# Prevalence and risk factors for Pre-eclampsia in Indian women: a national cross sectional study

**AUTHORS:** Sutapa Agrawal<sup>1\*</sup>, Gagandeep K Walia<sup>1</sup>

1 South Asia Network for Chronic Disease, Public Health Foundation of India, New Delhi, India

\*Correspondence to Sutapa Agrawal, Epidemiologist, South Asia Network for Chronic Disease, Public Health Foundation of India, C-1/52, Safdurjung Development Area, New Delhi-110016, India; email: <u>sutapa.agrawal@phfi.org</u> or sutapaiips@rediffmail.com

Word count: abstract-297; main text- 2,983

Number of tables: 3

Number of references: 35

Author's Contribution: SA and GKW conceived the article. SA conducted the statistical analysis. SA wrote the first draft and SA and GKW reviewed and revised it for important intellectual content.

# Prevalence and risk factors for Pre-eclampsia in Indian women: a national cross sectional study

# Abstract

**Background:** Pre-eclampsia is of considerable public health threat particularly in developing countries globally affecting approximately 8% of all pregnancies. We examined the prevalence of pre-eclampsia and associated maternal, behavioural, dietary and socioeconomic and demographic risk factors in India.

**Methods:** Data from a cross sectional survey of 124,385 women age 15-49 years included in India's third National Family Health Survey (NFHS-3, 2005-06) have been used. Information on symptoms of pre-eclampsia were obtained from 39,657 women who had a live birth in the five years preceding the survey and reported specific health problems during pregnancy for the most recent birth. Multiple logistic regression analysis was used to estimate the prevalence odds ratios for pre-eclampsia, adjusting for various risk factors.

**Results:** More than half of the respondents (n=22,061, 55.6%) reported pre-eclampsia. Rural– urban and marked geographic variation were found with rates for pre-eclampsia ranging from as low as 33% (Haryana) to 87.5% (Tripura). With various risk factors and background factors statistically controlled, the prevalence odds ratios of pre-eclampsia was higher among women with twin pregnancy (OR:1.53;95%CI:1.12-2.09), terminated pregnancy (OR:1.38;95%CI:1.30-1.48), women with severe to mild anemia (OR ranges from 1.08 to 1.32), tobacco smoking (OR:1.91;95%CI:1.19-1.91), diabetes (OR:1.89;95%CI:1.44-2.49), asthma (OR:2.05;95%CI:1.59-2.65), consuming fruits weekly/occasionally, eggs daily, fish weekly, and residing in eastern (OR:2.10;95%CI:1.89-2.33), northeastern (OR:1.49;95%CI:1.27-1.75) and central part (OR:1.37;95%CI:1.26-1.50) of India with reference to their counterparts.

**Conclusions:** Our study provides first empirical evidence of prevalence of pre-eclampsia and its associated risk factors in a large nationally representative sample of Indian women. Our findings indicate that modifiable risk factors exist. With the target of the Millennium Development Goals in sight, pre-eclampsia should be identified as a priority area in reducing maternal and infant morbidity and mortality in India. Further research to verify accuracy of reporting of symptoms of pre-eclampsia is needed in Indian setting.

Key words: pre-eclampsia; risk factors; women; India; NFHS-3

#### Introduction

Pre-eclampsia, a life threatening complication of pregnancy is a condition that typically starts after 20<sup>th</sup> week of pregnancy and is related to increased blood pressure (BP≥140/90 mmHg) and protein in mother's urine (urinary albumin protein ≥300 mg/24 h). The clinical spectrum of preeclampsia ranges from mild to severe. Preeclampsia occurs in 5–8% of pregnancies worldwide, and is the second leading cause of direct maternal and fetal deaths[1]. The etiology of pre-eclampsia is still obscure, despite many attempts to identify possible causes. Women with moderate pre-eclampsia generally have no symptoms. Women with severe pre-eclampsia, or with very high blood pressure, may feel unwell, with symptoms such as headache, upper abdominal pain, or visual disturbances[2]. The prevalence of preeclampsia varies in different populations and in different ethnic groups[1].

Preeclampsia has remained a significant public health threat in both developed and developing countries contributing to maternal and perinatal morbidity and mortality globally[2]. Numerous risk factors for pre-eclampsia have been suggested but only some have actually been established in multivariate models that permit simultaneous control for possible confounders. There has not been any previous large-scale report concerning the risk factors for pre-eclampsia in Indian population. Therefore, the objective of the present study is to identify population based risk factors associated with preeclampsia in a large sample of Indian women. India's third National Family Health Survey (NFHS-3,2005-06) collected data from 124,385 women residing in 109,041 households[3] and covered regions comprising more than 99% of India's population which provides a unique opportunity to study the prevalence of preeclampsia, its socio-demographic, maternal, lifestyle and dietary determinants. In this paper, we report the findings on self-reported symptoms of preeclampsia, and the risk factors associated with it.

# **Materials and Method**

*Data.* India's third National Family Health Survey conducted during 2005-06 was designed on the lines of the Demographic and Health Surveys (available at www.measuredhs.com) that have

been conducted in many developing countries since the 1980s. The NFHS 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 and 74,369 men aged 15–54 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[3]. The analysis presented here focuses on 39,657 ever married women who had a live birth in the five years preceding the survey and reported specific health problems during pregnancy for the most recent birth.

