

# Prevalence of Stillbirths during COVID-19 Pandemic at a Tertiary Referral Centre in Central Kerala, India: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Stillbirth is defined as a baby born with no signs of life after a given threshold. It is a sensitive indicator of quality of care received by the mother during antepartum and intrapartum period. There has been a renewed focus on stillbirth in the backdrop of COVID-19 pandemic, as pregnant women are at an increased risk for severe form of COVID-19 and are associated with adverse perinatal outcomes.

**Aim:** To estimate the prevalence of stillbirths and its characteristics during the pandemic and also, to classify the causes of stillbirths according to the International Classification of Diseases for use in Perinatal Mortality (ICD-PM) classification.

**Materials and Methods:** This cross-sectional study was conducted in the Department of Obstetrics and Gynaecology at Government Medical College, Thrissur, Kerala, India, during the COVID-19 pandemic from 1<sup>st</sup> August 2021 to 30<sup>th</sup> July 2022. A total of 106 mothers, who gave birth to stillbirths after 28 weeks of gestation were included in the study. When gestational age was not sure, stillbirth weighing more than 500 grams was considered as the inclusion criteria. Foetus, placenta, cord and membranes were examined after the delivery. The parameters studied were age, domicile, income, gestational age, order of pregnancy, mode of delivery, timing of foetal death, baby weight, gender, presence of anomalies and maternal medical complications. The causes were classified according to

International Classification of Diseases-10-to Perinatal Mortality (ICD-PM) classification system. Categorical variables were assessed by Chi-square test and continuous variables were assessed by unpaired Student's t-test.

**Results:** There were 106 stillbirths with a Stillbirth Rate (SBR) of 38.78 per 1000 births. Major proportions of stillbirths were antepartum. Mean maternal age was 28.7±4.7 years. There were 73 (68.86) rural women and 33 (31.1%) urban women with stillbirths. A total of 90 (84.9%) cases were referral, while 16 (15.1%) were registered in the Institute for antenatal care. A total of 67 (63.2%) stillborns were male babies, but there was no significant difference in SBR, according to the order of pregnancy. Causes were classified according to the ICD-PM classification system. Hypertensive disorders in pregnancy (36.79%) and the foetal growth restriction (39.62%) were the common maternal and foetal condition identified among the cases. There were 22 COVID-19 positive cases, but they were also having hypertension as co-morbidity.

**Conclusion:** In present study, antepartum stillbirth was the commonest type and occurred mostly in referral cases from periphery. Hypertensive diseases in pregnancy and foetal growth restriction were the leading causes. Early detection of high-risk conditions and timely referral, may reduce the rate of stillbirth.

**Keywords:** Coronavirus disease 2019, Foetal growth restriction, Preeclampsia, Pregnancy, Severe acute respiratory syndrome coronavirus 2

## INTRODUCTION

Stillbirth is one of the worst outcomes of pregnancy and often a neglected tragedy. SBR is a marker of maternal health and access to quality care during pregnancy and childbirth. Despite the universality of childbearing, changing environments result in varying patterns of obstetric morbidity. Decline in SBR has not been satisfactory across the nations, besides COVID-19 pandemic has worsened scenario [1].

Stillbirth is defined as delivery of a fetus after a given threshold related to gestational age or weight of the baby, showing no signs of life and who cannot be resuscitated following birth [2]. An early stillbirth occurs at 22 to 27 completed weeks of gestation and a late stillbirth occurs at 28 weeks or more of gestation. For international comparison, late gestation foetal deaths (28 weeks or more) are considered. SBR is defined as the number of babies born with no signs of life per 1000 total births. [3]. Foetal death can occur during antepartum or intrapartum period. The causes of stillbirths are traditionally classified into maternal, placental and foetal [4]. There are several determinants of stillbirths such as maternal age, gestational age, antenatal care, illiteracy, null or high parity,

infections, maternal medical and obstetric complications, congenital anomalies, intrapartum events and type of delivery [5].

