Original Research Article

Perinatal outcome of pregnancies with previous stillbirth: a prospective case control study in tertiary care center

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ABSTRACT

Background: Aim was to examine the association between stillbirth in first pregnancy and adverse perinatal outcome in second pregnancy. To determine risk factors causing recurrent stillbirth.
Methods: This study was conducted at Government Medical College, and hospital, Nagpur. It was prospective case control study with cases as patients who had stillbirth in previous pregnancy and control as patient who had live birth in previous pregnancy.
Results: There was 10 fold increased risk of recurrent stillbirth in cases compared to control. Preeclampsia was major risk factor followed by placental abruption; congenital anomaly and preterm labour were responsible for recurrent stillbirth.
Conclusions: History of stillbirth in first pregnancy is associated with adverse perinatal outcome in form of recurrent stillbirth, increased NICU admission and neonatal death. Risk reduction by elimination of risk factor, proper antenatal surveillance and close monitoring during labour helps to reduce recurrent stillbirth.

Keywords: Congenital anomaly, Fetal growth restriction, Neonatal death, NICU, Perinatal outcome, Placental abruption

INTRODUCTION

The birth of a newborn after twenty-eight completed weeks of gestation or weighing 1,000 grams or more, with baby showing no signs of life after delivery is a still born.[1] Such death includes both antepartum an intrapartum death.

Previous stillborn pregnancy is at high risk of stillbirth, preterm birth, IUGR, placental abruption in next pregnancy.[2] There is 2-to-10-fold increased risk of repeat fetal death.[3] Perinatal outcome in pregnancies with previous still born are more prone to perinatal death, fetal growth restriction, early preterm birth, hypoxic ischemic encephalopathy, intracranial hemorrhage, respiratory distress. Around 2 million stillbirths occurred worldwide in 2019.[4] Out of these, 0.34 million stillbirths occurred in India, making it the country with largest such burden according to first joint estimate. India, along with five other countries-Pakistan, Nigeria. The Democratic Republic of the Congo, China and Ethopia- accounted for nearly half of all stillbirths in the world. The country had substantial progress in reducing the stillbirth rate over the past two decades. The rate had declined to 13.9 stillbirths per 1000 in 2019 from 29.6 per 1000 in 2000, a 53% reduction.[5] Recurrence of stillbirth with similar gestational age in successive pregnancies is most likely due to recurring causes of stillbirth presenting at the same time in a next pregnancy. Several known causes of stillbirth have been shown to recur in pregnancies like placental abruption, preeclampsia, and birth defects. Studies have also shown that women with previous

stillbirth in general tend to repeat gestational age among their infant. So, this study was carried out to examine the association between stillbirth in first pregnancy and adverse perinatal outcomes in second pregnancies and to determine the risk factors that caused recurrent stillbirth.

METHODS

A prospective case control study of perinatal outcome of pregnancies with previous stillbirth was carried out at the Obstetrics and Gynecology Department of Government Medical College, Nagpur, after the approval of Institutional Ethics Committee between 1st January 2019 to 31st December 2020.

Study population included cases as women who had stillbirth in previous pregnancy and control as women who had live birth in previous pregnancy matched with gravidity and parity. Women with previous stillbirth due road traffic accidents or accidental injury were excluded. Total sample size was 200 (cases-100+ control -100). Data collection started prospectively from outpatient department and followed till delivery and puerperium.

Pregnant patients with previous stillbirth were enrolled at 1st ANC visit (preferably in 1st trimester). Information collected on obstetric history, the circumstances and cause of stillbirth, intrapartum events, previous investigation pointing out causative factor noted, gross placental abnormality, placental histology {if done} microbiological evaluation, neonate inspection to find out the cause of stillbirth.

Complete obstetric history about present pregnancy noted. Pregnancy dating from 1st trimester ultrasonography to rule out fetal growth restriction. Pregnancy complication such as fever, rash, hypertension, diabetes, genital infection, vaginal bleeding, PPROM. Personal history about drug and alcohol intake and family history about genetic, chromosomal disorder, congenital malformation was obtained.