*Outcome measures.* The survey included several questions related to health problems during pregnancy for the most recent birth in the five years preceding the survey. These questions were asked only to those women who had a live birth in the five years preceding the survey in order to account for recall lapse. The survey was conducted using an interviewer-administered questionnaire in the native language of the respondent using a local, commonly understood term for all the health problems during pregnancy. A total of 18 languages were used with back translation to English to ensure accuracy and comparability. The response to any of the symptom such as difficulty with vision during daylight, swelling of the legs, body or face, excessive fatigue, were designated as having symptoms of 'preeclampsia' in this study. However, no effort was made to confirm clinical diagnosis of these health problems from the respondents and thus ascertainment of preeclampsia was not possible.

*Risk factors.* The socio-demographic factors considered in the present analysis included age (15-29, 30-39, 40-49 years); education (no education, primary, secondary, higher); religion (Hindu, Muslim, Christian, Sikhs, Others); category (Scheduled Castes, Scheduled Tribes, Other Backward Class, General); 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) was computed using previously described methods[3]; place of residence

(urban, rural); and geographic regions (north, northeast, central, east, west, south). The following maternal reproductive risk factors were evaluated as potential confounding factors: total children ever born (CEB) (1, 2-3, 4+); preceding birth interval (first birth order, interval <2years, interval 2-3years, interval 3+years); antenatal care (ANC) visit during pregnancy (no visit, 1 visit, 2 visits, 3 visits, 4+ 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); anemia level (not anemic, mild, moderate, severe). The biological and lifestyle factors included Body Mass Index ( BMI) kg/m<sup>2</sup> categories (Indian adult population standard; Indian consensus group 1996): ≤18.4 kg/m<sup>2</sup> (underweight), 18.5 to 22.9 kg/m<sup>2</sup> (normal), 23.0 to 24.9 kg/m<sup>2</sup> (overweight), ≥25 kg/m<sup>2</sup> (obese); current tobacco smoke (no, yes); alcoholic (no, yes); diabetes (no, yes); asthma (no, yes); dietary intake variables include—frequency of consumption of milk/milk products, green leafy vegetables, fruits, pulses and beans, eggs, fish, chicken/meat— all categorized into daily, weekly, occasionally or/and never. For definition of some variables see Table 2.

*Data Analysis.* We first examined regional and rural/urban differentials in the prevalence of preeclampsia and then estimated their prevalence and its associations with eight socioeconomic and demographic variables, nine maternal factors, five BMI and lifestyle and disease related factors and seven diet variables. Potential risk factors were selected on the basis of previous knowledge of their association with preeclampsia. We used multiple logistic regression to estimate the prevalence odds ratios for each of these risk factors, adjusted for the others. As certain states and certain categories of respondents were oversampled, in all analyses weights were used to restore the representativeness of the sample[3].

Results are presented as odds ratios with 95% confidence intervals. The estimation of confidence intervals takes into account design effects due to clustering at the level of the primary sampling unit. Before carrying out the multivariate model, we assessed the possibility of multicollinearity between the covariates. In the correlation matrix of covariates, all pair wise

Pearson correlation coefficients were <0.5, suggesting that multicollinearity did not affect the findings. All analyses including the logistic regression models were conducted using the SPSS statistical software package Version 19.

*Ethical considerations.* The NFHS-3 survey received ethical approval from the International Institute for Population Science's Ethical Review Board. Prior informed written 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

Table 1 shows the findings for prevalence of pre-eclampsia by India's state and rural/urban residence. More than half of the respondents (n=22,061; 55.6%) had reported symptoms of pre-eclampsia. Almost similar prevalence for pre-eclampsia was found in rural (56.2%) and urban (54%) India, though higher rates (>70%) were observed in the states of Uttarakhand, Bihar, Jharkhand, Kerala with the highest being in Tripura (87.5%).

# <Table 1 here >

Table 2 shows associations between maternal, lifestyle, dietary and socioeconomic characteristics and risk of pre-eclampsia in Indian women. Strong associations (p<0.0001) between different factors and pre-eclamsia prevalence have been found: twin pregnancy (67.9%), terminated pregnancy (63.6%), ANC visit during pregnancy, whether received advise on pregnancy nutrition during ANC visit, whether alerted to pregnancy complications such as convulsions, first order birth (58.0%), severe anemia (58.0%), current tobacco smoking (64.1%), diabetes (67.1%), asthma (72.8%), never/occasionally consuming milk (57.3%), green leafy vegetables (59.1%), fruits (57.9%), pulses or beans (59.1%), consuming eggs, fish (61.2%), chicken/meat daily (59.7%), among Muslim (61.6%), non working (56.9), residing in eastern part of India (69.9%).

#### <Table 2 here>

With various risk factors and background factors statistically controlled (Table 3), the prevalence odds ratios of pre-eclampsia was higher among women who had 4 or more ANC visits during pregnancy (OR:1.31;95%CI:1.22-1.41), received advice on pregnancy nutrition during ANC visit (OR:1.23;95%CI:1.17-1.29), were alerted to pregnancy complications such as convulsions (OR:1.34;95%CI:1.26-1.43), blood pressure was measured during pregnancy (OR:1.31;95%CI:1.06-1.21), twin pregnancy (OR:1.53;95%CI:1.12-2.09), had a terminated pregnancy (OR:1.38;95%CI:1.30-1.48), suffering from severe to mild anemia (OR ranges from 1.08 to 1.32), smokes tobacco (OR:1.91;95%CI:1.19-1.91), had diabetes (OR:1.89;95%CI:1.44-2.49), asthma (OR:2.05;95%CI:1.59-2.65) with reference to their counterparts. The prevalence odds of pre-eclampsia was also higher among educated (OR ranges from 1.1 to 1.22), Muslim (OR:1.37;95%CI:1.23-1.41) and Christian women(OR:1.36;95%CI:1.13-1.56), women residing in rural areas (OR:1.08;95%CI:1.01-1.15) and in east (OR:2.10;95%CI:1.89-2.33), northeast (OR:1.49;95%CI:1.27-1.75) and central part (OR:1.37;95%CI:1.26-1.50) of India. Those, consuming fruits weekly/occasionally, eggs daily, fish weekly, were also more likely have higher odds of pre-eclampsia prevalence than those who never consumed them. However, women who are underweight, drinks alcohol, aged 30-39 years and resides in southern region of India, had at least 1 (OR:0.82;95%CI:0.74-0.91) or 2 ANC visit (OR:0.87;95%CI:0.78-0.96), who consumed milk daily, green leafy vegetables daily or weekly, pulses or beans at least weekly, eggs weekly, or occasionally consumes fish or chicken/meat had a reduced odds of preeclampsia prevalence.

