)	18,304 (89.9)	Reference	
Respondent has diabetes[#]				
No (*n*=52,755)	4990 (9.5)	47,765 (90.5)	Reference	
Yes (*n*=384)	58 (15.1)	326 (84.9)	1.61 (1.18, 2.20)	0.003
Respondent has hypertension[#]				
No (*n*=51,857)	4830 (9.3)	47,027 (90.7)	Reference	
Yes (*n*=1398)	231 (16.5)	1167 (83.5)	1.76 (1.49, 2.07)	<0.001
Respondent has thyroid disorder				
No (*n*=52,594)	4915 (9.4)	4679 (90.6)	Reference	
Yes (*n*=966)	189 (19.6)	777 (80.4)	2.06 (1.73, 2.46)	<0.001

[#]Some values are missing

Table 3: Association of fertility related factors with miscarriage by using univariate Poisson regression analysis

Variables	Miscarriage *n*=5104 (%)	Live birth *n*=48,456 (%)	PR (95% CI)	*P*
Consanguineous marriage				
No (*n*=48,446)	4547 (9.4)	43,899 (90.6)	Reference	
Yes (*n*=5114)	557 (10.9)	4557 (89.1)	1.09 (0.98, 1.21)	0.104
History of Miscarriage/abortion				
No (*n*=52,011)	4950 (9.5)	47,061 (90.5)	Reference	
Yes (*n*=1549)	154 (9.9)	1395 (90.1)	0.93 (0.77, 1.13)	0.488
History of Contraceptive use[#]				
Nil (*n*=43,275)	4177 (9.7)	39,098 (90.35)	Reference	
IUD (*n*=2902)	161 (5.6)	2741 (94.4)	0.49 (0.40, 0.60)	<0.001
Pills/emergency contraception (*n*=6071)	622 (10.3)	5449 (89.7)	1.06 (0.95, 1.19)	0.281
Others (*n*=1299)	144 (11.1)	1155 (88.9)	1.20 (0.98, 1.45)	0.072
Number of children ever born to the respondent				
0 (*n*=21,054)	1992 (9.5)	19,062 (90.5)	Reference	
1 (*n*=17,282)	1478 (8.6)	15,804 (91.4)	0.89 (0.82, 0.97)	0.007
2 (*n*=8318)	880 (10.6)	7438 (89.4)	1.13 (1.02, 1.25)	0.013
3 (*n*=3771)	397 (10.5)	3374 (89.5)	1.03 (0.95, 1.24)	0.222
4 or more (*n*=3135)	357 (11.4)	2778 (88.6)	1.30 (1.13, 1.49)	<0.001

[#]Some values are missing

young women of 15–19 years as well as among women aged above 29 years, a finding that is in line with a study conducted in Nepal.[22] This association may be attributable to age-related biological mechanisms such as a decrease in hormonal function, an increase in chromosomal abnormality, or very young girls are not physically developed to bear a child.[4,11,18,22,23] The prevalence of miscarriage was significantly higher among educated women, and similar findings were reported from Nepal, Iran, and

