

# Causes of Intrauterine Fetal Death during COVID-19 outbreak in a Tertiary Care Hospital in Lahore, Pakistan

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## Author's Contribution

<sup>1</sup> Conception of study

<sup>1</sup> Experimentation/Study conduction

<sup>1,2</sup> Analysis/Interpretation/Discussion

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<sup>1,2</sup> Critical Review

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## Abstract

**Objective:** To assess the frequency of IUDs and their possible causes since the Covid-19 pandemic.

**Material and Methods:**

**Study design:** Cross-sectional study

**Setting:** Department of Obstetrics and Gynaecology, Shalamar Hospital, Medical and Dental College, Lahore, Pakistan.

**Duration of study:** 15/03/2020 to 15/06/2020

This is a cross-sectional single-center study. The relevant details about IUDs like age, parity, social status, booked status, comorbidities, and social status were entered into a Performa and the data analyzed.

**Results:** The Intrauterine death rate from the study was 41.99 fetal deaths per 1000 live births (Total births: 643, IUDs: 27) while the mean age of the mothers was 29.67 with a minimum age of 22 years and a maximum of 37 years. According to the risk factors associated with the IUD, 11.1% had Pregnancy Induced hypertension, 11.1% had Pre-Eclampsia, 22.2% had Gestational Diabetes Mellitus and 22.2% Pregnancy Induced Hypertension and Gestational Diabetes Mellitus and 33.3% had no comorbidities. Amongst all the patients 33.3% of cases were unbooked.

**Conclusion:** We conclude that in the last one year the fetal deaths per 1000 at Shalamar Hospital were around 28.57 per 1000 live births, during the last 3 months they gone up to 41.99 fetal deaths per 1000 live births. The leading cause(s) for IUDs in Pregnancy during the Covid-19 were pandemic Induced Hypertension and Gestational Diabetes Mellitus, which cumulatively account for 44.4% cases but 33.3% cases had no co-morbidities and still ended up in an Intra-Uterine death, which may or may not have been influenced by a Covid-19 infection. From the looks of it, Non-clinical reasons seem to have a higher probability of increasing the IUD rate but clinical effects of the Covid-19 infection can also not be ruled out completely, further studies are required into the pathogenesis and the effect of Covid-19 on pregnancy.

**Keywords:** Intrauterine death, Intrauterine Growth retardation, Fetal death, Stillbirth, Pregnancy Induced Hypertension, Gestational Diabetes Mellitus, Covid-19, Fetal Hydrops, Amniotic Fluid Index, Placental Abruption.

## Introduction

On 12<sup>th</sup> March 2020, based on more than 20,000 confirmed cases and almost 1000 deaths in the continent of Europe, the World Health Organization announced the new coronavirus outbreak pandemic. Since then the world has been battling this disease to date in all walks of life. No one has been spared from the direct or indirect effects of this disease. The biggest challenge has been faced by doctors who have been made to handle another disease on top of pre-existing medical conditions of their respective patients. Obstetricians who have already had their hands full with dealing with two lives now need to look into this new disease as well to assess the maternal and fetal outcomes.

The purpose of this study is to see the frequency of Intrauterine deaths during the Covid-19 Pandemic. Intrauterine death has also been known as Fetal death has been a pressing issue and has always come as a challenge to obstetricians in all parts of the world. This has been a more prevalent issue in 3<sup>rd</sup> world countries like Pakistan due to the lack of resources and the sheer number of antenatal patients that the hospitals receive. In 2015 there were 2.6 million stillbirths worldwide, with more than 7178 deaths per day, developing countries were on the receiving end of the majority of these deaths, ninety-eight percent of deaths occurred in low and middle-income countries, about half of all stillbirths occur in the intrapartum period, the Estimated proportion of intrapartum stillbirths varies from 10% in developed regions to 59% in South Asia.<sup>1</sup> Worldwide, the number of stillbirths declined by 19.4% between 2000 and 2015, representing an annual rate of reduction (ARR) of 2%.<sup>1</sup> This mainly shows improvement in the healthcare facilities provided and a better understanding of fetomaternal monitoring especially those mothers with co-morbidities. There are a number of causes that can affect the fetus during the intrauterine life and can lead to fetal death, recently the world has seen a Pandemic rise exponentially and become a risk factor and a possible complicating factor in pre-existing health conditions or conditions like pregnancy. The aim of this study is mainly to look at whether or not the number of intrauterine deaths during the pandemic has gone up and how can obstetricians modify their practice to bring into account another possible risk factor (even if not fully understood) to ensure that the ante-natal period is not affected negatively.

## Materials and Methods

This cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Shalamar Hospital Lahore from 15/03/2020 to 15/06/2020. A total of 647 pregnant women having age 29-37 were selected for this study. The study was approved by the Ethical Committee and written informed consent was taken from every patient.