### <Table 3 here>

# Discussion

In this nationwide large scale cross-sectional study, we identified three main sets of findings relating to (i) overall self-reported symptoms of pre-eclampsia prevalence; (ii) geographical differences in prevalence; and (iii) risk factors for prevalence.

Firstly, we found that the prevalence of pre-eclampsia (55.6%) in this large nationally representative survey was high compared to earlier studies in Asian population[4]. This may be due to cross-sectional symptomatic nature of the study rather than clinical confirmation. Secondly, we found striking differences geographically and between specific states regarding pre-eclampsia prevalence. Prevalence ratios for pre-eclampsia showed more than two fold variation between the lowest prevalence state (Haryana-33.3%) and highest prevalence state (Tripura-87.5%). This substantial state wise differences in pre-eclampsia prevalence clearly warrant further investigation. State specific analysis using multilevel methods could be carried out to explore the substantial differences in prevalence in Indian states. Some potential explanations for these differences are that in high prevalence states there is a very high rate of smoking particularly among rural women, diabetes and more terminated pregnancy cases along with a high schedule tribe population coupled with poorer access to health care services (expect for Kerala) compared to rest of India. An alternative explanation may be related to climatic differences across Indian regions. Some studies in west have reported a higher incidence of preeclampsia associated with conception during the spring and summer months [5,6]. 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, are associated with blood pressure levels [5,6]. Thirdly, we identified a number of specific risk factors for pre-eclampsia prevalence. Some of the risk factors for pre-eclampsia among Indian women are similar as found among Asian women[4] or those of other ethnic groups, while some vary. It is well-established that the risk of preeclampsia is greater in twin rather than in singleton pregnancies and we found similar result in our study. The reported incidence of pre-eclampsia is 13%-37%, which is 2-3 times higher than singleton pregnancies [7-10] and about 24.3% in case of triplets and quadruplicate pregnancies[11].

The finding that obese women are at a higher risk of pre-eclampsia is similar to studies which showed obesity is a risk factor for pre-eclampsia[12-17], but the mechanisms involved are not

known. Women with the lowest BMI are relatively protected against preeclampsia[18], which is also confirmed in our study (OR:0.95;CI:0.90-1.00).

The finding that current tobacco smoking is associated with significantly increased risk of preeclampsia is also consistent with previous research[19,20]. We found similar findings with other studies regarding previous history of miscarriage or terminated pregnancy[21,22]; and ethnicity[23], socio-economic position[24] with pre-eclampsia risk. The likelihood of progression from gestational hypertension to pre-eclampsia may be increased by a prior miscarriage[25]. Underlying medical conditions[26,27] such as diabetes[28,29] or asthma is associated with higher prevalence odds of pre-eclampsia and our study findings are consistent with the earlier reports.

In our study, age and parity were not found to be associated with pre-eclampsia in contrast to other studies[29]. A study done in Saudi Arabia showed that women at extremes of maternal age, the nulliparous women, and high-parity women are at an increased risk of developing pre-eclampsia[30]. The variation in our study and other studies could be due to the differences in the population-based and hospital based study.

Our study found higher prevalence of preeclampsia in women who visited ANC during the pregnancy or who received advice on pregnancy nutrition and were alerted about pregnancy complications such as convulsions during their ANC visit. The identification and counseling of preeclampsia relies fundamentally on the frequency of antenatal care[31] and if their blood pressure was measured during the visit. Many women with pre-eclampsia, particularly, at the community level are missed due to the lack of antenatal care. These women are more likely to develop serious complications. Antenatal care utilization is around 68% in LMIC compared to 98% in high resource settings[32]. The region of the world with the lowest levels of use is South Asia, where only 54% of pregnant women have at least one antenatal care visit[32] and in India 22.8%[3]. Not surprisingly, there is marked urban/rural differential in accessing antenatal care in LMIC including India. Whereas 86% of women in urban settings will have one antenatal visit,

only 65% of women rural settings will have the same[32]. For repeated antenatal visits, 62.4% of women in urban India report four or more antenatal visits compared to 27.7% of rural women[3].