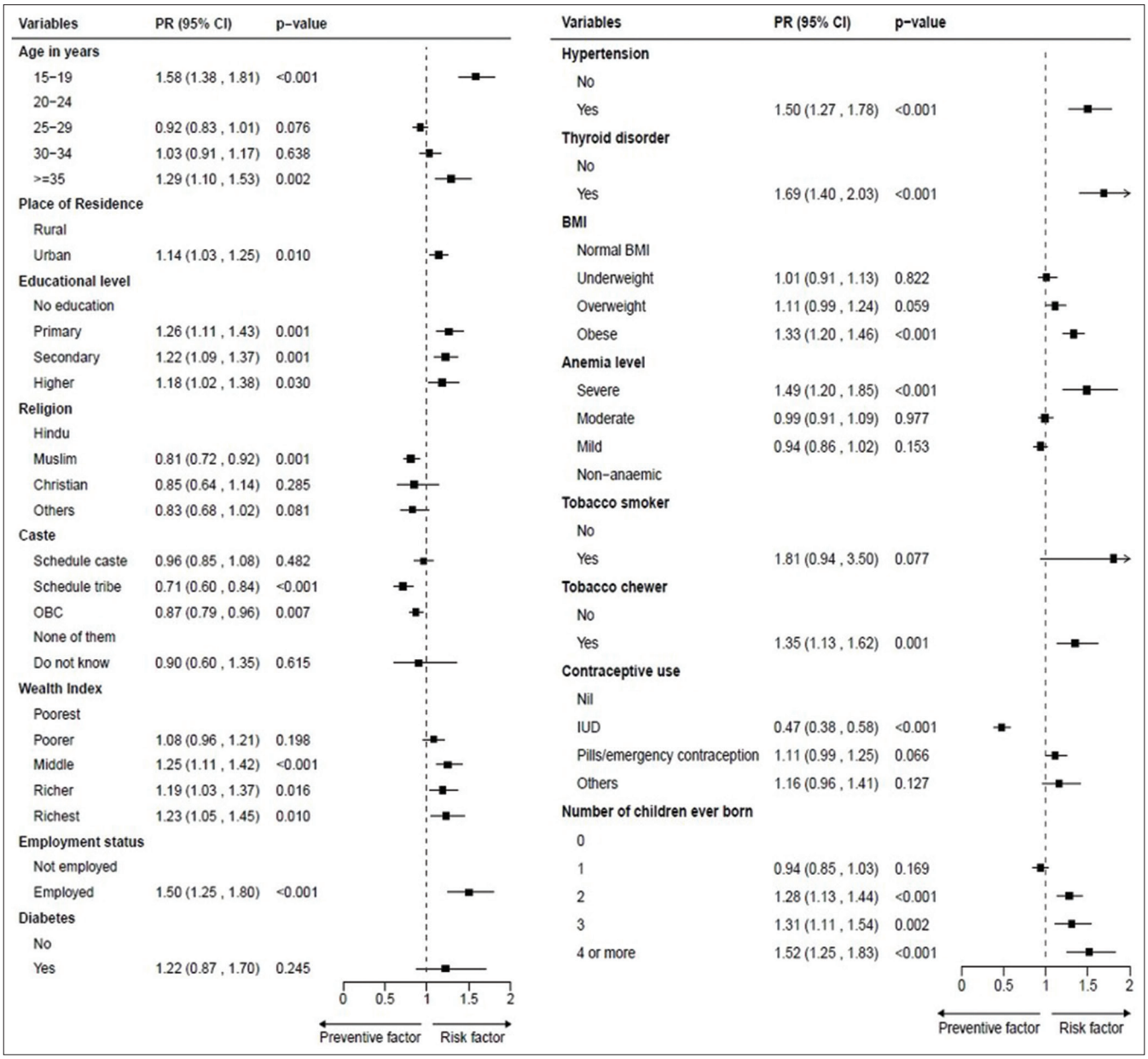

Figure 1: Results of multiple Poisson regression analysis

Ghana.[22,24,25] This association could be attributed to educated women having careers and getting married at a later age compared to illiterate women. Studies have shown that women from urban places have a higher prevalence of miscarriage compared to those from rural places, and our study corroborates this.[22,25,26] Negative impacts of urbanization such as air pollution and lifestyle factors could be the reasons for a higher rate of miscarriage among these women. However, conflicting findings were observed in studies from Ghana and China.[25,27] The prevalence of miscarriage was higher among women who belonged to higher wealth index families, a finding that is in line with other studies.[22,24,26] Wealthier women are more likely to be better educated with career options and tend to defer their marriage and pregnancy, which makes them more vulnerable to miscarriage. Occupational status was another significant sociodemographic risk factor for miscarriage, a similar finding reported from South Korea.[28] Workplace conditions such as night shift, work that involves lifting heavy items, and extreme temperatures may affect the development of embryos, leading to early pregnancy loss.[19,28] These lend credence to the findings of our study as the majority of the occupations were agricultural and non-skilled labor, which would expose them to extremes of temperature, pesticides, lifting weights, etc., The sociodemographic factors that were protective against miscarriage were Muslim religion and ST/OBC castes, and these findings are in line with a study carried out using NFHS-4 data.[26] However, how these factors protect against miscarriage does not have a clear construct. It may be due to the differences in cultural practices followed by them, such as younger age at marriage and pregnancy among both Tribal and Muslim communities, which placed them at lower risk.[13] Younger women are less likely to

miscarry than those who become pregnant later in life. Those of other castes get higher education and follow career paths that delay their age at marriage and pregnancy, which is not so among the ST/OBC castes. It could also be postulated that the effect seen is the result of under-reporting of miscarriages among these communities rather than real protection. Thus, there is a need for further research in this area to find real factors that protect against miscarriage so that they can be reduced.