Infection is a major maternal cause leading to stillbirth. Pregnant women are at an increased risk for severe form of COVID-19 and are associated with adverse perinatal outcomes. Epidemiological studies have reported a spike in SBR, but more evidence is needed to discriminate between direct effect and indirect effect of the epidemic [6,7]. Direct effects are those caused by maternal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, while indirect effects are those resulting from changes in access to healthcare or in the behaviour of pregnant women or clinicians during the COVID-19 pandemic [6]. The number of stillbirths among mothers, infected with COVID-19 doubled in the second wave [7].

Classification of stillbirths is a complicated process but it is vital for having a better obstetric result in future. Systematic assessment of each stillbirth is important, so, that risk factors and causes can be identified and strategies for prevention can be provided. ICD-PM is a universal classification system developed by World Health Organisation (WHO) for identifying the risk factors, causes and contributing factors [8].

United Nations International Children's Emergency Fund (UNICEF) report on projecting the indirect effect of COVID-19 on stillbirths predicted higher risk for stillbirth [9]. The reasons assumed are limited access to care, shortage of human resources, disrupted supply chains for essential medicine and equipment, obstacles to care such as reduced transport facilities and fear of contracting the virus. The effect of pandemic on SBR may vary depending on mitigation effects in the country, strength of existing health system and baseline stillbirth levels [9]. A study released by the United States (US) Centres for Disease control across US Hospital from March 2020-September 2021 found a significant elevated SBR among women with COVID-19 infection and recommended vaccination before or during pregnancy to reduce the impact of COVID-19 on stillbirth [1]. Increased SBR during the second wave of COVID-19 pandemic was also reported from Mumbai [7] but no similar study was conducted in Thrissur, Kerala, India. Hence, present study was conducted to find out the prevalence of stillbirths during the COVID-19 pandemic and to describe its characteristics, also to classify the causes of stillbirths according to the ICD-PM classification.

## MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of Obstetrics and Gynaecology of Government Medical College Hospital, Thrissur, a tertiary care centre in rural part of central Kerala, India, from 1<sup>st</sup> August 2021 to 30<sup>th</sup> July 2022. Institutional Ethics Committee approval was obtained (IRC protocol no:IEC/GMCTSR/151/2021). Written informed consent was obtained from the subjects after explaining the motive of the study and they were ensured that information collected shall be kept confidential. Out of 2733 total births, 106 mothers, who gave stillbirths within the study duration, were enrolled in the study.

**Inclusion criteria:** Mothers, who were admitted in COVID-19 and non COVID-19 maternity wards with intrauterine foetal deaths confirmed by absence of cardiac activity in ultrasonography, mothers who gave stillbirths in labour rooms of both COVID-19 and non COVID-19 wards were included in the study [10]. Stillbirths occurring, only after 28 weeks of gestation were included in the study. When gestational age was not sure, stillbirths weighing more than 500 grams were included.

**Exclusion criteria:** Mothers with severe mental disorders such as depression, bipolar disorders and schizophrenia and those cases suspected to have attempted for foeticide (if there is any history of any self-medication for termination of pregnancy or history of approaching quacks for the same) were excluded from the study.

### Study Procedure

Investigators collected the data from patients using proforma within 24 hours of delivery. Maternal data regarding socio-demographic variables including age, domicile (rura/urban), socio-economic status [11], data regarding gestational age, order of pregnancy, booking status of the women for antenatal care (Institutional or referral), details of COVID-19 infection and COVID-19 vaccination were noted. Presence of medical complications like hypertensive disorders of pregnancy, gestational diabetes mellitus, anaemia and heart disease, Obstetric complications like foetal growth restriction, oligamnios, polyhydramnios, and antepartum haemorrhage were enquired and details collected from case records.

Complete general, systemic and obstetric examination was conducted. Details of labour, like whether onset of labour was spontaneous or induced, method of induction of labour, indication for induction of labour, duration of labour, mode of delivery, interval between admission and time of delivery, stage of labour at which stillbirth occurred (in cases of intrapartum SBs) and any other complications during labour and childbirth were also noted. After the delivery of stillbirth, placenta, umbilical cord and membranes

were examined systematically. Foetal autopsy was not done due to social reasons. Every stillbirth was discussed in detail in the perinatal audit of the department and cause of death was assigned by senior obstetricians. The cause of death was further assigned according to the ICD-PM classification system by WHO [6].

