

## Research Article

### Risk Factors of Stillbirths: A Case Control Study in North India

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#### Abstract

**Introduction:** Stillbirth is not appreciated as a public health problem and given a high priority by the policy makers despite 2.6 million fetal deaths annually worldwide. About 98% stillbirths occur in Low and Middle Income Countries (LMIC). India is the largest contributor of all global stillbirths. The study aims to evaluate risk factors of stillbirths.

**Materials and Methods:** A hospital-based case-control study was conducted in medical college women's hospital in north India. The cases were mothers of stillborn babies. There were 38 stillbirths during the study period. Mother of liveborn babies were taken as controls. For each case, two controls were selected (76) from the same hospital during the corresponding time. The power of the sample was 80 percent at 95 percent confidence limit. The cases and controls were comparable, the respective mean age of mothers being 25.3 (+SD 3.7) and 23.9 (+SD 4.6) years ( $p > 0.05$ ). Bivariate analysis was carried out with stillbirth as outcome variable and age, sex of the baby, residence, maternal complications and fetal characteristics as independent variables. Rural residence, sex of the baby, pregnancy induced hypertension/eclampsia and preterm deliveries were statistically significantly associated with occurrence of stillbirth. Multivariate logistic regression was performed, and risk was estimated by measuring Odds Ratio (OR). The model included variables which were statistically significant on bivariate analysis.

**Results:** The risk of stillbirth was 10 times or more with pregnancy induced hypertension and preterm delivery, the adjusted OR being 12.75 (95% CI 2.95-55.00;  $p < 0.001$ ) and 12.54 (95% CI 3.95-39.00;  $p < 0.001$ ). Higher maternal age was also associated with significantly higher and independent risk of stillbirth (OR 1.90, 95% CI 1.10-3.27;  $p < 0.02$ ). Male fetus was more likely to be stillborn (OR 4.02, 95% CI 1.38-11.69). There effect was independent of all other risk factors in the model. The effect of rural residence was not significant in multivariate model.

**Conclusion:** The study showed a strong evidence of association pregnancy induced hypertension and preterm birth as risk factors for stillbirth. Maternal age and sex of the child also showed statistically significant risk of stillbirth. Rural residence which showed significant association in bivariate analysis, but it was removed in the model when adjusted for other risk factors.

**Keywords:** Case control; Multivariate regression model; Odds ratio; Risk factors; Stillbirth

#### Introduction

High incidence of stillbirths, a fetal death at and beyond 28 weeks of gestation of pregnancy, is an important maternal and child health problem in Low Middle Income Countries (LMIC) including India. An estimated 2.6 million stillbirths occur globally,

of which 98 percent occur in LMICs [1]. Despite being an important reproductive and child health problem, it is not on yet on the global agenda and constantly overlooked by the global community. While stillbirths are closely related to maternal mortality, yet it was not included in the tracking indicators of Millennium Development Goals (MDG), and as well as Sustainable Development Goals (SDG). WHO [2,3] has estimated that stillbirth rates are the highest 31.0 and 29.7 per 1000 births in the African Region and Eastern Mediterranean Region, respectively. Stillbirth rates are

estimated to be 25.9 per 1000 births in South East Asia Region (WHO). In 2009, 76.2% of all stillbirths occurred in South Asia and sub-Saharan Africa. Half the of world’s stillbirths occur in India, Pakistan, Nigeria, Bangladesh and China [4].

India tops the list of 195 countries in stillbirths worldwide, and about 75% all stillbirths in South East Asian countries [5]. During 2015, about 26 million births occurred in India, of which 592,000 were stillbirths. The estimated stillbirth rate of India is 22.2 per 1000 births down from 33.3 per 1000 births in the year 2000 [1]. The stillbirth rates range from 20 to 66 per 1000 births in various socio-economically diverse states in the country [6-11]. Varying estimates of stillbirths have also been reported due to using differential criteria for defining stillbirths and the methods used for input data from various sources [12-14]. Most stillbirths are preventable and the interventions to prevent and reduce them are well established. India has succeeded reducing maternal and child mortality by about 70% in the last one decade through universalization of health care and improving quality of antenatal care and institutional deliveries, and child health services [14]. The problem of large number of stillbirths is serious and deserves urgent attention of policy makers and researchers. However, there is a dearth of data on stillbirth in India as is it not reported in the country’s vital registration system as well as health information system of national health systems. There is a lack of systematically designed studies to identify causes and risk factors of stillbirth. The present study aims at assessment of risk factors associated with stillbirth in a tertiary care medical college women hospital in north India.

### Study Design and Methods

The study was conducted by using case control design in a tertiary care women hospital of the medical school in the Jaipur city in the state of Rajasthan in India in 2015. The cases were defined as fetal deaths at 28 or more weeks of gestation among pregnant women hospitalized for delivery. Live birth during the corresponding period in the hospital was taken as control. All cases of stillbirths were registered. For each case, two controls were selected. A total number of 38 stillbirths were identified during

the period, and 76 controls were randomly selected from 776 live births in the corresponding period. The power of sample was more than 80% at 95% confidence limits to derive valid estimates of risk.