Regarding the relation between comorbid conditions and miscarriage, our results are consistent with existing evidence of the association with obesity, severe anemia, hypertension, and thyroid disorder. Primary care physicians can educate their patients about these risk factors, identify them, and provide timely interventions so that miscarriage can be reduced among the population under their care. Obesity was reported as a risk factor for miscarriage in many studies conducted in various populations.[3,11,24,29] In cohort studies conducted in China and Spain, it was observed that women with severe anemia before pregnancy have increased odds of miscarriage compared to those with normal hemoglobin levels.[30,31] Though the exact physio-pathological mechanism behind the relationship between anemia and miscarriage remains unclear, iron deficiency could be the main reason as it increases hypoxia and oxidative stress. Our results are similar to previous findings that thyroid disorder and hypertension pose as risk factors for miscarriage.[3,24,32,33] Thyroid dysfunction is a common complication of pregnancy, and there is evidence for an association between thyroid dysfunction with pregnancy loss. A cohort study established an association between miscarriage and elevated blood pressure during preconception or early pregnancy period.[33] Similarly, there is evidence that pregestational and gestational diabetes are risk factors for miscarriage.[22] In our study, this association was not significant after adjusting for other variables in the multiple regression model. Prevention and treatment of obesity, hypertension, anemia, and thyroid disorders among the patients presenting in the primary care settings would enable primary care physicians to contribute to reduction of miscarriage at their level. Many studies have found tobacco smoking to be a risk factor for miscarriage; however, in our study, this association was not significant. This could be due to a smaller number of smokers in our sample, which may not be enough to get a significant association in the multiple regression model. Smokeless tobacco usage increases the risk of miscarriage, preterm births, stillbirths, loss of functional placentae components, pregnancy-related elevated glucose concentrations, low birth weight, reduced gestational age at birth, etc.[34] This indicates that reducing miscarriages should involve active efforts to reduce tobacco use among women, for which family physicians and primary care providers have a major role to play.

In our study, the prevalence of miscarriage was 53% less among those women who had ever used an IUD compared to women who never used any method of contraception, whereas no association was observed between oral contraceptive use and miscarriage. There is contradicting evidence on the association between the use of contraception and miscarriage.[22] Though in the NFHS-5, data were collected on the ever-usage of various contraceptives, there could be a high possibility that the majority of IUD-ever users had recently started using it, especially after having a live birth. This reverse causality could be the reason for the low prevalence of miscarriage among IUD users compared to women who never used any contraception. This study found that the prevalence of miscarriage increased with the number of children ever born, which was used as a surrogate measure for the number of previous pregnancies. Similar results were observed in studies conducted in Australia and Israel; however, a conflicting finding was reported from Ghana.[25,35,36] This contradicting finding could be the result of differences in fertility characteristics such as the age at marriage, age at first pregnancy, inter-pregnancy interval, etc., and some socioeconomic factors between the populations of Ghana and other developing/developed nations.

There were some limitations in our study. The design is cross-sectional, which limits the casual association of a few variables. The data on diabetes, thyroid disorder, hypertension, and miscarriage were self-reported and were not confirmed using lab reports. Hence, there could be possibilities of response bias, under-reporting, and misclassification biases. This study only examined the sociodemographic, lifestyle, and a few fertility and comorbid conditions, and did not consider the association with diet, inter-pregnancy interval, and chromosomal abnormalities. Despite all these limitations, by selecting only women who were pregnant in the 12 months preceding the survey, recall bias was eliminated to some extent; in addition, a nationally representative sample provides a much more reliable inference on various factors associated with miscarriage in India.

Conclusion

The study identified various sociodemographic, lifestyle, comorbid, and fertility-related risks as well as protective factors associated with miscarriage in India. The sociodemographic risk factors were age less than 20 years or greater than 34 years, urban residence, primary or more education level, high income, and employment status, whereas the protective factors were Muslim religion and SC/OBC caste. Obesity, severe anemia, hypertension, and thyroid disorder were the comorbid risk factors for miscarriage. Tobacco chewing and two or more ever-born children were respectively the lifestyle and fertility-related risk factors. The use of IUDs was the only fertility-related protective factor for miscarriage. To reduce the incidence of miscarriage in developing countries like India, the respective governments, and healthcare providers should develop intervention programs, especially targeting women in well-educated and high-income families. A multipronged approach should be used, including enabling family physicians and primary care providers to contribute toward the same by equipping them with knowledge about the risk factors of miscarriage.

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Conflicts of interest

There are no conflicts of interest.

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