This system classifies foetal conditions and maternal conditions associated with stillbirths. The ICD-PM classification requires information on timing of death, clinically defined causes and associated conditions. Foetal conditions associated with the antepartum stillbirths were designated as codes with prefix A (A-1 to A-6) and intrapartum SBs with prefix I (I-1 to I-7). Maternal conditions associated with stillbirths were coded with prefix M (M-1 to M-5). Categories and examples of ICD-PM are shown in [Table/Fig-1].

Category	Description	Example
A1	Congenital malformations and chromosomal abnormalities	Neural tube defects, trisomies etc.,
A2	Infections	Congenital syphilis, congenital rubella syndrome
A3	Antepartum hypoxia	Intrauterine hypoxia
A4	Other specified antepartum disorder	Vasa praevia, ruptured cord, TTTS, Rhesus isoimmunisation
A5	Disorders related to foetal growth	Foetal growth restriction, macrosomia, post-term
A6	Antepartum death of unspecified cause	IUD of unspecified cause
I1	Congenital malformations and chromosomal abnormalities	Neural tube defects, trisomies etc.,
I2	Birth trauma	Intracranial laceration and haemorrhage due to birth injury
I3	Acute intrapartum event	Intrauterine hypoxia
I4	infection	Congenital syphilis, congenital rubella syndrome
I5	Other specified intrapartum disorder	Vasa praevia, ruptured cord, TTTS, Rhesus isoimmunisation
I6	Disorders related to foetal growth	SGA, macrosomia, post-term
I7	Intrapartum death of unspecified cause	Foetal death of unspecified cause
M1	Complications of placenta, cord and membranes	Abruptio placenta, placenta praevia, cord prolapse, Chorioamnionitis
M2	Maternal complications of pregnancy	PROM, oligo- and polyhydramnios, multiple pregnancy, maternal death
M3	Other complications of labour and delivery	Breech delivery, malpositions and presentations, disproportions instrumental delivery, caesarean delivery, preterm delivery
M4	Maternal medical conditions	Hypertensive disorders, DM, renal disorders, infectious diseases, nutritional disorders, maternal use of tobacco, alcohol and drugs
M5	No maternal conditions	No condition identified (healthy mother)

**[Table/Fig-1]:** ICD-PM categories with description and example-specific causes [8].

ICD-PM: International Classification of Diseases, ICD-10 for use in Perinatal Mortality

TTTS: Twin to twin transfusion syndrome; IUD: Intrauterine death; SGA: Small for gestational age;

PROM: Premature rupture of membranes; DM: Diabetes mellitus

### Operational definitions [9]

Registered gravida: Four or more antenatal visits

Stillbirth: Birth of a baby with no signs of life

Preterm stillbirth: Stillbirth occurring before 37 weeks

Post-term stillbirth: Stillbirth occurring after 41 weeks

Antepartum stillbirth: Intrauterine foetal demise occurred before the onset of labour

Intrapartum stillbirth: Intrauterine foetal demise occurred during labour

Stillbirth Rate (SBR):  $1000 \times \frac{\text{sb}}{\text{sb}+\text{lb}}$  sb=stillbirths with >28 or more weeks, lb=live births regardless of gestational age or birth weight.

## STATISTICAL ANALYSIS

Descriptive data analyses consisted of frequency proportions and mean (standard deviation). Categorical variables were analysed using cross tabulations and Chi-square test for significance ( $p < 0.05$ ). The analysis was done using Statistical Package for the Social Sciences (SPSS), version 16.0.

## RESULTS

There were 2733 total births and 106 stillbirths during the study period. The SBR was 38.78 per 1000 births in present study. There were 73 (68.87%) antepartum and 33 (31.13%) intrapartum stillborns. A total of 95 (89.62%) women with stillbirths were in 21-35 years age group, while 11 (10.31%) women were in extremes of age, i.e., six women below 20 and five above 35 years. Mean age in present study was  $28.7 \pm 4.7$  years. A total of 92 (86.79%) babies were preterm and 14 (13.21%) were more than 37 weeks, while none of them were post-term. A total of 46 (43.40%) babies weighed less than 1 kg and 49 (46.22%) babies weighed 1-2.5 kg [Table/Fig-2].

