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Prevalence of and risk factors for eclampsia in pregnant women in India

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Abstract

Objective: Eclampsia is a potentially fatal disorder in pregnant women and remains an important cause of maternal and perinatal child morbidity and death worldwide. We aimed to assess the prevalence of and risk factors for convulsions (not occurring from fever) during pregnancy in Indian women. Convulsion is a key symptom suggestive of eclampsia.

Methods: Cross-sectional data from India's third National Family Health Survey, conducted during 2005–2006 were used. Self-reported information on convulsions during pregnancy was obtained from 39,657 women aged 15–49 years who had a live birth in the 5 years preceding the survey. Multiple logistic regression analysis was used to explore risk factors for convulsion in pregnancy.

Results: Overall, 1 in 10 women reported having convulsions in their most recent pregnancy. The prevalence was significantly higher in women living in rural areas compared with those living in urban areas (11.3% vs. 7.4%; $P<0.0001$), with marked state and geographic variation. The odds of convulsions were significantly higher in women with a twin pregnancy [odds ratio (OR) 2.12; 95% confidence interval (CI) 1.45–3.11], a previously terminated pregnancy (OR 1.32; 95% CI 1.20–1.45), diabetes (OR 1.37; 95% CI 0.99–1.89), or asthma (OR 1.85; 95% CI 1.35–2.54), in women who were alerted to pregnancy complications (OR 2.78; 95% CI 2.50–3.08), in Sikh women (OR 1.73; 95% CI 1.28–2.33), in women in a low social group (OR 1.40; 95% CI 1.25–1.58), and in women residing in central India (OR 1.51; 95% CI 1.31–1.74) or eastern India (OR 1.33; 95% CI 1.14–1.54) with reference to their counterparts.

Conclusion: Our findings from a large population-based nationally representative sample of Indian women indicate a high prevalence of convulsions, a symptom suggestive of eclampsia, and its association with several maternal, lifestyle risk factors and sociodemographic characteristics.

Keywords: Convulsions; eclampsia; risk factors; women; Indian

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Introduction

'Eclampsia' refers to the occurrence of new-onset, generalized, tonic–clonic seizures or coma in a woman with preeclampsia. It is the convulsive manifestation of preeclampsia and one of several clinical manifestations at the severe end of the preeclampsia spectrum [1, 2]. It is a potentially fatal disorder in pregnant women and remains an important cause of maternal and perinatal child morbidity and death worldwide, accounting for more than 50,000 maternal deaths annually

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[3–7]. World Health Organization estimated, at least 16% of maternal deaths in low- and middle-income countries (LMICs) result from hypertensive disorders of pregnancy, of which eclampsia is the primary contributor [8]. Preeclamptic women in LMICs are also three times likelier to progress to eclampsia than women in high-income countries [9]. Largely on the basis of clinical data, the incidence of eclampsia ranges between 2% and 10%, depending on the population studied and the definition of eclampsia used [10]; clinical studies suggest that the proportion of deliveries impacted by eclampsia in Indian women ranges from as low as 0.9% to as high as 7.7% [11–14]. However, these clinical studies likely suffer from selection bias on the basis of severity of the condition, especially among populations with limited access to prenatal care, and therefore may underestimate the prevalence of the condition. Precise country-specific population-level estimates of eclampsia prevalence are largely unavailable.

Risk factors for eclampsia reported in high-income countries include young and old maternal age, obesity before pregnancy, being unmarried, excessive weight gain during pregnancy, multiple gestations, nulliparity, chronic hypertension, low socioeconomic status, prolonged birth interval, lack of prenatal care, and current smoking [15–21]. Very few population-based epidemiological studies of eclampsia have been conducted in LMICs. Prior studies were largely undertaken in clinical settings [13, 22–24], and do not provide representative data on risk factors as they are based on highly selected samples. Available information suggests that predisposing factors in LMICs may include poverty, illiteracy, low educational attainment, lack of health awareness, and poor access to antenatal care (ANC) during pregnancy. Previous studies have also found that beliefs about seeking medical advice during pregnancy may also be a factor in some LMICs, and can result in delayed diagnosis and inappropriate treatment of patients with preeclampsia or eclampsia [25, 26].

India is in the midst of a demographic, epidemiological, and nutrition transition characterized by a growing population, increasing urbanization, a shift in the patterns of diseases, and changes in lifestyle [27]. The past decade has seen a dramatic increase in lifestyle-related noncommunicable diseases, including obesity, diabetes mellitus, hypertension, coronary heart disease, stroke, and cancers [28]. Given that preeclampsia shares many risk factors with cardiovascular disease (e.g., obesity, type 2 diabetes, and hypertension), it is expected that the increase in cardiovascular disease risk factors to occur in women of childbearing age will translate into a higher incidence of preeclampsia and its complications (e.g., eclampsia). The objective of this study was thus to quantify the prevalence and predictors of convulsions (not occurring from fever), a symptom suggestive of eclampsia, with use of nationally representative data among Indian women.

Methods

Study setting and participants

Cross-sectional data from the third National Family Health Survey (NFHS-3), conducted in India in 2005–2006, was used for this study. NFHS-3 was designed on the lines of the Demographic and Health Surveys (available at www.measuredhs.com), which have been conducted in many LMICs since the 1980s. The National Family Health Survey has been conducted in India for three successive rounds, each at an interval of 5 years. NFHS-3 collected demographic, socioeconomic, and health information from a nationally representative probability sample of 124,385 women aged 15–49 years residing in 109,041 households. The sample is a multistage cluster sample with an overall response rate of 98%. All states of India are represented in the sample (except the small union territories), covering more than 99% of the country's population. Full details of the survey have been published [29] and are available at www.nfhsindia.org. To assess symptoms suggestive of eclampsia, we restricted the sample to those women who had had a live birth in the 5 years preceding the survey. We further restricted our analyses to data pertaining to the most recent birth, both to minimize recall bias and to draw on antenatal care (ANC) measures, which were available only for the most recent pregnancy. This resulted in a final sample size of 39,657 participants.

Outcome measures

To assess the occurrence of eclampsia, we constructed a measure based on women's self-reports of symptoms during pregnancy. Specifically, mothers were asked: "During this pregnancy, did you have convulsions not from fever?".

The response options were "Yes," "No," and "Don't know." Following World Health Organization [30] and National Institute for Health and Care Excellence [31] guidelines, we created a dichotomous indicator of eclampsia: women who reported experiencing convulsions (not from fever) were coded as eclamptic. However, it was not possible to confirm clinical diagnosis of these symptoms. Data on physician-reported diagnosis of convulsions (not from fever) or clinical test results were not available in the NFHS-3 to verify a self-reported diagnosis.