#### Strength and limitations of the study

To our knowledge, this is the largest nationally representative cross-sectional study of the risk factors for preeclampsia in an Asian population. 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 socio-economic and lifestyle patterning of pre-eclampsia risk. 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, body mass index, and tobacco smoking. However, due to the general challenges of measuring hypertensive disorders in population-based studies, the measurement of preeclampsia in the NFHS also has apparent limitations. Self reported symptoms during last pregnancy preceding the survey were used to diagnose pre-eclampsia and eclampsia and therefore, ascertainment of pre-eclampsia was performed in view of a research context, rather than a clinical context. The information of the symptoms of preeclampsia and eclampsia presented here is based on women's self reports and should therefore be interpreted with care. Although we cannot exclude misclassification within this context, it is unlike that we missed severe preeclampsia cases. Also we could not identify the gestational onset of preeclampsia. As this is not a clinical study, we could perform only prevalence odds ratios for pre-eclampsia and eclampsia. Moreover no information is available on the pre-pregnancy pre-eclampsia risk factors of the women as health problems during pregnancy was assessed only for the most recent birth within five 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 reason that we could not found any substantial association between some of the important risk

factors and pre-eclampsia in this population based survey which was otherwise proven in clinical studies. For e.g., we could not obtain maternal pre-pregnancy body mass index[27,33,17], familial aggregation[34] and genetic factors[34,35] which are important risk factor for pre-eclampsia confirmed in some studies. However, the NFHS, by collecting wideranging social, demographic, maternal health care factors, BMI, lifestyle, chronic disease and diet data, and being nationally representative, provides a unique opportunity to draw descriptive inferences on the social distribution and patterning of pre-eclampsia risk in Indian women.

#### Conclusion

Well documented population level studies to assess the determinants of pre-eclampsia are few in India. This study is important because few others have reported prevalence rates based on population-level data, and none reflect the results of analysis carried out through 2007, the latest year for which NFHS data are available. The NFHS dataset is remarkable for its depth in terms of national representation.

Pregnant women in low and middle income countries (LMIC) are amongst the most vulnerable populations in the world. Preeclampsia follows second and cause significant maternal and perinatal morbidity and mortality. Community health care workers, specifically lady health care workers, are an integral part of the health care force in many LMIC and can be employed to provide timely care to women with pre-eclampsia. Prevention strategies should be applied to every pregnant woman since we cannot predict who will develop pre-eclampsia given the limitation in resources. Measuring blood pressure and proteinuria is challenging in LMIC due to financial cost and lack of training. A detection tool that is affordable and can be easily applied is needed.

Our study findings may serve as an important call for health care providers to heighten their awareness of the increased population-level risk for pre-eclampsia originating in pregnancy. An

increase in the risk for such as preeclampsia underlines the importance of regular healthcare during the preconception, antenatal, and inter-conception periods. More epidemiological research in India should focus on uncovering preventable causes of preeclampsia, while public health practice and policy must promote improved access to health care prior and mandatory ANC visit and reduction of social and behavioral risk factors.

In conclusion, pre-eclampsia remains an important maternal health problem in India. This study provides empirical evidence of prevalence of pre-eclampsia and their associated risk factors in India. Our findings from a large nationally representative sample of Indian women indicate that, modifiable risk factors exist. With the target of the Millennium Development Goal in sight, preeclampsia should be identified as a priority area in reducing maternal and infant mortality in India. Further research to verify accuracy of reporting of symptoms of pre-eclampsia is needed.

#### Acknowledgements

SA and GKW are supported by a Wellcome Trust Strategic Award Grant No Z/041825. We acknowledge the support of International Institute for Population Sciences and Macro International (www.measuredhs.com) for providing us the access to the 2005-06 Indian National Family Health Survey data.

# References

- 1. Roberts JM, Lain KY : Recent insights into the pathogenesis of pre-eclampsia. *Placenta* 2002, **23**: 359–72.
- Duley L: Maternal mortality associated with hypertensive disorders of pregnancy in Africa, Asia, Latin America and the Caribbean. Br J Obstet Gynaecol 1992, 99:547-553.
- 3. International Institute for Population Sciences & Macro International: *National Family Health Survey (NFHS-3), 2005–06: India: Vol. I.* Mumbai, IIPS; 2007.
- 4. Lee CJ, et al.: Risk factors for pre-eclampsia in an Asian population. International Journal of Gynecology & Obstetrics 2000, **70**:327-333.
- 5. Phillips JK, *et al.*: Seasonal variation in preeclampsia based on timing of conception. *Am J Obstet Gynecol* 2004, **104**:1015–1020.
- Rudra CB, Williams MA: Monthly variation in preeclampsia prevalence: Washington State, 1987–2001. J Matern Fetal Neonatal Med 2005, 18:319–324.
- 7. Sibai BM, et al.: Hypertensive disorders in twin versus singleton pregnancies. Am J Obstet Gynecol 2000, **182**: 938 – 942.
- Prasannan-Nair C, Reynolds SF, Budden G: Partial molar pregnancy with severe preeclampsia at 19 weeks' gestation. J Obstet Gynaecol 2006, 8: 817.
- 9. Wong LFA , Stuart B, Gleeson N: **Triploidy partial mole and proteinuric hypertension**. *J Obstet Gynaecol* 2007, **4**: 424–425.
- Bdolah Y, et al.: Twin pregnancy and the risk of preeclampsia: bigger placenta or relative ischemia? American Journal of Obstetrics & Gynecology 2008, 198:428.e1-6.
- 11. Cassell KA, O'Connell CM, Baskett TF: The origins and outcomes of triplet and quadruplet pregnancies in Nova Scotia: 1980 to 2001. Am J Perinatol 2004, 21:439-45.
- 12. Rosenberg TJ, et al.: Prepregnancy weight and adverse perinatal outcomes in an ethnically diverse population.

*Obstet Gynecol* 2003, **102**:1022–1027.