Parameters	N	Percentage (%)
<b>Age</b>		
18-20 y	6	5.66
21-30 y	63	59.44
31-35 y	32	30.18
35 y	5	4.72
<b>Gestational age</b>		
28-37 wk	92	86.79
37-40 wk	14	13.21
<b>Baby weight</b>		
<1 kg	46	43.40
1-2.5 kg	49	46.22
2.5-3 kg	8	7.55
>3.5 kg	3	2.83

[Table/Fig-2]: Distribution of maternal age, gestational age and baby weight (N=106).

Stillbirths occurred more in rural women compared to urban women and women below poverty line had more stillbirths compared to the women above poverty line and the difference was statistically significant ( $p < 0.001$ ). All women with stillbirths gave history of attending antenatal clinics during the current pregnancy. A total of 90 (84.91%) women were referred from periphery and 16 (15.09%) women were booked with this Institution. There were 57 (53.57%) multies and 49 (46.23%) primies. Stillbirths were more in multiparas compared to primies, but the difference was not significant ( $p = 0.437$ ). A total of 67 (63.21%) babies were male and 39 (36.79%) were female babies and the difference in gender was found to be significant ( $p < 0.007$ ) [Table/Fig-3].

There were 73 (68.87%) antepartum stillbirths (category-A) and 33 (31.13%) intrapartum stillbirths (category-I). Among the foetal conditions associated with SBs in ICD-PM classification, foetal growth restriction (A-5) topped the antepartum group 29 (39.72%). In this category, there were Doppler abnormalities like absent end diastolic flow in five cases, abnormal cerebro-placental ratio in three cases, reduced diastolic flow in four cases and two cases with reversal of flow. There were 15 (20.54%) cases of infections in the antepartum category (A2). There were seven cases of congenital malformations (subcategory A1); three cases of Arnold-Chari malformations two cases with multiple anomalies, one with congenital diaphragmatic hernia and one case of Dandy-Walker syndrome. Ten (13.68%) came under A3 category (antepartum hypoxia) and no causes could be identified in another ten cases (A6) identified. Antepartum stillbirths were induced and delivered by vaginal route, unless there was a contraindication.

Characteristics	N (%)	Chi-square/df	p-value
<b>Domicile</b>			
Rural	73 (68.87)	15.094/1	<0.001**
Urban	33 (31.13)		
<b>Economic status</b>			
BPL	82 (77.36)	31.736/1	<0.001**
APL	24 (22.64)		
<b>Booking status</b>			
Referral	90 (84.91)	51.660/1	<0.001**
Booked	16 (15.09)		
<b>Parity</b>			
Multi	57 (53.77%)	0.604/1	0.437
Primi	49 (46.23%)		
<b>Gender</b>			
Male	67 (63.21)	7.396/1	0.007*
Female	39 (36.21)		

[Table/Fig-3]: Socio-demographic and foetomaternal characteristics of stillbirths.

\*\*significant at  $p < 0.001$ ; \*significant at  $p < 0.05$

BPL: Below poverty line; APL: Above poverty line

There were 33 cases of intrapartum stillbirths. In this group, also disorders related to foetal growth (I-6) was the major subcategory (N=13; 39.39%). Seven cases were associated with infection (I-4) and five cases had abruption (I-3). No causes could be attributed to seven cases of intrapartum SBs (21.22%). Among the intrapartum deaths, 30 stillbirths occurred during vaginal delivery and three cases had undergone caesarean section for abruption [Table/Fig-4].