Predictor variables

The following maternal reproductive risk factors were evaluated in the adjusted analysis: total number of children ever born (one, two or three, four or more); preceding birth interval (first birth order, interval <2 years, interval 2–3 years, interval >3 years); ANC visit during pregnancy (no visits, one visit, two visits, three visits, four of more visits); blood pressure measured during pregnancy (no, yes); received advice on pregnancy nutrition during ANC visit (no, yes); alerted to pregnancy complications such as convulsions (no, yes); type of pregnancy (singleton, twin); ever had a terminated pregnancy (no, yes); and anemia level (not anemic, mild anemia, moderate anemia, severe anemia). The biological and lifestyle factors included body mass index (BMI) categories (Indian adult population standard) [32] – 18.4 kg/m^2 or less (underweight), 18.5–22.9 kg/m^2 (normal), 23.0–24.9 kg/m^2 (overweight), 25.0 kg/m^2 or more (obese); current tobacco smoking (no, yes); alcohol consumption (no, yes); self-reported diabetes (no, yes); and self-reported asthma (no, yes). Sociodemographic predictors included age (15–29 years, 30–39 years, 40–49 years); education (no education, primary education, secondary education, higher education); religion (Hindu, Muslim, Christian, Sikh, others); caste (Scheduled Castes, Scheduled Tribes, Other Backward Class, others); employment status (not working, working); wealth index (measured by an index based on household ownership of assets and graded as lowest, second, middle, fourth, and highest) that was computed by previously described methods [29]; place of residence (urban, rural); and geographic regions (north, northeast, central, east, west, south). For the definition of some variables, see Table 1.

Statistical analyses

We first examined observed and expected regional and rural/urban differences in the prevalence of seizures and then estimated associations with eight socioeconomic and demographic variables, nine maternal factors, and five BMI- and lifestyle-related and disease-related factors. We did this analysis since we anticipated a striking difference in the prevalence of eclampsia by state since all the states in India are in different levels of demographic, epidemiological, and fertility transition and the differences in health-care and health-seeking behavior among women is also discernible. To do this analysis, firstly we ran a multiple regression model (not including the following geographic variables: state and region and place of residence) but including the identified potential risk factors. By using the "predict" command in the logistic regression, we 'estimated' the risk (log odds) of eclampsia for every participant in this study. Then, using this estimated risk, we obtained the average by each state and then compared the estimates with the observed prevalence (see Table 2). We then plotted the results as bar plots sorted from the lowest to the highest prevalence of eclampsia, and for each state we have the observed and the estimated rates based on our model. This is a simple way to try to quantify what accounts for the massive difference in the states.

Potential risk factors were selected on the basis of previous knowledge of their association with seizures presented in earlier literature. Lastly we used multiple logistic regression models to estimate the prevalence odds ratios (ORs) for each of these risk factors, adjusted for the above-mentioned confounders and risk factors. As certain states and certain categories of respondents were oversampled, sample weights were used to restore the representativeness of the sample [29].

The results are presented as ORs with 95% confidence intervals (CIs). The estimation of CIs takes into account design effects due to clustering at the level of the primary sampling unit. We assessed the possibility of multicollinearity between the covariates. In the correlation matrix of covariates, all pairwise Pearson correlation coefficients were less than 0.5, suggesting that multicollinearity did not affect the findings. Analyses were conducted with the IBM SPSS Statistics version 19 (IBM, Armonk, NY, United States).

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Table 1. Characteristics of the study participants and reported prevalence of eclampsia during pregnancy for the most recent live birth among women aged 15–49 years (*n*=39,657) who had a live birth in the 5 years preceding the survey according to selected characteristics, India, 2005–2006

Characteristics	Sample distribution		Eclampsia		*P* value
	n	%	*n*	%	
Maternal factors					
Parity					<0.0001
1	10,453	26.4	907	8.7	
2–3	18,199	45.9	1699	9.3	
4+	11,005	27.8	1465	13.3	
Preceding birth interval					<0.0001
First-order birth	10,546	26.6	913	8.7	
Interval <2 years	7124	18.0	801	11.3	
Interval 2–3 years	9538	24.1	1019	10.7	
Interval 3+ years	12,448	31.4	1337	10.8	
ANC visit during pregnancy					<0.0001
No visits	9035	23.0	1222	13.5	
1 visit	2377	6.0	341	14.4	
2 visits	7329	18.6	765	10.4	
3 visits	5953	15.1	588	9.9	
4+ visits	14,663	37.3	1116	7.6	
Blood pressure measured during pregnancy[a]					<0.0001
No	9756	32.0	1113	11.4	
Yes	20,764	68.0	1808	8.7	
Received advice on pregnancy nutrition during ANC visit[a]					0.002
No	10,413	34.0	1038	10.0	
Yes	20,198	66.0	1809	9.0	
Alerted to pregnancy complications such as convulsions during ANC visit[a]					<0.0001
No	25,887	84.6	2088	8.1	
Yes	4715	15.4	760	16.2	
Type of pregnancy					<0.0001
Singleton	39,298	99.1	4014	10.2	
Twin	359	0.9	57	15.9	
Ever had a terminated pregnancy[b]					<0.0001
No	32,319	81.5	3150	9.8	
Yes	7338	18.5	921	12.6	
Anemia level[c]					0.013
Not anemic	14,939	40.1	1490	10.0	
Mild	15,082	40.4	1613	10.7	
Moderate	6616	17.7	754	11.4	
Severe	652	1.7	65	10.0	
BMI and lifestyle factors					
BMI[d]					<0.0001
Underweight (≤18.4 kg/m^2)	12,837	38.0	1969	11.0	
Normal (18.5–22.9 kg/m^2)	15,863	46.9	1603	11.1	
Overweight (23.0–24.9 kg/m^2)	2525	7.3	242	8.7	

Table 1 (continued)

Characteristics	Sample distribution		Eclampsia		*P* value
	n	%	*n*	%	
Obese (≥25.0 kg/m^2)	2789	7.8	175	5.9	
Current tobacco smoker					<0.0001
No	39,049	98.5	3980	10.2	
Yes	608	1.5	91	15.0	
Alcohol drinker					0.008
No	38,735	97.7	3954	10.2	
Yes	911	2.3	116	12.7	
Diabetes[e]					<0.0001
No	39,123	98.7	3984	10.2	
Yes	160	1.3	85	16.6	
Asthma[e]					<0.0001
No	39,163	98.8	3979	10.2	
Yes	470	1.2	91	19.4	
Background factors					
Age (years)					0.127
15–19	2982	7.5	348	11.7	
20–24	13,269	33.5	1341	10.1	
25–29	12,908	32.6	1286	10.0	
30–34	6685	16.9	699	10.5	
35–39	2723	6.9	279	10.2	
40–44	835	2.1	97	11.6	
45–49	210	0.5	21	10.0	
Mean age 34.89 (±7.87) years					
Education[f]					<0.0001
No education	18,783	47.4	2277	12.1	
Primary	5550	14.0	591	10.7	
Secondary	12,959	32.7	1089	8.4	
Higher	2365	6.0	114	4.8	
Religion					0.019
Hindu	31,280	78.9	3191	10.2	
Muslim	6482	16.3	686	10.6	
Christian	814	2.1	65	8.0	
Sikh	514	1.3	70	13.7	
Others[g]	568	1.4	59	10.4	
Caste/tribe[h]					<0.0001
Scheduled Caste	7945	20.1	778	9.8	
Scheduled Tribe	3742	9.5	420	11.2	
Other Backward Class	15,878	40.2	1825	11.5	
General	10,845	27.5	971	9.0	
Missing caste	1089	2.8	63	5.8	
Employment status					<0.0001
Not working	27,699	70.0	2958	10.7	
Working	11,898	30.0	1110	9.3	

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Table 1 (continued)

Characteristics	Sample distribution		Eclampsia		*P* value
	n	%	*n*	%	
Wealth index[i]					<0.0001
Lowest	9566	24.1	1296	13.6	
Second	8600	21.7	955	11.1	
Middle	7769	19.6	779	10.0	
Fourth	7256	18.3	611	8.4	
Highest	6466	16.3	431	6.7	
Place of residence					<0.0001
Urban	10,622	26.8	789	7.4	
Rural	29,035	73.2	3282	11.3	
Geographic region[j]					<0.0001
North	5678	12.8	489	9.6	
Northeast	1613	4.1	121	7.5	
Central	11,111	28.0	1424	12.8	
East	10,042	25.3	1510	15.1	
West	5117	12.9	195	3.8	
South	6696	16.9	332	5.0	
Total[k]	39,657		4071	10.3	

ANC, antenatal care; BMI, body mass index.