The details of presenting complaints, history, menstrual history, examination findings, per vaginal examination findings, mode of delivery, and fetal outcomes, and investigation reports were recorded. The records of babies born below 28 weeks of gestation, fetuses weighing below 1000 were excluded. The parity of patients, booking status, and associated comorbidities were assessed and entered in pre-designed performa along with a demographic profile of the patients.

All the collected was entered in SPSS version 20 and analyzed. Mean and SD was calculated for numerical data and frequencies and percentages were calculated for categorical data.

## Results

From Mid-March 2020 to Mid-June 2020 we have seen a total of 643 pregnant women and the outcome of 27 of those was a stillbirth and 617 were live births, making the stillbirth rate to be 41.99 per 1000 live births. Out of which 77 (11.98%) had PIH, 71 (11.04%) had Pre-Eclampsia, 161 (25.04%) had GDM, 129 (20.06%) had PIH plus GDM and 212 32.97% had no known co-morbidities. Out of these 33.32% were Primi-Gravidas and 66.74% were Multi-Gravidas. 55.62% were over the age of 30 and 44.43% were under 30. In terms of Parity Primi-Gravidas were 33.33% while Multi-Gravidas was 66.68%.

Out of all these patients, 59.7% were booked and 40.3% were unbooked. Also since Shalamar Hospital has the facility for Private/Company (Insurance) cases as well as General cases another important stat is that out of these majority of the patients 572 (88.96%) were general and 71 (11.04%) were a company or private. This is important to understand and take into consideration as it shows the socio-economic class the women belonged to:

FREQUENCIES VARIABLES=Facility Insurance Parity Disease /ORDER=ANALYSIS

**Table 1: Statistics**

	Facility	Insurance	Parity	Disease
Valid	643	643	643	643
Missing	0	0	0	0

**Table 2: Facility**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	383	59.6	59.6	59.6
Booked				
Unbooked	260	40.4	40.4	100.0
Total	643	100.0	100.0	

**Table 3: Insurance**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	572	89.0	89.0	89.0
General				
Private/Company	71	11.0	11.0	100.0
Total	643	100.0	100.0	

**Table 4: Parity**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid PRIMIGRAVIDA	264	41.1	41.1	41.1
MULTIGRAVIDA	379	58.9	58.9	100.0
Total	643	100.0	100.0	

**Table 5: Disease**

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid PIH	76	11.8	11.8	11.8
GDM	161	25.0	25.0	36.9
PRE-ECLAMPSIA	71	11.0	11.0	47.9
PIH+GDM	129	20.1	20.1	68.0
No Cormidities	206	32.0	32.0	100.0
Total	643	100.0	100.0	

## Discussion

To be able to analyze this study in the best possible way there needs to be an understanding of how frequently stillbirths had been happening in this world (especially in countries like Pakistan) before the Covid-19 Pandemic.

There are a number of factors that influence the stillbirth rate. We can classify them as clinical factors and non-clinical factors. Maternal and fetal health would fall into clinical factors while other variables like socioeconomic status, access to skilled healthcare, general awareness, etc would come under non-clinical factors. Developed countries have achieved low fetal and intrauterine mortality.<sup>5,6,7</sup> The occurrence of an intrapartum stillbirth in a developed country is considered the result of inadequate care.<sup>8</sup> Hence, whatever intrauterine deaths that occur in these countries are mostly attributed to non-preventable reasons or close calls and near misses.<sup>8</sup>

Overall the stillbirth rate of the developed world had been much less than the developing world. According to WHO Estimated stillbirths that occur intrapartum are seen as 10% in developed countries to 59% in South Asia.<sup>1</sup>

According to another study the world's largest stillbirth rates ranging from 25 to 40/1000 births were seen in South Asia and in addition, Pakistan, reported stillbirth rates from 36 per 1000 to 70 or more per 1000 in some rural areas.<sup>9-14</sup> In another study Pakistan was shown to be the country with the highest stillbirth rate (43.1 stillbirths per 1000 total births compared to a global estimate of 18.4) globally in 2015.<sup>15</sup> Intrapartum stillbirths in developing countries may represent inadequate access to essential obstetric care and inadequate care.<sup>16</sup>

So a country like Pakistan In which the stillbirth rate has been very high even before a pandemic like the Covid-19 it would not be wrong to say that any additional risk factor might be posing a threat to increase the stillbirth rate should be looked into. As discussed above the number of stillbirths in Pakistan can be attributed to lack of specialized healthcare or lack of awareness regarding certain ante-natal risk factors like PIH and GDM, two very prevalent risk factors in Pakistani society, primarily due to strong family history for both Hypertension and Diabetes.<sup>17</sup> In a nutshell stillbirths have been a pressing issue for obstetricians around the world, while the developed world has been able to curb this through better antenatal monitoring, regular follow-ups, creating awareness, etc, the developing world especially countries like Pakistan are still to tame this menace spreading like wildfire. Possible factors being, lack of facilities, limited access to specialized healthcare (although we at Shalamar hospital have tried to neutralize that variable to some extent), lack of awareness, nonchalant attitude towards diseases, and feto-maternal health by extension. Similar problems

have also been seen in our neighbouring country where Most of the population is not aware of the need for antenatal follow-up.<sup>1,17,18,19</sup>