Patient’s consent was obtained for interview and collecting data. The data was extracted from the case records, notes of the obstetrician, and in person interview of the mother during the week following parturition before discharge from the hospital. Information was collected by trained investigators on the age of the women, parity, gravidae, previous history medical and obstetric history, utilization of antenatal care, complications during pregnancy and child birth, gestation age at delivery, type of delivery, person conducting delivery, presence of pediatrician, and questions related to urban/rural residence, and access and availability of health care. Cases and controls were compared on socio-demographic characteristics. Bivariate analysis was conducted to test association between independent variables and outcome (dependent variable). Subsequently, multi-variate logistic regression was performed to adjust for confounding effect of various factors to derive adjusted risk estimates of risk associated with stillbirths. Statistical Software SPSS version 22.0 was used for data analysis.

### Results

The study included 38 cases of stillbirth (Mothers) and 76 Live births as controls (Mothers). The mothers of the cases and controls were interviewed while they were in the hospital after delivery and patient records were reviewed. The mean age of the mothers of cases was 25.3 (SD+3.7) years, and those of controls 23.9 (SD+4.6) years. There was no significant difference in the mean age of the mothers (p>0.05). A bivariate analysis was performed for exploring association of stillbirth with various sociodemographic, maternal and fetal factors, such as age of the mother, urban-rural residence, sex of the baby, complications during pregnancy (ante partum hemorrhage and pregnancy induced hypertension), severe anemia, prematurity and type of delivery as independent risk factors, and birth outcome as dependent variable (Table 1).

Variables	Case (Stillbirth) n=38		Control (Live Birth) n=76		$\chi^2$	p Value
	No.	Percent	No.	Percent		
Mother’s Age (Years)						
Below 24	17	44.6	45	59.2	2.629	0.10
25 and more	21	55.3	31	40.8		
Sex of Child						

Male	25	65.8	28	34.8	8.533	0.003
Female	13	34.2	48	65.2		
Residence						
Urban	8	21.1	34	44.7	6.107	0.01
Rural	30	97.4	42	55.3		
Antepartum Hemorrhage						
Yes	1	1.3	1	2.6	0.254	0.614
No	37	97.4	75	97.4		
Pregnancy Induced Hypertension/Eclampsia						
Yes	6	15.8	1	2.6	9.208	0.002
No	32	84.2	75	97.4		
Severe Anemia						
Anemic	1	1.3	1	2.6	0.252	0.614
Non-Anemic	37	97.4	75	97.4		
Type of Delivery						
Caesarian	12	31.6	26	34.2	0.0789	0.778
Normal	26	68.4	50	65.8		
Premature Delivery						
Yes	22	55.6	4	2.7	42.28	0.0001
No	16	44.4	72	97.3		

**Table 1:** Bivariate Analysis of Cases (Stillbirth) and Controls (Live Birth).

No significant difference was observed in categories of age groups of mothers ( $p > 0.10$ ). Majority of women, both cases (97.4 percent) and controls (55.3 percent) hailed from rural areas, however, there was a significantly higher number of stillbirths in women with rural residence ( $p < 0.01$ ). Significantly higher number male babies were still born than females ( $p < 0.003$ ). Preterm birth was highly significantly associated with higher stillbirths ( $p < 0.001$ ). Maternal complications during pregnancy, namely, Pregnancy Induced Hypertension (PIH) and eclampsia were also highly significantly associated with increased number of stillbirths ( $p < 0.002$ ). Antepartum hemorrhage, severe anemia and type of delivery were not found to be associated with stillbirths.

A multivariate logistic regression analysis was performed to adjust for the effect of multiple risk factors (Table 2). PIH/Eclampsia was the most critical factor found to be strongly associated with the risk of stillbirth (Adjusted OR 11.6, 95% CI 1.5, 47.9) and the increased risk was independent of any other risk factor in the model. Preterm fetus was more likely to be a stillbirth, the risk being 10 times higher (Adjusted OR 10.5, 95% CI 2.3, 34.2). Male fetus was more likely to be still born, more the risk being more than twice than the female fetus. Maternal age, which was not associated with stillbirth in the bivariate analysis, showed a significantly higher risk among women in higher age group (25 and above years) than their younger counter parts (Adjusted OR 2.14, 95% CI 1.10, 7.04). The association of rural residence with stillbirths observed in the bivariate analysis, when included in the multivariate model, lost its statistical significance. Though rural residence showed a higher risk of stillbirth (Adjusted OR 2.14, 95% CI 0.79, 5.72), but failed to be statistically significant.

Factors	$\beta$ Coefficient	Std. Error	pValue	Odds Ratio	CI 95% LL – UL
Mother’s Age	0.981	0.495	0.047	2.14	1.10-7.042
Residence Rural/Urban	0.759	0.503	0.131	2.14	0.798-5.722
Sex of Child Female/Male	0.947	0.471	0.044	2.55	1.37-6.485
Preterm Delivery	2.358	0.771	0.002	10.56	2.33-34.22
Postpartum Hemorrhage /Eclampsia	2.454	0.766	0.021	11.63	1.47-47.89

**Table 2:** Multivariate Logistic Regression of Factors Associated with Stillbirths.

The final model included higher maternal age, male sex of the fetus, preterm birth and PIH/Eclampsia to be the most significant risk factors of stillbirth among women (Table 2A).