[a]Based on 30,583 total cases, and 9029 missing cases for which there was no ANC visit.

[b]Includes miscarriages/spontaneous abortion and induced abortion.

[c]Mild anemia (hemoglobin 10.0–10.9 g/dL for pregnant women, 10.0–11.9 g/dL for nonpregnant women, and 12.0–12.9 g/dL for men), moderate anemia (7.0–9.9 g/dL for women and 9.0–11.9 g/dL for men), and severe anemia (<7.0 g/dL for women and <9.0 g/dL for men). In the survey appropriate adjustments in these cutoff points were made for respondents living at altitudes above 1000 m and for respondents who smoke, since both of these groups require more hemoglobin in their blood [33].

[d]In the third National Family Health Survey, all respondents were weighed with a solar-powered scale with an accuracy of ±100 g. Their height was measured with an adjustable wooden measuring board, specifically designed to provide accurate measurements (to the nearest 0.1 cm). Women who were pregnant at the time of the survey or who had given birth during the 2 months preceding the survey were excluded from these anthropometric measurements.

[e]From self-reports only.

[f]No education, 0 years of education; primary education, 1–5 years of education; secondary education, 6–8 years of education; higher education, at least 9 years of education.

[g]Others include Buddhist, Jain, Jewish, and Zoroastrian.

[h]Scheduled Castes and Scheduled Tribes are identified by the Government of India as socially and economically backward and needing protection from social injustice and exploitation. Other Backward Class is a diverse collection of intermediate castes that were considered low in the traditional caste hierarchy but are clearly above Scheduled Castes. Others are thus a default residual group that enjoys higher status in the caste hierarchy.

[i]Items included in the wealth index in the third National Family Health Survey household include electrification, type of windows, drinking water source, type of toilet facility, type of flooring, material of exterior walls, type of roofing, cooking fuel, house ownership, number of household members per sleeping room, ownership of a bank or post office account, and ownership of a mattress, a pressure cooker, a chair, a cot/bed, a table, an electric fan, a transistor radio, a black and white television, a color television, a sewing machine, a cell phone, any other

Table 1 (continued)

telephone, a computer, a refrigerator, a watch or clock, a bicycle, a motorcycle or scooter, an animal-drawn cart, a car, a water pump, a thresher, and a tractor.

[j]North, Delhi, Haryana, Himachal Pradesh, Jammu and Kashmir, Punjab, Rajasthan, Uttaranchal; northeast, Assam, Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, Tripura; central, Chhattisgarh, Madhya Pradesh, Uttar Pradesh; East: Bihar, Jharkhand, West Bengal, Orissa; west, Maharashtra, Goa, Gujarat; south, Andhra Pradesh, Karnataka, Kerala, Tamil Nadu.

[k]The number of women varies slightly for individual variables depending on the number of missing values.

Ethical considerations

The NFHS-3 survey received ethics approval from the International Institute for Population Science's Ethical Review Board and the Indian Government. Prior written informed consent was obtained from each respondent. The analysis presented in this study is based on secondary analysis of existing survey data with all identifying information removed.

Results

Observed and expected prevalence of convulsions in pregnancy by area of residence and state. Overall, 1 in 10 participants (10.3%; n=4071) in our sample reported convulsions (not from fever) during pregnancy, symptoms suggestive of eclampsia (Table 2). The observed prevalence was significantly higher in women living in rural areas than in those living in urban areas (11.3% vs. 7.4%; P<0.0001; Figs. 1–3). There was marked state-level variation in the observed prevalence of convulsions, with rates ranging from 1.1% in Tamil Nadu to 24.5% in Jharkhand (Fig. 4). The observed prevalence of convulsions was greater than 20% in Uttarakhand, Bihar, Jharkhand, Arunachal Pradesh, and Sikkim and between 10% and 20% in Punjab, Madhya Pradesh, Uttar Pradesh, Orissa, Nagaland, and Tripura.

Characteristics of the study participants

Table 1 presents the characteristics of the study participants. One quarter of the mothers had given birth once, 31% of the births were preceded by an interval of more than 3 years, and 1% of the pregnancies resulted in multiple births. Approximately one fifth (18.5%) of the mothers reported having terminated a pregnancy. Malnutrition rates were high: almost one fifth of the mothers were moderately or severely anemic, 31% were underweight, and 22% were either overweight or obese. More than half the mothers had had four or more ANC visits during their last pregnancy, for 68% blood pressure was measured during an ANC visit during their last pregnancy, 66% reported receiving advice on pregnancy nutrition during an ANC visit, and only 15% were alerted to the possibility of pregnancy-related complications such as convulsions. Very few were current smokers (1.5%) or alcohol drinkers (2.3%). The prevalence of diabetes (1.3%) and asthma (1.2%) was low. Most mothers (almost three quarters) were aged between 15 and 29 years (the mean age being 34.89 years), and almost half (47.4%) had no education. Most of the mothers (four in five) were identified as Hindu, and two fifths belonged to Other Backward Class. Seventy percent of the mothers were not working and one quarter belonged to the poorest households. More than 70% of the mothers were residing in rural areas, whereas 28% were residents of central India.

Prevalence of convulsions in pregnancy

The prevalence of reported convulsions was highly significant (P<0.0001) in the following groups: parity greater than four (13.3%); a preceding birth interval of less than 2 years (11.3%); no ANC (13.5%); women alerted to pregnancy complications such as convulsions (16.2%); women with a twin pregnancy (15.9%); women with a previously terminated pregnancy (12.6%); women with moderate anemia (11.4%) to severe anemia (10.0%); underweight (11.0%) and normal-weight women (11.1%); current smokers (15.0%); current alcohol drinkers (12.7%); women with diabetes (16.6%) or asthma (19.4%); women with no education (12.1%); Sikh women (13.7%); women belonging to Scheduled Tribes and Other Backward Class; women belonging to households in the lowest wealth quintile (13.6%); women who do not work (10.7%);

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Table 2. Observed versus expected prevalence of eclampsia during pregnancy for the most recent live birth among women aged 15–49 years (*n*=39,657) who had a live birth in the 5 years preceding the survey, by state and residence, India, 2005–2006