Investigation like full blood count, blood group, rhesus typing, nuchal tralusancy scan, oral glucose challenge test (75grams), glycosylated hemoglobin, coagulation profile test for autoantibody/thrombophilia were done.

During third trimester, fetal monitoring by growth scan, doppler, biophysical profile, cardiotocography and upcoming antenatal complication noted and treatment given. All delivery events noted (spontaneous/induced). Mode of delivery, duration of labor, intrapartum complication was noted. After delivery, APGAR at 1minute and 5 minute was noted. Neonates were followed up for 7 days.

Statistical analysis

Collected data were entered into Microsoft spreadsheet. Tables and charts were prepared using Microsoft word and excel spreadsheet. Continuous variables (demographic, biochemical and hemodynamic parameters) were presented as Mean±SD. Categorical variables were expressed in frequency and percentages. Continuous variable were compared between Cases and Control performing independent t-test for normalized data and for non-normalized data, Mann-Whitney test. Categorical variables were compared between cases and control by performing chi-square test. For small numbers, Fisher exact test was used wherever applicable. Odds ratio, 95% confidence interval were calculated to find association of different factors with previous still births. Multivariate logistic regression was performed to determine independent predictors of in cases of previous still births. $p<0.05$ was considered as statistical significance. Statistical software STATA version 14.0 was used for statistical analysis.

RESULTS

Most of study population belongs to young age group {20-25}, (Table 1) and rural background (Table 2). Preeclampsia, abruption, congenital abnormalities were high risk factors responsible for stillbirth. Reason for most of stillbirth remains unexplained. Preeclampsia is leading cause for most of recurrent stillbirth (Table 3).

Cesarean section rate increased in cases with previous stillbirth (Table 4). Most of study population belongs to referral category (Table 5).

Table 1: Age distribution of cases and controls.

Age in years	Cases		Control	
	Frequency	%	Frequency	%
<20	28	28.00	48	48.00
20-25	45	45.00	40	40.00
26-30	16	16.00	10	10.00
31-35	7	7.00	1	10.00
>35	4	4.00	1	10.00

Table 2: Distribution of study population according to residence.

Residence	Cases		Control		P value
	Frequency	%	Frequency	%	
Rural	83	83.00	79	79.00	Chi2=0.5198
Urban	17	17.00	21	21.00	P=0.471,NS

Table 3: Distribution of cases and control according to high risk factor in pregnancy.

High risk factors	Previous pregnancy		P value	Present pregnancy		P value
	Cases	Control		Cases	Control	
Inrauterine growth restriction	0	0	-	1	0	1.000,NS
Preeclampsia	15	1	OR=15.63 (2.29-664.43) p<0.001, HS	32	3	OR=15.21 (4.43-79.82) p<0.001,HS
Diabetes melitus	1	0	1.000,NS	1	0	1.000,NS
Abruption	7	0	0.014,S	2	0	0.497,NS
Congenital anamoly	6	0	0.029,S	3	0	0.246,NS
Sickle cell disease/other haemoglobinopathy	3	0	0.246,NS	3	0	0.246,NS
Other medical disorder	1	0	1.000,NS	0	0	1.000,NS
Labour abnormalities	19	0	<0.001,HS	8	1	OR=8.60 (1.10-385.7) p=0.0147S
Unexplained	47	0	<0.001,HS	2	0	0.497,NS
Not otherwise classified	0	0	-	0	0	-
No risk factor	1	99	<0.001,HS	45	96	OR=0.034 (0.008-0.10) p<0.001,HS

Table 4: Distribution of cases and control according to mode of delivery.

Mode of delivery	Previous pregnancy		P value	Present pregnancy		P value
	Cases	Control		Cases	Control	
Vaginal	77	72	Chi2=0.6580 p=0.417,NS	48	69	Chi2=9.0825 p=0.003,HS
Caesarean	23	28		52	31	
Instrumental	0	0		0	0	

Table 5: Distribution of study population according to booked/referral.

	Cases		Control		P value
	Frequency	%	Frequency	%	
Booked	11	11.00	19	19.00	Chi2=2.5098 p=0.113, NS
Referral	89	89.00	81	81.00	

Table 6: Distribution of study population according to weight of baby in previous pregnancy and present pregnancy.