- 13. Cedergren MI: Maternal morbid obesity and the risk of adverse pregnancy outcome. *Obstet Gynecol* 2004, **103**:219–224.
- Weiss JL, et al.: Obesity, obstetric complications and cesarean delivery rate-a population based screening study. *Am J Obstet Gynecol* 2004, **190**:1091–1097.
- 15. Ramos GA, Caughey AB: The interrelationship between ethnicity and obesity on obstetric outcomes.
   Am J Obstet Gynecol 2005, 193:1089–1093.
- 16. Nohr EA et al.: Prepregnancy obesity and fetal death: a study within the Danish national birth cohort.
   Obstet Gyne Col 2005, 106:250–259.
- Bodnar LM, Ness RB, Harger GF, Roberts JM: Inflammation and triglycerides partially mediate the effect of pre pregnancy body mass index on the risk of preeclampsia. *Am J Epidemiol* 2005, 162: 1198– 1206.
- 18. Belogolovkin V, et al.: The effect of low body mass index on the development of gestational hypertensi on and preeclampsia.
   J Matern Fetal Neonatal Med 2007, 20:509–513.
- 19. England L, Zhang J: **Smoking and risk of preeclampsia: a systematic review.** *Front Bioscience* 2007, **12**: 2471–2483.
- 20. Pipkin FB, & on behalf of The Genetics of Preeclampsia Consortium: Smoking in moderate/severe preeclampsia worsens pregnancy outcome, but smoking cessation limits the damage.
   Hypertension 2008, 51:1042–1046.
- 21. Trogstad L, et al.: The effect of recurrent miscarriage and infertility on the risk of preeclampsia.
  B J Obstet Gynecol 2009, 116:108 –113.
- 22. Hiby SE, et al.: Association of maternal killer-cell immunoglobulin-like receptors and parental HLA-C genotypes with recurrent miscarriage. Hum Reprod 2008, 23:972–976.
- 23. Dempsey JC, *et al.*: Weight at birth and subsequent risk of preeclampsia as an adult. Am J Obstet Gynecol 2003, **189**:494 –500.
- **24.** Silva LM, et al.: Low socioeconomic status is a risk factor for preeclampsia: the Generation R Study.

*J Hypertens* 2008, **26**:1200–1208.

- **25.** Saudan P, et al.: Does gestational hypertension become pre-eclampisa? British Journal of Obstetrics and Gynaecology 1998, **105**:1177-84.
- 26. Sibai BM: Risk factors, pregnancy complications, and prevention of hypertensive disorders in women with pregravid diabetes mellitus. *J Matern Fetal Med* 2000, **9**:62–65.
- Chappell LC, et al.: Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension. A prospective study. Hypertension 2008, 51:1002–1009.
- 28. Bryson CL, Ioannou GN, Rulyak SJ, Critchlow C: Association between Gestational Diabetes and Pregnancy-induced Hypertension. *Am J Epidemiol* 2003, 158:1148–1153.
- 29. Duckitt K, Harrington D: Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. *BMJ* 2005, **330**:565.
- 30. Lawoyn TO, Ani F: **Epidemiologic aspects of pre-eclampsia in Saudi Arabia.** *East Afr Med J* 1996, **73**:404–6.
- 31. Shennan AH, Redman C, Cooper C, Milne F: Are most maternal deaths from preeclampsia avoidable?
   The Lancet 2012, 379:1686-7.
- Abdou-Zahar C, Wardlaw T: Antenatal care in developing countries. Antenatal care in developing countries: promises, achievements and missed opportunities: an analysis of trends, levels and differentials, 1990–2001. Bulletin of World Health Organization 2003, 67:13–25.
- Svensson E, Reas DL, Sandanger I, Nygård JF: Urban-rural differences in BMI, overweight and obesity in Norway (1990 and 2001).
   Scand J Public Health 2007, 35: 555 – 558.
- 34. Esplin MS, et al.: Paternal and maternal components of the predisposition to preeclampsia.
   N Engl J Med 2001, 344:867–872.
- **35.** Laivuori H, et al.: Susceptibility loci for preeclampsia on chromosomes 2p25 and 9p13 in Finnish families.

Am J Hum Genet 2003, **72**:16 8–177.

**Table 1:** Reported prevalence of Pre-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 five years preceding the survey, by state and residence, India, 2005-06

	Pre-eclampsia					
	Url	Urban Rural			Total	
India/States	N	(%)	Ν	(%)	Ν	(%)
India	5738	54.0	16323	56.2	22,061	55.6
Northern region						
Delhi	403	50.2	30	43.5	433	49.7
Haryana	88	37.3	201	31.8	289	33.3
Himachal Pradesh	36	47.4	313	46.9	349	46.9
Jammu and Kashmir	113	58.5	402	58.2	515	58.3
Punjab	197	56.4	306	52.8	503	54.1
Rajasthan	207	67.2	496	45.3	703	50.1
Uttaranchal	145	67.1	467	71.2	612	70.2
Central region						
Chhattisgarh	127	59.3	501	50.9	628	52.4
Madhya Pradesh	327	59.8	1027	59.8	1354	59.8
Uttar Pradesh	529	51.4	2110	53.8	2639	53.3
Eastern region						
Bihar	150	75.4	1143	77.8	1293	77.5
Jharkhand	150	64.1	748	77.4	898	74.8
Orissa	106	52.2	679	58.9	785	57.9
West Bengal	297	63.7	1015	63.4	1312	63.5
Northeastern region						
Arunachal Pradesh	121	75.6	275	63.4	396	66.7
Assam	85	52.5	641	58.1	726	57.4
Manipur	161	36.7	426	41.3	587	39.9
Meghalaya	99	68.8	399	59.4	498	61.0
Mizoram	203	70.5	201	63.6	404	66.9
Nagaland	167	50.0	535	49.0	702	49.2
Sikkim	54	59.3	306	67.4	360	66.1
Tripura	73	89.0	383	87.2	456	87.5
Western region						
Goa	253	56.9	209	59.7	462	58.1
Gujarat	298	69.5	407	61.8	705	64.8
Maharashtra	531	46.1	435	33.6	966	39.5
Southern region						
Andhra Pradesh	208	36.7	426	36.3	634	36.4
Karnataka	231	38.0	355	36.9	586	37.3
Kerala	207	78.4	431	76.4	638	77.1
Tamil Nadu	290	47.4	346	48.7	636	48.1