	Urban			Rural			Total		
	n	Observed (%)	Expected (%)	*n*	Observed (%)	Expected (%)	*n*	Observed (%)	Expected (%)
India	789	7.4	19.4	3282	11.3	80.6	4071	10.3	8.5
Northern region									
Delhi	53	6.6	6.4	7	10.1	0.2	60	6.9	1.5
Haryana	17	7.2	2.1	40	6.3	1.3	57	6.6	1.5
Himachal Pradesh	7	9.1	0.8	79	11.9	2.6	86	11.6	2.2
Jammu and Kashmir	1	0.5	0.1	38	5.5	1.2	39	4.4	1.0
Punjab	54	15.5	6.5	92	15.9	3.0	146	15.7	3.7
Rajasthan	40	13.0	4.8	73	6.7	2.4	113	8.1	2.9
Uttaranchal	38	17.6	4.6	149	22.7	4.8	187	21.4	4.8
Central region									
Chhattisgarh	18	8.4	2.6	84	8.5	2.7	102	8.5	2.6
Madhya Pradesh	53	9.7	8.7	287	16.7	9.3	340	15.0	8.7
Uttar Pradesh	108	10.5	13.0	514	13.1	16.0	622	12.6	15.9
Eastern region									
Bihar	45	22.6	5.4	300	20.4	9.7	345	20.7	8.8
Jharkhand	32	13.7	3.9	261	27.1	8.4	293	24.5	7.5
Orissa	25	12.4	3.0	171	14.9	5.5	196	14.5	5.0
West Bengal	10	2.1	1.2	75	4.7	2.4	85	4.1	2.2
Northeastern region									
Arunachal Pradesh	54	34.0	6.5	75	17.4	2.4	129	21.8	3.3
Assam	11	6.8	1.3	59	5.4	1.9	70	5.6	1.8
Manipur	19	4.3	2.3	66	6.4	2.1	85	5.8	2.2
Meghalaya	9	6.3	1.1	64	9.6	2.1	73	9.0	1.9
Mizoram	9	3.1	1.1	8	2.5	0.3	17	2.8	0.4
Nagaland	49	14.7	5.9	190	17.4	6.1	239	16.8	6.1
Sikkim	14	15.4	1.7	103	22.7	3.3	117	21.5	3.0
Tripura	9	11.0	1.1	69	15.7	2.2	78	15.0	2.0
Western region									
Goa	23	5.2	1.3	27	7.7	0.9	50	6.3	1.3
Gujarat	16	3.7	1.8	56	8.5	1.8	72	6.6	1.8
Maharashtra	24	2.1	1.4	30	2.3	1.0	54	2.2	1.4
Southern region									
Andhra Pradesh	28	4.9	2.3	61	5.2	2.0	89	5.1	2.3
Karnataka	47	7.7	3.4	86	9.0	2.8	133	8.5	3.4
Kerala	7	2.7	0.8	24	4.3	0.8	31	3.8	0.8
Tamil Nadu	9	1.5	0.4	5	0.7	0.2	14	1.1	0.4

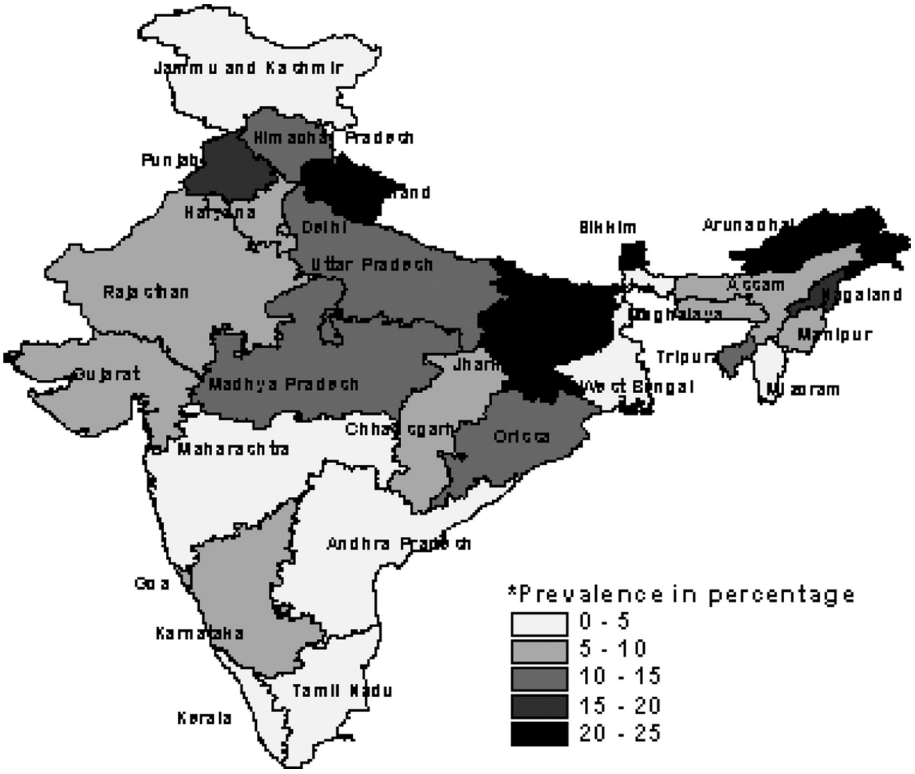

Fig. 1. Prevalence of eclampsia in India, 2005–2006.

women residing in rural areas (11.3%); and among women living in the eastern part of India (15.1%).

Associations between convulsion and predictor variables

The adjusted odds for convulsion were significantly higher in women with a twin pregnancy compared with a singleton (OR 2.12; 95% CI 1.45–3.11), in women with a previous terminated pregnancy (OR 1.32; 95% CI 1.20–1.45), among women who were alerted to pregnancy complication such as convulsions during an ANC visit (OR 2.78; 95% CI 2.50–3.08), in women with diabetes (OR 1.37; 95% CI 0.99–1.89) or asthma (OR 1.85; 95% CI 1.35–2.54), among Sikh women (OR 1.73; 95% CI 1.28–2.33) compared with Hindu women, among women belonging to Other Backward Class (OR 1.40; 95% CI 1.25–1.58) compared with women belonging to Scheduled Castes, women residing in rural areas (OR 1.22; 95% CI 1.09–1.37) or in central (OR 1.51; 95% CI 1.31–1.74) or eastern (OR 1.33; 95% CI 1.14–1.54) regions of India compared with women residing in northern regions (Table 3).

Women with at least one ANC visit during pregnancy (OR 0.68–0.77; 95% CI: 0.59–0.79), overweight (OR 0.86; 95% CI: 0.73–1.02) or obese women (OR: 0.70; 95%CI: 0.58–0.85), women older than 20 years of age, women who are employed (OR 0.85; 95% CI 0.79–0.92), women with higher educational attainment (OR 0.68; 95% CI 0.54–0.87), women with higher household wealth status, and women living in north eastern (OR 0.74; 95% CI 0.56–0.98), western (OR 0.38; 95% CI 0.31–0.47), and southern (OR 0.44; 95% CI 0.36–0.52) regions of India had a lower likelihood of having symptoms suggestive of eclampsia.