Grade	M1	M2	M3	M4	M5	Total (%)
A1	2	0	0	0	5	7 (9.58)
A2	4	2	2	5	2	15 (20.54)
A3	1	3	0	6	0	10 (13.68)
A4	0	2	0	0	0	2 (2.73)
A5	4			21	4	29 (39.72)
A6	0	0	0	10	0	10 (13.69)
Total	11 (15)	7 (9.5)	2 (2.73)	42 (57.53)	11 (15.68)	73 (68.86)
I1	1	0	0	1	0	2 (6.06)
I2	0	0	0	0	0	0
I3	0	0	0	3	0	3 (9.09)
I4	2	1	0	1	0	7 (21.22)
I5	0	1	0	0	0	1 (3.03)
I6	3	2	0	7	1	13 (39.38)
I7	0	0	0	8	2	7 (21.22)
Total	6 (18.18)	4 (12.12)	0	20 (60.60)	3 (9.09)	33 (31.14)

[Table/Fig-4]: Cause of death as per ICD-PM classification.

A total of 42 cases (57.53%) of antepartum SBs and 20 cases (60.6%) of intrapartum SBs were in the M4 category. Hypertension and its complications were the predominant component in M4 (Maternal medical complications). Maternal condition M-1 (complications of placenta, cord and membranes) was associated with 11 cases of antepartum SBs and six cases of intrapartum cases. Among these placental abruption was the main contributor leading to eight antepartum and five intrapartum stillbirths [Table/Fig-4]. There were 28 cases of severe preeclampsia, three cases of eclampsia, four cases of non severe preeclampsia, three cases of gestational hypertension and one case of chronic hypertension. Fourteen cases of gestational diabetes were also in the M4 category and all of them had preeclampsia also [Table/Fig-5].

There were the 22 COVID-19 positive mothers and all of them had hypertensive diseases of pregnancy. Among them, 15 cases had antepartum stillbirths and seven cases had intrapartum deaths.

Maternal medical conditions	n (%)
<b>Hypertensive diseases of pregnancy</b>	39 (62.90%)
Gestational hypertension	3
Non severe preeclampsia	4
Severe preeclampsia	28
Eclampsia	3
Chronic hypertension	1
<b>Diabetes Mellitus</b>	14 (22.58)
Pregestational DM	4
Gestational DM	10
<b>Iron deficiency anaemia</b>	6 (9.68%)
<b>Hypothyroidism</b>	3 (4.84%)

**[Table/Fig-5]:** Distribution of maternal medical condition M4.

Seven mothers gave history of COVID-19 infection during pregnancy and all of them had antepartum stillbirths. They were also having hypertensive diseases of pregnancy. None of them had serious infection or required admissions in intensive care unit. All mothers with stillbirths had been vaccinated for COVID-19.

## DISCUSSION

Among the 2733 total births, 106 were stillbirths and SBR was calculated to be 38.78/1000 births. SBR in India varies from 13 to 26.48/1000 births and this wide interstate variation may be due to differences in population characteristics and the risk factors [12,13]. SBR was similar to the pre-pandemic rate as it was 38.56/1000 births in a study conducted in the same Institute for a period of two years from March 2014 to February 2016.

Many studies from different parts of the world were showing increase in SBR and finding in the present study was compared with contrast studies as shown in [Table/Fig-6] [1,6,7,14].

Author name (ref no.)	Place and year of the study	Sample size	Prevalence% of stillbirths
DeSisto CL et al., [1]	USA, March 2020-September 2021	21,653	1.26%
Chmielewska B et al., [6]	Systematic review and meta- analysis (17 countries including India) January 2020-January 2021	1,68295	OR1.28 (95%CI 1.07-1.54)
Mahajan NN et al., [7]	Mumbai, April 2020-July 2021	1,645	3.48%
Ajith S et al., [14]	North Kerala, April 2020-October 2020	350	0.89%
Present study	Central Kerala, August 2021-July 2022	2733	3.87%

**[Table/Fig-6]:** Studies reporting on the Stillbirth Rate (SBR) during COVID-19 pandemic.

The reason for high SBR in this study was due to referral even from neighbouring districts. A study by Flenady V et al., in Lancet attributed 20-30% of stillbirths to suboptimal obstetric care [15]. The quality of care in peripheral health services is usually compromised due to overcrowding and shortage of skilled health personnel and mothers are referred late to tertiary care centres [16]. Results showed more stillbirths in rural women in concurrence to a study from Bihar state by Dandona R et al., [17].