Weight of baby in kg.	Previous pregnancy			Present pregnancy		
	Cases	Control	Odds Ratio,95%C.I. P value	Cases	Control	Odds Ratio, 95% C.I. P value
1.0-1.5	48	0	<0.001, HS	16	0	p<0.000, HS
				11	1	OR=20.11 (2.65-
1.5-2.0	4	0	0.0003, HS			878.75)
						p=0.0002, HS
			OR=2.72 (1.21-	38	35	OR=1.98 (1.02-3.85)
2.0-2.5	36	55	6.38)			p=0.0285,S
			p=0.0082, HS			
2.5-3	8	42	OR=1.0 (reference)	30	55	OR=1.0 (reference)
3.0-3.5	4	8	-	4	9	-
>3.5	0	0	_	1	0	-

Table 7: Still birth rate, NICU admission and neonatal death rate among cases and control.

Outcome of present pregnancy	Cases	Control	P value
	N (%)	N (%)	
Stillbirth	15	2	0.002,HS
Normal	70	98	<0.0001,HS
NICU admission	0	0	--
Birth asphyxia	0	0	--
Respiratory distress	3	0	0.246,NS
Low birth weight	5	0	0.059,NS
Sepsis	3	0	0.264,NS
Neonatal death	4	0	0.121,NS
NICU admission and Neonatal death	15	0	<0.0001

Most of baby born are belong to low birth weight (Table 6). 15% stillbirth occurred in cases with previous stillbirth. NICU admission and neonatal death are 15 % in cases with stillbirth (Table 7). Common causes of stillbirth in cases are preeclampsia, antepartum hemorrhage and preterm delivery (Table 8).

Table 8: Distribution of cases and control according to cause of stillbirth.

Cause of stillbirth	No. of cases	No. of control
Hypertensive disorder	7	0
Antepartum hemorrhage	2	0
Spontaneous preterm labour	2	1
Fetal abnormality	1	1
Fetal growth restriction	1	0
Intrapartum asphyxia	1	0
Unexplained intrauterine death	1	0
Infection	0	0
Maternal disease	0	0
Trauma	0	0
Unclassified	0	0

DISCUSSION

This study was conducted at Department of Obstetrics and Gynecology, at a Tertiary Care Centre. In our study, we compared pregnancy outcome between cases who had stillbirth in previous pregnancy with control who had live birth in previous pregnancy and determine the risk factors for recurrent stillbirth.

In our study, significant number of stillbirths occurred in age group of 20-25{Chi2=13.2419, p=0.010} which was similar to study done by Bhattacharya et al {mean age - 24}.[6] Gordon et al study suggestive of significant number of stillbirth in younger one{<20}, whereas significant number of stillbirth occurred in advanced age group {>35yrs} in Salihu et al and in Onwude et al, Ofi et al, Robson et al study, there was no significant association of maternal age with stillbirth.[7-11]

In our study, most of woman belonged to rural area. There is no significant association with adverse perinatal outcome with area of residence. Most of cases and control were from referral category but no significant correlation between adverse perinatal outcome and booking status. In our study, high risk factors e.g., preeclampsia {OR=15.63, 95%C.I. (2.29-664.43) p<0.001}, placental abruption {p=0.014}, preterm labour {p<0.001}, congenital anomaly {p=0.029} had significant association with adverse perinatal outcome. Preeclampsia {OR=15.63, 95% C.I. (2.29-664.43) p<0.001} was associated with 15 fold increased risk of adverse perinatal outcome whereas in Ofir et al, Bhattacharya et al, Salihu et al, Maried Black et al and Yildiram et al, there was 3-4 fold increased risk, in Gethaun et al study, 2 fold increased risk.[10,6,8,12-14] However, fetal growth restriction rates were similar between cases and controls. In our study, some causes recurred in subsequent pregnancies such as preeclampsia {OR=15.21, 95% C.I. (4.43-79.82) p<0.001}, preterm labour {OR=8.60, 95%C.I. (1.10-385.7) p=0.0147}. Finding of increased incidence of preeclampsia in subsequent pregnancies may have remained unnoticed in previous pregnancies which had contributed to stillbirth. In our study, cause of stillbirth in 40 % of cases remained unexplained {as karyotyping and fetal autopsy not performed} similar to study done by Bhattacharya et al (44%) but higher than Maignien et al (22%).[6,15]