Discussion

In this nationwide large-scale cross-sectional study we identified three main sets of findings relating to (1) overall self-reported prevalence of convulsions (not from fever), which are the main symptoms of eclampsia, (2) massive geographic differences in prevalence, and (3) risk factors for prevalence. We found that the prevalence of reported convulsions (10.3%) was high compared with that in earlier studies of clinical eclampsia in Asian populations, notably in Singapore [34].

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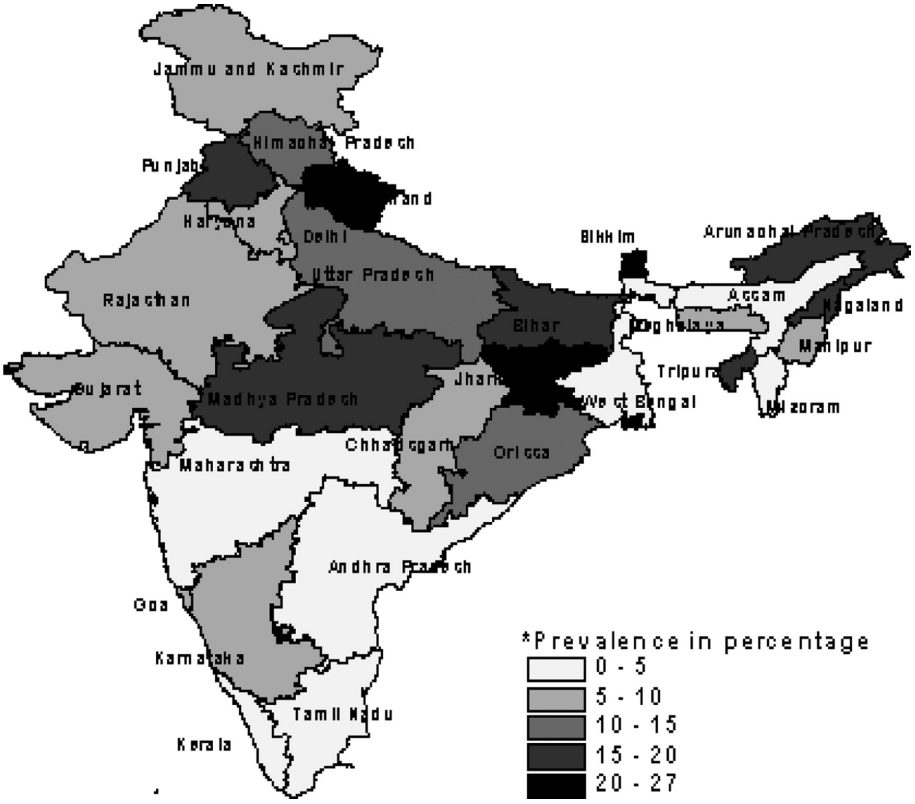

Fig. 2. Prevalence of eclampsia in rural India, 2005–2006.

The prevalence in our study is higher than not only that of high-income countries but also that of most LMICs and the incidence is higher than that reported in other parts of India. This may be due to the cross-sectional symptomatic nature of the study rather than clinical confirmation. The only other study that gives an incidence similar to that of our study is from the Dhaka Medical College and Hospital, Bangladesh, which is the largest tertiary referral government hospital in Bangladesh and deals mostly with referral cases, where the incidence of eclampsia is 9% [25]. Therefore from the study we can safely say that approximately 10% of the Indian women surveyed who had been pregnant during the previous 5 years self-reported convulsions. The diagnosis of convulsions was suspected and was not confirmed by a clinician. The cause of the convulsions was not specified. Some (perhaps a small minority of the seizures) were associated with eclampsia.

In this study we used the occurrence of convulsions (not from fever) as a proxy for eclampsia. There are other causes of nonfebrile seizures in pregnancy and it is not justified to make that presumption without our talking about the general prevalence of epilepsy in the general population. In various studies the overall prevalence of epilepsy in India is estimated to be between 2.5 and 11.9 per 1000 population [35–39]. The prevalence is reported to be about 1% of the overall population [35], being higher in the rural population (1.9%) than in the urban population (0.6%) [40, 41]. However, there are almost to 1.5 million women with epilepsy in the reproductive age group (15–49 years) in India [42]. There are very few incidence studies from India, and the most recent one suggests an age-standardized incidence rate of 27.3 per 100,000 per year [43].

Convulsions (during pregnancy) are a common manifestation of epilepsy and eclampsia [44], and in the case of no history of epilepsy before conception, eclampsia remains the major cause of convulsions that are a result of untreated hypertension during pregnancy. Apart from eclampsia and idiopathic causes, the various other causes of convulsions during pregnancy include antiphospholipid syndrome, cerebral vein thrombosis, thrombotic thrombocytopenic purpura, cerebral

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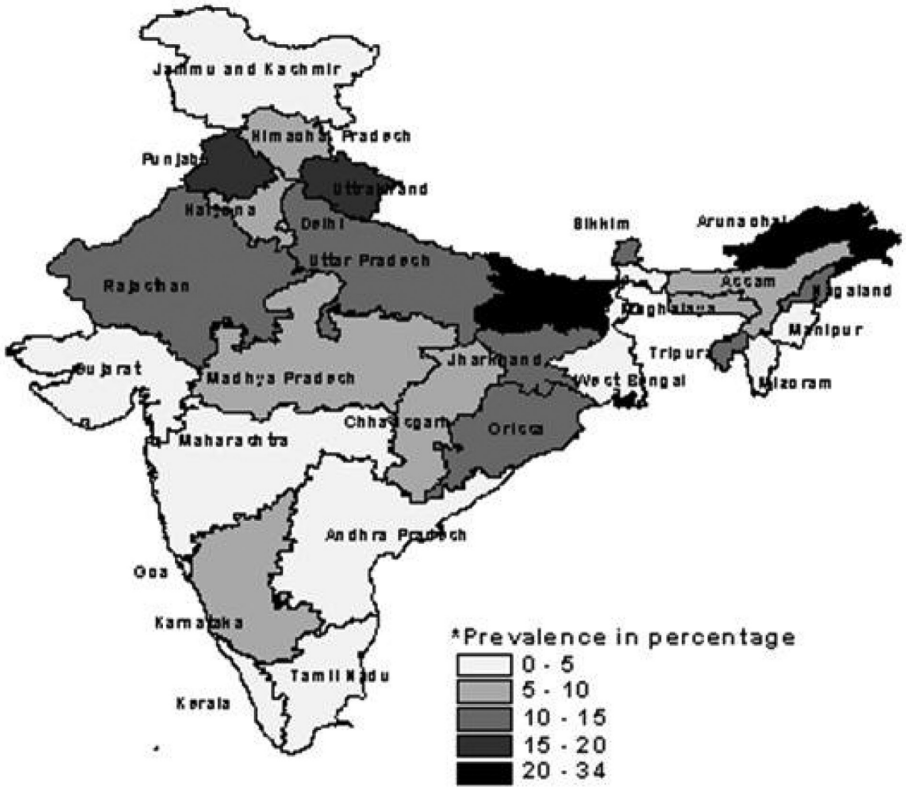

Fig. 3. Prevalence of eclampsia in urban India, 2005–2006.