according to selected characteristics, India, 2005-06							
Characteristics		nple	Pre-ecl	ampsia	$\chi^2 p$		
	distrik	distribution		ses	value		
	Number	Percent	Number	Percent	-		
Maternal factors							
Total children ever born					<0.0001		
1	10453	26.4	6057	57.9			
2-3	18199	45.9	9727	53.4			
4+	11005	27.8	6277	57.0			
Preceding birth interval					<0.0001		
First order birth	10546	26.6	6122	58.0			
Interval <2 years	7124	18.0	3855	54.1			
Interval 2-3 years	9538	24.1	5146	54.0			
Interval 3+ years	12448	31.4	6938	55.7			
ANC visit during pregnancy					<0.0001		
No visit	9035	23.0	5199	57.5			
1 visit	2377	6.0	1413	59.4			
2 visits	7329	18.6	3960	54.0			
3 visits	5953	15.1	3257	54.7			
4+visits	14663	37.3	8070	55.0			
Blood Pressure measured					0.095		
during pregnancy							
No	9756	32.0	5346	54.8			
Yes	20764	68.0	11502	55.4			
Received advise on					<0.0001		
pregnancy nutrition during							
ANC visit							
No	10413	34.0	51.7	5386			
Yes	20198	66.0	56.8	11472			
Alerted to pregnancy					<0.0001		
complications such as							
convulsions during ANC							
visit							
No	25887	84.6	53.9	13966			
Yes	4715	15.4	61.1	2882			

39298

359

32319

7338

14939

15082

6616

652

11592

99.1

0.9

81.5

18.5

40.1

40.4

17.7

1.7

30.5

Type of pregnancy

Ever had a terminated

*BMI and Lifestyle factors* Body Mass Index <sup>c</sup>

Underweight ( $\leq 18.5 \text{ kg/m}^2$ )

Singleton

pregnancy<sup>a</sup> No

Anaemia level b

Not anaemic

Moderate

Severe

Twin

Yes

Mild

**Table 2:** Sample distribution and reported prevalence of Pre-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 five years preceding the survey according to selected characteristics, India, 2005-06

21817

243

17394

4666

8077

8696

3825

378

6431

55.5

67.9

53.8

63.6

54.1

57.7

57.8

58.0

55.5

< 0.0001

< 0.0001

< 0.0001

0.414

Normal (18.5-22.9 kg/m <sup>2</sup> )	20714	54.4	11605	56.3	
Overweight (23.0-24.9	2770	7.3	1566	56.5	
kg/m <sup>2</sup> )					
Obese ( $\geq 25.0 \text{ kg/m}^2$ )	3226	14.7	1828	56.7	
Current tobacco smoking					<0.00
No	39049	98.5	21670	55.5	
Yes	608	1.5	390	64.1	
Drinks Alcohol					0.00
No	38735	97.7	21584	55.7	
Yes	911	2.3	468	51.4	
Diabetes <sup>d</sup>					<0.00
No	39123	98.7	21703	55.5	
Yes	160	1.3	345	67.1	
Asthma <sup>d</sup>					<0.00
No	39163	98.8	21703	55.4	
Yes	470	1.2	342	72.8	
Dietary intake					
Milk or curd					<0.00
Daily	14424	36.4	7397	51.3	
Weekly	6160	15.5	3515	57.1	
Occasionally	14393	36.3	8468	58.8	
Never	4675	11.8	2681	57.3	
Green leafy vegetables					0.00
Daily	23820	62.1	12924	54.3	
Weekly	11288	29.6	6248	55.4	
Never/Occasionally	3186	8.3	1885	59.1	
Fruits					<0.00
Daily	4915	10.8	2538	51.6	
Weekly	9885	25.2	5374	54.4	
Occasionally	22085	60.0	12329	55.8	
Never	1400	4.0	811	57.9	
Pulses and beans					0.03
Daily	18219	46.7	9843	54.0	
Weekly	14854	39.4	8249	55.5	
Occasionally	4880	13.0	2766	56.7	
, Never	345	0.9	204	59.1	
Eggs					<0.00
Daily	1394	3.0	768	55.1	
Weekly	10739	26.6	5829	54.3	
Occasionally	15283	38.5	8614	56.4	
Never	10868	31.9	5841	53.7	
Fish		-			<0.00
Daily	2825	6.4	1729	61.2	
Weekly	8787	21.7	4758	54.1	
Occasionally	14982	39.1	8454	56.4	
Never	11697	32.8	6117	52.3	
Chicken or meat	,	52.0	511/	52.5	<0.00
Daily	481	1.2	287	59.7	
Weekly	8581	21.0	4474	51.6	
Occasionally	18410	47.0	10655	57.9	
Never	10819	30.8	5690	52.6	
Backaround factors	10015	50.0	5050	52.0	
					0.01