Many national programmes such as Janany Suraksha Yojanana (maternity security programme) and Pradhan Mantri Surakshit Natritva Abhiyan-a once a month fixed antenatal programme) are there to improve maternal care [18]. All women with stillbirths gave history of regular attendance in antenatal clinics giving the impression that pandemic did not disrupt the access to healthcare in Kerala.

A systematic review had shown that older mothers have increased risk for stillbirths, but majority of mothers with stillbirth in present study were in the 20-30 years group [19]. High prevalence of early

completion of family before 35 years in Indian culture can explain the higher number of births and stillbirths among this age group [20]. Analysis revealed that stillbirths were more in multigravidas (57.8%) than the primies, but the difference between primies and multies was not significant similar result was shown in a study from Hyderabad [21] But another study by Saleem S et al., reported an increased risk of stillborns in first (95% CI, RR 1.23-1.41) and after fifth pregnancy (95%CI, RR 1,24-1.53) in Indian women [22]. Male foetuses have around a 10% increased risk of stillbirths compared to female foetuses and hence the sex ratio for SBs is slightly higher than the sex ratio for live births [23]. Foetal growth restriction and prematurity are important cause stillbirths with low birth weight [19].

Low intrapartum stillbirths in the Institute reflected close monitoring during labour, protocol based care and timely interventions [24]. Intrapartum stillbirths drop by 1.6/1000 births with every percentage rise in caesarean section rates from 0-8% in low middle income countries [25]. Early detection of high-risk pregnancies and need based termination should be ensured [26]. Prompt diagnosis of hypertensive diseases in pregnancy, diabetes mellitus and early pick-up of foetal growth restriction can prevent many foetomaternal complications [19]. Antenatal care by skilled healthcare professionals and early diagnosis with prompt effective management is very important in improving the obstetric outcomes [27]. Screening during antenatal visits with allotment of cards of varied identity with appropriate precedence can be an important measure in monitoring high-risk obstetric cases, which can also prove crucial in timely referral to tertiary care centres [28].

Classification by ICD-PM differentiates SBs into antepartum and intrapartum depending on the timing of death [8]. Major proportion of cases belonged to antepartum stillbirths similar to the results in middle income countries [29]. This can be interpreted as quality of intrapartum care is improving and further improvement is possible only by increasing the quality of antenatal care [30]. Two major conditions identified were hypertensive disorder in pregnancy and foetal growth restriction. Early detection and timely intervention of high-risk cases appears very crucial for better foetomaternal outcome in such conditions [31]. Infectious diseases also come under the maternal medical complications (M4). COVID-19 positive mothers as well as mothers with history of COVID-19 infection in the past during the current pregnancy were having co-existing hypertension also. During the second wave of pandemic, preeclampsia was reported higher [7]. According to the inter COVID-19 study, which looked at nearly 2100 inter COVID-19 women in 18 countries, the SARS-CoV-2 infection predispose pregnant women to a greater risk of preeclampsia due to its pro-inflammatory effect [31]. Multiple co-existing conditions make the application of this classification a challenging one and need further modification [32]. Similar results were reported in a study from Sri Lanka [33].

## Limitation(s)

The small sample size was a limitation. Social and emotional concerns of parents limited foetal autopsy and financial constraints limited advanced tests, which prevented further exploration of conditions in the unspecified category. Future studies should focus on foetal autopsy or minimally invasive tissue sampling and cytogenetic analysis, so that further evaluation of cases is possible.

## CONCLUSION(S)

Prevalence of stillbirth in present study was found to be 3.8%, foetal deaths were more in women with hypertensive diseases in pregnancy and in foetuses with growth restriction. SBR is sensitive marker of quality of care received by pregnant women. Majority of stillbirths occurred during the antepartum period among the rural women referred from peripheral health services, suggesting the need for improved antenatal care. More awareness should be generated

among women regarding the early detection and management of medical conditions like hypertension and diabetes mellitus. Protocol-based management should be implemented in peripheral health facilities and timely referral to tertiary care centre should be ensured to reduce the SBR. Allotment of cards of varied identity of high-risk obstetric cases, may help in better monitoring and timely referral to higher centres, where better facilities are available.

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