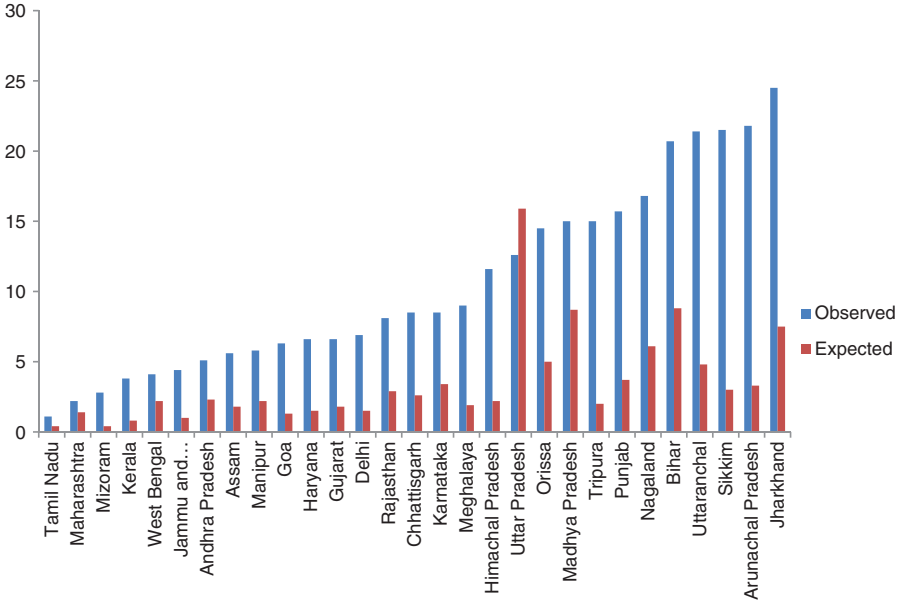

Fig. 4. Observed and expected prevalence of convulsions (not from fever) among women in the last pregnancy, India 2005–2006.

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Table 3. Unadjusted and adjusted odds ratios and 95% confidence interval for the risk of eclampsia during pregnancy for the most recent birth among women aged 15–49 years who had a live birth in the 5 years preceding the survey, India, 2005–2006

Characteristics	Unadjusted		Adjusted[a]	
	OR	95% CI	OR	95% CI
Maternal factors				
Total children ever born				
1 (Ref)	1.00	Ref	1.00	Ref
2–3	1.08	1.00–1.18	0.41	0.14–1.24
4+	1.62	1.48–1.76	0.54	0.18–1.63
Preceding birth interval				
First-order birth (Ref)	1.00	Ref	1.00	Ref
Interval <2 years	1.34	1.21–1.48	2.73	0.91–8.19
Interval 2–3 years	1.26	1.15–1.39	2.68	0.90–8.02
Interval 3+ years	1.27	1.16–1.39	2.66	0.89–7.94
ANC visit during pregnancy				
No visits (Ref)	1.00	Ref	1.00	Ref
1 visit	1.07	0.94–1.22	0.68	0.59–0.79
2 visits	0.74	0.68–0.82	0.69	0.59–0.80
3 visits	0.70	0.63–0.78	0.72	0.62–0.84
4+ visits	0.53	0.48–0.57	0.77	0.64–0.95
Blood pressure measured during pregnancy				
No (Ref)	1.00	Ref	1.00	Ref
Yes	0.77	0.71–0.83	1.21	1.08–1.35
Received advice on pregnancy nutrition during ANC visit				
No (Ref)	1.00	Ref	1.00	Ref
Yes	0.89	0.82–0.96	1.07	0.96–1.19
Alerted to pregnancy complications such as convulsions during ANC visit				
No (Ref)	1.00	Ref	1.00	Ref
Yes	2.19	2.01–2.40	2.78	2.50–3.08
Type of pregnancy				
Singleton (Ref)	1.00	Ref	1.00	Ref
Twin	1.67	1.25–2.22	2.12	1.45–3.11
Ever had a terminated pregnancy				
No (Ref)	1.00	Ref	1.00	Ref
Yes	1.33	1.23–1.44	1.32	1.20–1.45
Anemia level				
Not anemic (Ref)	1.00	Ref	1.00	Ref
Mild	1.08	1.00–1.16	0.97	0.89–1.07
Moderate	1.16	1.06–1.27	1.02	0.91–1.15
Severe	0.99	0.76–1.28	1.12	0.83–1.53
BMI and lifestyle factors				
BMI				
Underweight (≤18.4 kg/m^2)	0.99	0.92–1.06	0.93	0.85–1.02
Normal (18.5–22.9 kg/m^2) (Ref)	1.00	Ref	1.00	Ref

Table 3 (continued)

Characteristics	Unadjusted		Adjusted[a]	
	OR	95% CI	OR	95% CI
Overweight (23.0–24.9 kg/m^2)	0.77	0.67–0.88	0.86	0.73–1.02
Obese (≥25.0 kg/m^2)	0.54	0.46–0.64	0.70	0.58–0.85
Current tobacco smoker				
No (Ref)	1.00	Ref	1.00	Ref
Yes	1.55	1.24–1.95	1.18	0.80–1.73
Alcohol drinker				
No (Ref)	1.00	Ref	1.00	Ref
Yes	1.29	1.06–1.57	1.17	0.89–1.55
Diabetes				
No (Ref)	1.00	Ref	1.00	Ref
Yes	1.76	1.40–2.23	1.37	0.99–1.89
Asthma				
No (Ref)	1.00	Ref	1.00	Ref
Yes	2.11	1.68–2.66	1.85	1.35–2.54
Background factors				
Age (years)				
15–19 (Ref)	1.00	Ref	1.00	Ref
20–24	0.85	0.75–0.97	0.85	0.73–1.00
25–29	0.84	0.74–0.95	0.74	0.62–0.88
30–34	0.88	0.77–1.01	0.67	0.54–0.83
35–39	0.87	0.73–1.02	0.65	0.51–0.84
40–44	0.99	0.78–1.26	0.81	0.56–1.15
45–49	0.83	0.52–1.32	0.20	0.06–0.67
Education				
No education (Ref)	1.00	Ref	1.00	Ref
Primary	0.86	0.79–0.95	1.09	0.98–1.21
Secondary	0.66	0.62–0.72	0.99	0.89–1.09
Higher	0.37	0.30–0.45	0.68	0.54–0.87
Employment status				
Not working (Ref)	1.00	Ref	1.00	Ref
Working	0.86	0.80–0.93	0.85	0.79–0.92
Religion				
Hindu (Ref)	1.00	Ref	1.00	Ref
Muslim	1.04	0.96–1.14	1.13	0.98–1.29
Christian	0.77	0.59–0.99	1.14	0.80–1.63
Sikh	1.40	1.08–1.80	1.73	1.28–2.33
Others	1.02	0.78–1.34	1.05	0.71–1.55
Caste/tribe				
Scheduled Caste (Ref)	1.00	Ref	1.00	Ref
Scheduled Tribe	1.17	1.03–1.32	1.12	0.94–1.33
Other Backward Class	1.20	1.10–1.31	1.40	1.25–1.58
General	0.91	0.82–1.00	1.11	0.97–1.27

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Table 3 (continued)