15-29	29190	73.6	16235	55.6	
30-39	9421	23.8	5234	55.6	
40-49	1047	2.6	592	56.6	
Education <sup>e</sup>					0.005
No education	18783	47.4	10348	55.1	
Primary	5550	14.0	3200	57.7	
Secondary	12959	32.7	7174	55.4	
Higher	2365	6.0	1338	56.6	
Religion					< 0.0001
Hindu	31280	78.9	17010	54.4	
Muslim	6482	16.3	3996	61.6	
Christian	814	2.1	464	57.1	
Sikhs	514	1.3	284	55.3	
Others <sup>f</sup>	568	1.4	307	54.0	
Caste/tribe <sup>g</sup>					< 0.0001
Scheduled caste	7945	20.1	4366	55.0	
Scheduled tribes	3742	9.5	1950	52.1	
Other backward class	15878	40.2	8813	55.5	
General	10845	27.5	6177	57.0	
Missing caste	1089	2.8	679	62.4	
Employment status					<0.0001
Not working	27699	70.0	15753	56.9	
Working	11898	30.0	6278	52.8	
Wealth index <sup>h</sup>					<0.0001
Lowest	9566	24.1	5516	57.7	
Second	8600	21.7	4816	56.5	
Middle	7769	19.6	4166	53.6	
Fourth	7256	18.3	3948	54.4	
Highest	6466	16.3	3570	55.2	
Place of residence					< 0.0001
Urban	10622	26.8	5738	54.0	
Rural	29035	73.2	16323	56.2	
Geographic Regions <sup>i</sup>					< 0.0001
North	5678	12.8	2534	49.9	
Northeast	1613	4.1	959	59.4	
Central	11111	28.0	6082	54.7	
East	10042	25.3	7024	69.9	
West	5117	12.9	2485	48.6	
South	6696	16.9	2978	44.5	
Total <sup>j</sup>	39657		22061	55.6	

Note: <sup>a</sup> Includes miscarriages/spontaneous abortion and induced abortion both;

<sup>b</sup> Mild anaemia (Haemoglobin 10.0-10.9 grams/deciliter for pregnant women, 10.0-11.9 g/dl for non-pregnant women, and 12.0-12.9 g/dl for men), moderate anaemia (7.0-9.9 g/dl for women and 9.0-11.9 g/dl for men), and severe anaemia (less than 7.0 g/dl for women and less than 9.0 g/dl for men). In the survey, appropriate adjustments in these cutoff points were made for respondents living at altitudes above 1,000 metres and respondents who smoke, since both of these groups require more haemoglobin in their blood (Centers for Disease Control and Prevention, 1998);

<sup>c</sup> In NFHS-3, all respondents were weighed using a solar-powered scale with an accuracy of ±100 g. Their height was measured using 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 two months preceding the survey, were excluded from these anthropometric measurements;

<sup>d</sup> From self reports only;

<sup>e</sup> Education: No education (0 years of education), primary (1–5 years of education), secondary (6–8 years of education), higher (9+ years of education);

<sup>f</sup> Others include Buddhist, Jain, Jewish, Zoroastrian;

<sup>g</sup> 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. General are thus a default residual group that enjoys higher status in the caste hierarchy;

<sup>h</sup> Items comprising the wealth index in the third National Family Health Survey Household includes 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 radio/transistor, a black and white television, a colour television, a sewing machine, a mobile telephone, any other 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;

Region: 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;

<sup>1</sup>Number of women varies slightly for individual variables depending on the number of missing values

Characteristics	Pre-eclampsia				
-	Unadjusted Adjuste			usted*	
-	OR	95%CI	OR	95%CI	
Maternal factors					
Total children ever born					
1 <sup>Ref</sup>	1.00	ref	1.00	ref	
2-3	0.83	0.79-0.88	1.13	0.64-2.02	
4+	0.96	0.91-1.02	1.27	0.71-2.28	
Preceding birth interval					
First order birth <sup>Ref</sup>	1.00	ref	1.00	ref	
Interval <2 years	0.85	0.80-0.91	0.74	0.41-1.32	
Interval 2-3 years	0.85	0.80-0.90	0.72	0.41-1.29	
Interval 3+ years	0.91	0.86-0.96	0.75	0.42-1.33	
ANC visit during pregnancy					
No visit <sup>Ref</sup>	1.00	ref	1.00	ref	
1 visit	1.08	0.99-1.19	0.82	0.74-0.91	
2 visits	0.87	0.82-0.92	0.87	0.78-0.96	
3 visits	0.89	0.83-0.95	1.04	0.93-1.15	
4+ visits	0.90	0.86-0.95	1.31	1.22-1.41	
Blood Pressure measured					
during pregnancy					
No	1.00	ref	1.00	ref	
Yes	1.03	0.99-1.08	1.13	1.06-1.21	
Received advise on					
pregnancy nutrition during					
ANC visit					
No	1.00	ref	1.00	ref	
Yes	1.23	1.17-1.29	1.33	1.25-1.41	
Alerted to pregnancy					
complications such as					
convulsions during ANC visit					
No	1.00	ref	1.00	ref	
Yes	1.34	1.26-1.43	1.31	1.22-1.41	
Type of pregnancy					
Singleton <sup>Ref</sup>	1.00	ref	1.00	ref	
Twin	1.69	1.35-2.11	1.53	1.12-2.09	
Ever had a terminated					
pregnancy					
No <sup>Ref</sup>	1.00	ref	1.00	ref	
Yes	1.50	1.42-1.58	1.38	1.30-1.48	
Anaemia level					
Not anaemic <sup>Ref</sup>	1.00	ref	1.00	ref	
Mild	1.16	1.11-1.21	1.08	1.05-1.16	
Moderate	1.16	1.10-1.23	1.16	1.10-1.24	
Severe	1.17	1.00-1.37	1.32	1.10-1.54	
BMI and Lifestyle factors					
Body Mass Index <sup>c</sup>					
Underweight (≤18.5 kg/m²)	0.97	0.93-1.01	0.95	0.90-1.00	
Normal (18.5-22.9 kg/m <sup>2</sup> )	1.00	ref	1.00	ref	