Now let's look at how the dynamics of the world and Obstetrics have changed ever since the Pandemic has arrived. The largest case series so far on pregnancies with Covid-19 has concluded that The available data on pregnant patients with COVID-19 do not provide a clear verdict on the effect of the infection on fetomaternal health, the outcome thus far is favorable but erring on the side of caution is still advised, The number of Preterm deliveries has gone up which was mostly associated with elective interventions but despite the interventions, a trend toward spontaneous prematurity was present.<sup>20</sup>

In the last 1 year, the fetal deaths per 1000 at Shalamar Hospital were around 28.57 per 1000 live births, during the last 3 months they gone up to 41.99 fetal deaths per 1000 live births, at the same time the number of unbooked patients has also increased. Primarily due to the closure of small-unregulated private clinics and basic private health care facilities where all these people used to go before.

Looking at non-clinical reasons, unbooked patients seemed to bring uncontrolled diseases like PIH and GDM as they presented in a very later stage to the hospital, most of them having developed complications like Pre-Eclampsia, IUGR, or decreased AFI, etc. A lot of booked patients were also not able to make it to the hospital for regular ante-natal follow-ups due to the lockdown being imposed which served as a catalyst in deteriorating their condition by contributing to their risk factors like PIH and GDM not being monitored and treated promptly. Secondly because of the lockdown and the overall panic that was created lack of ante-natal follow-ups made regular ultrasound scans and general fetal monitoring difficult. This may have led to fetal health problems which could have been diagnosed earlier to be ignored.

Speaking of clinical reasons, although no strong evidence has been identified in terms of Covid-19 directly affecting fetomaternal health or evidence of vertical transmission (in the largest case series), previous experiences with similar viruses like SARS AND MERS<sup>21</sup> warns that vertical transmission should not be kept as the only reason to attribute with fetal morbidity and mortality.

There has been evidence seen in a study conducted on the placenta of mothers with the infection which showed signs of maternal vascular malperfusion on the placenta<sup>22</sup> which may imply adverse outcomes like

Pre-mature birth, fetal growth restriction, pre-eclampsia, and the topic of our discussion Stillbirth. This in addition to any pre-existing maternal conditions (PIH, GDM) can have serious implications on fetal life. In our study, we saw 23.58% of cases undergo placental abruption with no pre-existing maternal conditions. Evidence of placental abnormalities associated with maternal vascular malperfusion in the absence of any other risk factors like Hypertension has also been seen.<sup>23</sup> This makes sense since a lot of patients having Covid-19 infection have been seen to develop DIC.<sup>24</sup>

According to RCOG,<sup>25</sup> a recent report from a UK study showed that so far all pregnant women who are affected adversely are after 28 weeks, which emphasizes the point that women need to be more careful during their third trimester since their health can get worse if they contract the virus during this time leading to premature delivery. RCOG guidelines encourage pregnant mothers to maintain social distancing, take extra care of their health avoid public gatherings and avoid going into crowding places. Another very important message they have given is regarding breastfeeding which says that there has been no significant evidence regarding the spread of the virus from breastmilk and they feel that the benefits of breastmilk outweigh the possible risks (which are not yet fully understood).

## Conclusion

In our study, we have seen that the fetal death rate has gone up as compared to the last year from 28.57 to 41.99 per 1000 live births. The major factors contributing to the fetal demise being PIH and GDM. The majority of the increase can be linked to non-clinical factors like the increase in unbooked patients who came for their booking visit very late in their pregnancy, the majority of them having uncontrolled PIH and GDM due to lack of specialised ante-natal care and lack of follow-ups. The lack of follow-ups of booked patients was due to the lockdown and a hindrance to the commute of the patients. The general lack of responsibility towards health in a country is always a factor as well. In terms of clinical reasons, given that our study also showed placental abnormalities in 23.58% it can be said that maternal vascular malperfusion can also be a cause and if that is present in a mother already suffering from conditions like PIH and GDM can be detrimental for the fetus.

The non-clinical factors like lack of access to healthcare and lack of follow-ups can be improved and we feel

that if these variables can be controlled by creating awareness and encouraging people to have regular follow-ups even over the phone can make a huge difference in making the outcome of the pregnancy favorable. As far as the clinical reasons are concerned further research is required in terms of the pathogenesis and maybe if there is sufficient evidence on uteroplacental insufficiency due to the coagulopathy associated with this disease it can be treated along the lines of uteroplacental insufficiency like in hypertensive patients.

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