Characteristics	Unadjusted		Adjusted[a]	
	OR	95% CI	OR	95% CI
Missing caste	0.57	0.44–0.74	0.51	0.36–0.73
Wealth index				
Lowest (Ref)	1.00	Ref	1.00	Ref
Second	0.80	0.73–0.87	0.85	0.75–0.96
Middle	0.71	0.65–0.78	0.81	0.71–0.92
Fourth	0.59	0.53–0.65	0.77	0.66–0.90
Highest	0.46	0.41–0.51	0.72	0.59–0.87
Place of residence				
Urban (Ref)	1.00	Ref	1.00	Ref
Rural	1.59	1.47–1.72	1.22	1.09–1.37
Geographic region				
North (Ref)	1.00	Ref	1.00	Ref
Northeast	0.77	0.62–0.94	0.74	0.56–0.98
Central	1.38	1.24–1.54	1.51	1.31–1.74
East	1.66	1.49–1.85	1.33	1.14–1.54
West	0.37	0.31–0.44	0.38	0.31–0.47
South	0.49	0.43–0.57	0.44	0.36–0.52
Number of cases			36,772	

ANC, antenatal care; BMI, body mass index; CI, confidence interval; OR, odds ratio; Ref, Reference category.

[a]Adjusted for all other variables in the table.

infarction, drug and alcohol withdrawal, and hypoglycemia, but these are very rare compared with eclampsia [45]. However, convulsions during pregnancy that are unrelated to preeclampsia need to be distinguished from eclampsia. Such disorders include seizure disorders as well as brain tumor, aneurysm of the brain, and medication- or drug-related seizures. Since convulsions during pregnancy could be a clinical manifestation of a number of medical disorders and thus a different pathophysiology, it is recommended to carefully diagnose the cause of convulsions in pregnant women and women of childbearing age and then accordingly manage them to avoid any future complications.

The striking geographic variations in the prevalence of eclampsia between specific states in India in our study needs specific mention. There was a more than 20-fold variation in eclampsia rates between the states with the lowest (Tamil Nadu 1.1%) and highest (Jharkhand 24.5%) prevalence. These substantial statewise differences in the prevalence of eclampsia clearly warrant further investigation. State-specific analysis using multilevel methods could be conducted to explore the substantial differences in prevalence in Indian states. One possible explanation for the state differential may be related to how well the question on convulsion was delivered and/or understood in the different states. Other potential explanations for these differences are that in high-prevalence states there are high rates of diabetes cases, more terminated pregnancy cases among women, and a high Scheduled Tribe population coupled with poorer access to health care services (expect for Kerala) compared with the rest of India [29]. Also this can be attributed to health care infrastructure, health service availability, and health-seeking behavior. An alternative explanation may be related to climatic differences across Indian regions. Some studies in the West have reported a higher incidence of eclampsia associated with conception during the spring and

summer months [46]. Potential mechanisms include seasonal variation in exposure to infections, dietary changes, and alteration in vitamin D regulation and calcium metabolism as a consequence of exposure to sunlight, which are, in turn, associated with blood pressure levels [46, 47].

Thirdly, we identified a number of specific traditional and nontraditional risk factors for symptoms suggestive of eclampsia. Some of the risk factors for eclampsia among Indian women are similar to those found among Asian women [48] and other ethnic groups, whereas some others differ. In line with published reports, symptoms of eclampsia were associated with a maternal age of more than 35 years, nulliparity, multiple pregnancies, poor socioeconomic conditions, and poor education [13, 22, 23]. The evidence for young maternal age as an independent risk factor for preeclampsia is still controversial [24–26]. The age distribution of the women in our study is similar to that in other reported studies and suggests that eclampsia is, probably, a disease of low-parity young women [49]. However, a study done in Saudi Arabia showed that women at extremes of maternal age, nulliparous women, and high-parity women are at an increased risk of developing eclampsia [50]. The difference between our findings and those of other studies could be due to differences in the population-based and hospital-based settings.

It is well established that the risk of eclampsia is greater in twin rather than in singleton pregnancies, and we found similar result in our study. Various studies have reported the incidence of eclampsia in twin pregnancies to be between 13% and 37%, which is two to three times higher than in singleton pregnancies [51–54], and about 24.3% in the case of triplet and quadruplicate pregnancies [55]. In a clinical study, analysis of 37 cases of twin pregnancy complicated by eclampsia showed that the incidence of twins in the total 1030 cases of eclampsia was three times the incidence in the general population [56]. Our findings were similar to those of other studies regarding the association of a history of miscarriage or a terminated pregnancy [57] with eclampsia risk.

Underlying medical conditions such as diabetes [52], asthma, or a previous preeclampsia [58] are associated with higher prevalence odds of eclampsia, and our study findings are consistent with earlier reports from high-income countries. A contrasting finding from our study that obese women are at lower risk of eclampsia is different from the findings of studies conducted in the West [59], but the mechanisms involved are not known. Women with the lowest BMI are relatively protected against eclampsia [60], which is also confirmed in our study (OR 0.93; 95% CI 0.85–1.02).

Our findings are similar to those of other studies that evaluated the risk factors for eclampsia in other populations regarding socioeconomic status [23, 61] such as ethnicity [62], education, employment status, and place of residence. Studies from high-income countries have been largely inconclusive on this, given the low incidence of eclampsia, but in our study we found a clear pattern: no difference from other health conditions. We found women belonging to the Sikh religion and Other Backward Class and women residing in rural areas were at more risk of symptoms suggestive of eclampsia. The reason for this increased risk is unclear but may be associated with maternal poverty and social deprivation. The high odds of eclampsia risk among Sikh women in our study might be mediated through obesity, which is highest among Sikh women (4.7% vs. 1.2% among Hindu women for obesity defined as BMI >30 kg/m^2). Maternal prepregnancy BMI classified as overweight and obese has long been associated as a modifiable risk factors for preeclampsia/eclampsia [5, 6]. Obese pregnant women (BMI >30 kg/m^2) experience a nearly threefold increase in the risk of developing preeclampsia/eclampsia compared with women of normal weight (BMI 18.5 to <25.0 kg/m^2) [7], which has been confirmed in several large-scale US studies. In India a recent study assessing the risk factors for early onset of severe preeclampsia and eclampsia among north Indian women found overweight (>120%–150% of prepregnancy ideal body weight, adjusted OR 4.65) and lower socioeconomic class (Kuppuswamy class III–V) (adjusted OR 3.00) to be related to the increased risk [23]. We also found a link with education, with a 32% reduced risk in women who had a higher level of education (9 years or more). These novel risks were independent of other risk factors, including adequacy of prenatal care.

The new information linking symptoms suggestive of eclampsia risk to the mother's socioeconomic characteristics is an important first step toward identifying new, nontraditional risk factors. Although traditional risk factors (mostly clinical)

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for eclampsia are well recognized, these diseases remain unknowable, and there is no known effective way to reduce their incidence. Therefore nontraditional risk factors may be of great importance in the design of future interventions to prevent the occurrence of eclampsia or eclampsia symptoms in a low-resource setting such as India, but data regarding these risk factors are scarce in LMICs.