**Table 3:** Unadjusted and adjusted odds ratios (ORs) and 95% confidence interval (95%CI) for the risk of Preeclampsia during pregnancy for the most recent birth among women age 15-49 years who had a live birth in the five years preceding the survey, India, 2005-06

Rei				
Overweight (23.0-24.9	1.01	0.93-1.09	0.98	0.90-1.0
kg/m²)				
Obese (≥25.0 kg/m²)	1.02	0.94-1.11	1.08	0.98-1.1
Current Tobacco smoking				
No	1.00	ref	1.00	ref
Yes	1.43	1.21-1.70	1.91	1.41-2.5
Drinks Alcohol				
No <sup>Ref</sup>	1.00	ref	1.00	ref
Yes	0.84	0.74-0.96	0.81	0.67-0.9
Diabetes				
No <sup>Ref</sup>	1.00	ref	1.00	ref
Yes	1.65	1.37-1.98	1.50	1.19-1.9
Asthma				
No	1.00	ref	1.00	ref
Yes	2.15	1.75-2.64	2.05	1.59-2.6
Dietary intake				
Milk or curd				
Daily	0.78	0.73-0.84	0.89	0.81-0.9
Weekly	0.99	0.92-1.07	1.04	0.94-1.1
Occasionally	1.06	0.99-1.14	0.97	0.89-1.0
Never <sup>Ref</sup>	1.00	ref	1.00	ref
Green leafy vegetables			-	-
Daily	0.87	0.80-0.94	0.68	0.61-0.7
Weekly	0.88	0.81-0.96	0.77	0.70-0.8
Never/ Occasionally Ref	1.00	ref	1.00	ref
Fruits				
Daily	0.81	0.72-0.91	0.93	0.81-1.0
Weekly	0.87	0.78-0.97	1.14	1.04-1.2
, Occasionally	0.93	0.83-1.02	1.14	1.07-1.2
Never <sup>Ref</sup>	1.00	ref	1.00	ref
Pulses and beans				
Daily	0.94	0.74-1.20	0.98	0.73-1.3
Weekly	0.98	0.77-1.25	0.84	0.77-0.9
, Occasionally	1.03	0.80-1.32	0.92	0.84-1.0
Never <sup>Ref</sup>	1.00	ref	1.00	ref
Eggs		-		-
Daily	0.99	0.88-1.12	1.22	1.11-1.3
, Weekly	1.00	0.95-1.05	0.88	0.77-1.0
Occasionally	1.15	1.10-1.21	0.98	0.91-1.0
Never <sup>Ref</sup>	1.00	ref	1.00	ref
Fish	2.00			
Daily	1.65	1.50-1.81	0.97	0.87-1 0
Weekly	1 10	1.04-1 16	1.20	1.07-1 3
Occasionally	1.23	1.17-1.29	0.90	0.83-0.9
Never <sup>Ref</sup>	1 00	ref	1 00	0.00 0.0 ref
Chicken or meat	1.00		1.00	101
Daily	1 38	1 11-1 72	0.88	0 78-0 9
Weekly	0.90	0 85-0 95	0.00	0.76-0.9
	1 72	1 73-1 2/	0.27	0.74-1.2
Never <sup>Ref</sup>	1.20	1.23-1.34 ref	1 00	0.01-0.9 raf
Rackaround factors	1.00	101	1.00	101

15-29 <sup>Ref</sup>	1.00	ref	1.00	ref
30-39	1.00	0.95-1.05	0.91	0.85-0.98
40-49	1.04	0.92-1.18	0.88	0.73-1.07
Education				
No education Ref	1.00	ref	1.00	ref
Primary	1.11	1.05-1.18	1.15	1.08-1.23
Secondary	1.01	0.97-1.06	1.11	1.05-1.19
Higher	1.06	0.98-1.16	1.22	1.09-1.37
Employment status				
Not working <sup>Ref</sup>	1.00	ref	1.00	ref
Working	0.85	0.81-0.88	0.97	0.92-1.02
Religion				
Hindu <sup>Ref</sup>	1.00	ref	1.00	ref
Muslim	1.35	1.28-1.43	1.37	1.23-1.41
Christian	1.16	0.97-1.28	1.36	1.13-1.56
Sikhs	1.04	0.87-1.23	1.09	0.89-1.33
Others	0.99	0.84-1.17	0.95	0.77-1.17
Caste/tribe				
Scheduled caste Ref	1.00	ref	1.00	ref
Scheduled tribes	0.89	0.83-0.96	0.92	0.84-1.00
Other backward class	1.02	0.97-1.08	1.05	0.99-1.12
General	1.08	1.02-1.15	0.95	0.89-1.12
Missing caste	1.36	1.11-1.54	0.88	0.75-1.02
Wealth index				
Lowest <sup>Ref</sup>	1.00	ref	1.00	ref
Second	0.96	0.90-1.01	0.99	0.91-1.07
Middle	0.85	0.80-0.90	0.91	0.84-1.00
Fourth	0.88	0.82-0.93	0.97	0.88-1.07
Highest	0.91	0.85-0.97	1.00	0.89-1.12
Place of residence				
Urban <sup>Ref</sup>	1.00	ref	1.00	ref
Rural	1.09	1.05-1.14	1.08	1.01-1.15
Geographic Regions				
North <sup>Ref</sup>	1.00	ref	1.00	ref
Northeast	1.47	1.31-1.65	1.49	1.27-1.75
Central	1.22	1.14-1.30	1.37	1.26-1.50
East	2.34	2.18-2.51	2.10	1.89-2.33
West	0.95	0.88-1.03	0.94	0.88-1.04
South	0.81	0.75-0.87	0.74	0.66-0.82
Number of Cases			32703	

Ref for reference category\*Adjusted for all other variables in the table