It was found in our study that significant increased risk of adverse perinatal outcome at term gestation {37-40 weeks}{Chi2=40.7905, p<0.0001}, whereas Bhattacharya et al, Ofir et al, Gethaun et al, Gordon et al studies showed significant association at gestational age of <37 weeks.[6,10,13,16] Significant increase in number of cesarean section {Chi2=9.0825, p=0.003} in pregnancies with previous stillbirth similar with study done by Bhattacharya et al, Francesca Monari et al, Robson et al, Black et al.[6,17,11,12] Increase in cesarean section may be due to increase in number of induction of labour as well

as early decision by obstretician by considering it as precious pregnancy to improve the perinatal outcome in pregnancies with previous stillbirth. In our study, most of stillbirth in previous pregnancies belonged to 1kg to 1.5 kg group. Outcome in terms of birth weight (most of babies delivered fall in birth weight group of 2 to 2.5 kg {OR=1.98, 95% C.I. {1.02-3.85} p=0.0285} has been improved due to intervention done to prevent recurrent stillbirth. In our study, there was significant increase in risk low birth weight in present pregnancy which was similar to study done by Robson et al, Bhattacharya et al, Monari et al, Heinonen et al, Gokhan Yildiram et al, Black et al.[16,11-12,17,18] Mean birth weight has been reduced in cases in present pregnancy it may be due prior induction to prevent recurrent stillbirth.

There were total 15 stillbirths in present pregnancy. Total number NICU admission and neonatal death was 15. There is 10-fold increased risk of stillbirth {Chi2=13.48, OR=10.5, 95% C.I. (2.30-96.480 p<0.0002} after previous stillbirth whereas 22 fold increased risk by Ofir et al, 3.5 to 5 fold increased risk by Bhattacharya et al, Gethaun et al, Gordon et al, 2 fold increased risk by Sharma et al, 1.2 fold by Black et al but Robson et al, Lurie et al, Heinonen et al shows no significant increase in risk of stillbirth in exposed group.[10,6,13,7,18,12,11,19,20] Significant increased risk of NICU admission and neonatal death occurred in our study but no significant difference in Yildiram et al.[13]

In our study out of 15 stillbirths occurred in cases (present pregnancy), cause of stillbirth for seven pregnancies was preeclampsia, for two of them was placental abruption, two of them due to spontaneous preterm birth, others are intrapartum asphyxia, congenital anomaly, fetal growth restriction. Cause for one stillbirth remains unexplained. There were two stillbirths in control (present pregnancy), cause for one was spontaneous preterm birth and for second was congenital anomaly.

Limitations of study are, autopsies were not performed on stillborn due unwillingness of parents and social issues, so it is difficult to establish the cause in unexplained category. Due to financial constraints, certain advanced tests such as polymerase chain reaction (PCR) for infective pathology and cytogenetic analysis could not be performed.

CONCLUSION

Study was carried out to obtained perinatal outcome of pregnancies with previous stillbirth. Our aims are to examine the association between stillbirth in first pregnancy and adverse perinatal outcomes in second pregnancies and to determine the risk factors that causing recurrent stillbirth. Most of stillbirth occurred in young and advanced age group. High risk factor such as preeclampsia, placental abruption, fetal growth restriction, preterm labour is responsible for recurrent stillbirth. Preeclampsia remains the leading cause for

recurrent stillbirth. Reason for most of stillbirth remain unexplained. Caesarean section rate has been increased in pregnancies with previous stillbirth due to increased number of inductions of labour and early decision by obstetrician to improve the perinatal outcome. Newborn had a risk to be born at earlier gestation and have low birth weight due to induction of labour for fear of risk of recurrent stillbirth. There was 10fold increased risk of recurrent stillbirth in pregnancies with previous stillbirth. Risk reduction by elimination of risk factor, proper antenatal surveillance and close monitoring during labour helps to reduce recurrent stillbirth.

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