Our study indicates higher prevalence of symptoms suggestive of eclampsia in women who never visited an antenatal clinic during the pregnancy or who never received advice on pregnancy nutrition (OR 1.07, P=0.080) and were not alerted to pregnancy complications such as convulsions during their ANC visit. This may also be due to 'reverse causation.' For example, ANC personnel treat pregnant women at high risk of preeclampsia/eclampsia or who report symptoms such as blurred vision and headache, thus resulting in a positive association. The identification of eclampsia and counseling of women with eclampsia relies fundamentally on the frequency of ANC [63] and if blood pressure was measured during the visit. Globally, the absence of ANC is strongly associated with eclampsia and death [18]. Despite this, the absence of preconception care coupled with a lack of effective and universal ANC remains a serious challenge in LMICs. Many women with preeclampsia, particularly, at the community level, are missed because of the lack of ANC. These women are likelier to develop serious complications such as eclampsia during the latter part of the pregnancy. ANC utilization is approximately 68% in LMICs compared with 98% in high-resource settings [64]. The regions of the world with the lowest levels of use are South Asia, where only 54% of pregnant women have at least one ANC visit [64] and India (22.8%) [29]. Not surprisingly, there is marked urban–rural differential in accessing ANC in LMICs, including India. Whereas 86% of women in urban settings will have one antenatal visit, only 65% of women in rural settings will have the same [64]. For repeated antenatal visits, 62.4% of women in urban India report four or more antenatal visits compared with 27.7% of rural women [29].

Strength and limitations of the study

The strengths of our study include the large nationally representative study sample allowing comparisons to be made between states and urban versus rural settings, and the ability to examine socioeconomic and lifestyle patterning of symptoms suggestive of eclampsia risk in a population-based survey. Further, the large sample size provided adequate power to identify the potential risk factors and compensated for the ethnic variations in Indian populations. We could evaluate the association of well-known risk factors as potential confounders and effect modifiers, including birth intervals, maternal age, type of pregnancy, diabetes, asthma, BMI, and tobacco smoking. Furthermore, the survey was conducted with an interviewer-administered questionnaire in the native language of the respondent with a local, commonly understood term for all the health problems during pregnancy. Eighteen languages were used, with back translation to English to ensure accuracy and comparability.

However, because of the general challenges of measuring hypertensive disorders in population-based studies, the measurement of symptoms suggestive of eclampsia in the National Family Health Survey also has apparent limitations. These include the cross-sectional study design, thereby preventing conclusions regarding causality. Second, an important drawback of the study is that we report on seizures/convulsions during pregnancy and used this outcome as a proxy for eclampsia, which is likely to be a poor proxy, but these are the best available data we have at the national level. The 10% prevalence of 'eclampsia' is too high for a population-based survey, and might be due to overreporting, probably because some women do not understand the question. Also, NFHS-3 data did not have as a variable hypertension, which is considered the hallmark for the diagnosis of eclampsia, and convulsions sometimes may be due to cerebrovascular accidents or some brain lesion or medication- or drug-related seizures; these may be some of the reasons for the higher prevalence reported in this study. Third, the symptoms suggestive of eclampsia were all self-reported by women, and are therefore subject to bias. Case ascertainment was based on self-reported convulsions/seizures during the last pregnancy rather than a clinical assessment. Although we cannot exclude misclassification within this context, it is unlikely that we missed severe symptoms suggestive of eclampsia cases. Fourth, we could not identify the gestational onset of eclampsia. Fifth, no information is available on the prepregnancy eclampsia risk factors of the women as health problems during pregnancy

were assessed only for the most recent birth within 5 years preceding the survey. So there was a time gap between the information on all the covariates/risk factors and pregnancy-related health problems, which may be one of the reasons that we could not find any substantial association between some of the important risk factors (e.g., obesity, age of women) and eclampsia in this population-based survey which was otherwise proven in clinical studies. Sixth, the study database did not include information on some potentially important factors; for example, we could not obtain maternal prepregnancy BMI [65], familial aggregation [66], and genetic factors [67], which are important risk factor for eclampsia as proved in studies from high-income countries.

This study has potential implications for the possible prevention of pregnancy-related complications in India. Pregnant women in LMICs, including India, are among the most vulnerable populations in the world. Hypertensive disorders in pregnancy such as preeclampsia, eclampsia, and gestational hypertension are one of the three (apart from hemorrhage and sepsis) leading causes of maternal death and morbidity [68–72]. Community health care workers, specifically female health care workers, are an integral part of the health care force in many LMICs and can be employed to provide timely care to women with preeclampsia and eclampsia. Prevention strategies should be applied to every pregnant woman since we cannot predict who will develop preeclampsia and eclampsia given the limitation in resources. Measuring blood pressure and urinary protein levels is challenging in LMICs because of the financial cost and lack of training. A detection tool that is affordable and can be easily applied is needed.

Eclampsia has remained a significant public health threat in both high-income countries and LMICs, contributing to maternal and perinatal morbidity and mortality globally [69–72]. The Millennium Development Goals have placed maternal health at the core of the struggle against poverty and inequality as a matter of human rights. Ten percent of women have high blood pressure during pregnancy, and eclampsia and preeclampsia complicate 2%–8% of pregnancies [72]. Increasing awareness of maternal death as a public health priority, for both maternal and child health, has been important, and has helped implementation of improved health services. Millennium Development Goal 5 calls for a reduction by three quarters, between 1990 and 2015, in the maternal mortality ratio (www.un.org/millenniumgoals).

Our study findings may serve as an important call for health care providers to increase their awareness of the increased population-level risk of eclampsia. An increase in the risk of conditions as potentially dangerous as eclampsia underlines the importance of regular health care during the preconception, interconception, and antenatal periods. However, more epidemiological research in India should focus on uncovering preventable causes of eclampsia, and public health practice and policy must promote improved access to health care and mandatory ANC visits and reduction of traditional and nontraditional risk factors.

To conclude, the high prevalence of symptoms suggestive of eclampsia observed in the present analyses highlights that hypertensive disorders of pregnancy remain unaddressed in India, with a huge epidemiological burden especially when we are aware that ANC is poorly utilized in Indian settings. Our findings from a large nationally representative sample of Indian women indicate that modifiable lifestyle risk factors related to different geographic ethnic groups, regions, and locations exist that can be addressed while specific preventive and management strategies are developed. We found that higher education level, high household wealth status, and the mother's employment status acted as protective factors for eclampsia among Indian mothers. Further research to examine the clinically diagnosed prevalence of eclampsia is needed in LMICs.

With the target of the Millennium Development Goals in sight, hypertensive disorders of pregnancy (including eclampsia and preeclampsia) should be identified as a priority area in reducing maternal and infant morbidity and mortality in India. This calls for coordinated efforts and close involvement of the community, governmental/nongovernmental organizations, clinicians, nurses, and paramedical staff. Since for most Indian mothers ANC is still the main source of blood pressure measurement, nutrition education, and counseling on the signs of pregnancy complications such as convulsions, ensuring universal provision of mandatory comprehensive ANC, as emphasized in India's 11th 5 year plan (2007–2012) [73], is vital for improving maternal health in India.

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Data availability

The authors confirm that all data underlying the findings are fully available without restriction. The data are publicly available from the Demographic and Health Surveys website: http://dhsprogram.com/what-we-do/survey/survey-display-264.cfm.

Conflict of interest

The authors declare no conflict of interest.

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