Factors	$\beta$ Coefficient	Std. Error	pValue	Odds Ratio	CI 95% LL - UL
Mother’s Age	0.642	0.277	0.021	1.90	1.10-3.27
Sex of Child Female/Male	1.391	0.545	0.011	4.02	1.38-11.69
Preterm Delivery	2.529	0.589	0.001	12.54	3.95-39.00
Pregnancy Induced Hypertension/Eclampsia	2.545	0.746	0.001	12.75	2.95-55.00

**Table 2A:** Final Good-Fit Model.

## Discussion

Stillbirth is an unsung malady of the humankind, especially in the low and middle-income countries where 98 percent fetuses were stillborn [1,15]. Stillbirth is increasingly assuming public health importance with the decline in the infant and under-five mortality rates in the developing countries. However, no reliable estimates of stillbirth are available in most countries. Out of 2.6 million global stillbirths, 1.8 million stillbirths occur only in 10 countries with India on the top of the list, accounting for almost half of the global stillbirths. More recently, the Lancet special series has brought to focus the enormity the problem of stillbirth and issues and challenges of high stillbirths faced by the developing countries [16,17]. The psychological effects of stillbirth on the parents and families have remained unrealized. The economic costs, both direct and indirect, due to stillbirth are high and have not been appreciated [18].

The causes and the risk factors associated with stillbirths are now well known and studied in various countries including India. Higher maternal age, rural residence, maternal complications during pregnancy, especially hypertension, eclampsia, severe anemia and antepartum and intrapartum hemorrhage, and preterm birth have been found to be associated with the increased risk of stillbirth. Findings of our study corroborated with the findings of these studies. Our study found pregnancy induced hypertension/eclampsia and preterm births as important and highly significant

risk factors of stillbirths, the risk being more than 10 times. The male child had higher preponderance of stillbirths. The women of relatively higher age and those lived in rural areas had higher risk of stillbirths. India being the biggest contributor to the world’s all stillbirths, faces a major challenge of preventing stillbirths. This huge human loss can be prevented by simple and cost-effective health care interventions and the available technology through the current health systems in the countries. It is clearly noticeable, except male sex, most of the risk factors are amenable to currently available maternal and child health interventions. India has demonstrated success in reducing maternal deaths in the last one decade by 70 percent, and infant mortality has been reduced to one-half, 34 per 1000 in 2015 from 68 per 1000 live births in 2000 [14]. The recent national survey<sup>18</sup> showed that 79 percent child births occurred in public health facilities and hospitals, the immunization coverage of infants was 62 percent. However, full coverage with antenatal care during pregnancy was only 31.1 percent in the urban and 16.7 percent rural areas. About one-fourth women were poorly nourished (BMI<18.5 kg/m<sup>2</sup>) and 50.3 percent anemic during pregnancy. The survey also reported 8.8 percent women in 15-49-year age suffered from varying degree of hypertension.

This quintessentially points to urgent need for enhancing access and availability of maternal and child health services and improving quality of care during pregnancy and child birth. Detection and effective management of hypertension and eclampsia, and the intrapartum delivery process can turn around

the situation by drastic reduction in stillbirth [19-21]. India's National Health Mission launched India Newborn Action Plan (INAP) [22], in 2014 that aims to reduce stillbirth rate by one-third by 2030. Strengthening surveillance and tracking system for stillbirths and improving coverage and quality of antenatal care are among the core strategies of INAP. Future strategies for reducing and preventing stillbirths will be guided by standardizing definition of stillbirth and making data available through improved data collection system [23].

## Conclusion

The scourge of stillbirth can be mitigated by effective implementation of evidence-based health interventions to prevent and manage pregnancy induced hypertension, eclampsia, antepartum hemorrhage, preterm delivery, anemia; and strengthening health systems to enhance access and coverage effective and good quality care during pregnancy and child birth. Surveillance and tracking stillbirth will go a long way in monitoring progress and develop meaningful data on stillbirth and its distribution across the vastly diverse social-demographic regions in India.

## Strengths and Limitations

The study was a hospital-based case control study and would have had limitations of atypical case control design. The study was conducted in tertiary care referral hospital in a urban setting, and hence a possibility of selection bias may not be ruled out. However, the study had many strengths. It was more a case cohort study rather than usual case control design. The information bias was minimal as we used current cases and controls before the discharge from the hospital. The ascertainment of stillbirth was done by a senior gynecologist and the possibility of misclassification was minimal. Further, the records were available, and the missing information was obtained from the hospital staff and the patients while they were still in the hospital. The estimates of risk are likely to be quite valid and reliable as the sample size had a power with 95 percent confidence levels.

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## Author Contribution

SDG conceptualized, designed and prepared final manuscript, SG participated in conceptualization and final analysis, NPJ data management and preliminary analysis, SV data extraction and interview with patients, VJ supervised data collection and quality in hospital. All authors have read and approved the manuscript.

## Competing Interests

The authors declare that they have no competing interests.

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