

International Journal of Medical Science and Current Research (IJMSCR) Available online at: www.ijmscr.com Volume3, Issue 6, Page No: 512-516 November-December 2020



## **Evaluation of Diabetes as a Risk Factor for Stillbirth**

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Type of Publication: Original Research Paper Conflicts of Interest: Nil

#### ABSTRACT

**Background**: Antepartum stillbirth is a major contributor to perinatal mortality. There are many risk factors which may be socioeconomic, cultural or biological. With changing lifestyle, various diseases like diabetes and hypertension are on the increase. The objective of the study was to evaluate maternal diabetes as a risk factor for antepartum stillbirth.

**Methods:** The study was conducted over a period of six months in the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur. Women with documented singleton pregnancy more than 28 weeks were selected from those admitted in labour room for delivery. Forty antepartum stillbirths and eighty live births were included. Intrapartum stillbirth and pregnancies with either hypertensive disease of pregnancy or other medical diseases were excluded. Data collected was analyzed.

**Results:** Stillbirth rate was 86.5 per 1000 births.7.5% women were diabetic. Among women with antepartum stillbirth, 5% had pre-existing diabetes and gestational diabetes developed in 10%. The difference in the diabetes status of women with still birth and those with live birth was statistically significant (p=0.026).Odds ratio 11.286 (1.271 to 100.202).

**Conclusion:** Diabetic women were at high risk for stillbirth. Hence, women should be screened and diabetic women should have increased antenatal surveillance.

# Keywords: Antepartum Stillbirth, Diabetes mellitus, Gestational Diabetes, Glycosylated Haemoglobin INTRODUCTION

Stillbirth is an important indicator of the health status of a population. Globally 2.65 million stillbirth occur every year[1].The stillbirth rate for India is 4 per 1000 birth and 6 per 1000 birth for Rajasthan in 2015[2].For international comparison, the World Health Organization defines stillbirth as a baby born with no signs of life at or after 28 weeks gestation or if weight is more than 1000 gm if period of gestation is not available[3].Stillbirth may be antepartum (death before the onset of labour) or intrapartum (death after onset of labour).More than half of the stillbirths occur during the antepartum period (International Classification of Diseases-ICD 10 code- P 95) [3]. Across the world, there is a rising

trend among women towards delaying pregnancy and child birth.This trend is observed universally, irrespective of the race and economic status[4].Also, lack of physical activity leads to chances of obesity and diabetes which also increase the risk of antepartum stillbirth. Gestational diabetes mellitus, defined as diabetes mellitus associated with pregnancy, is present in about 2-5% of pregnancies in the United States. Due to current screening guidelines, it is generally not diagnosed until after 24 weeks of gestation[5].

#### **OBJECTIVE**

International Journal of Medical Science and Current Research | November-December 2020 | Vol 3 | Issue 6

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The objective of this study was to evaluate maternal diabetes as a risk of antepartum stillbirth and maternal morbidity associated with it.

#### METHODOLOGY

This was a prospective observational study done over a period of six months in a tertiary care centre. Women with documented singleton pregnancy more than 28 weeks were selected from those admitted in labour room for delivery. Forty antepartum stillbirths and eighty live births (one born before and one after each stillbirth) were included for evaluation of diabetes as a risk factor for stillbirth. Sample size was calculated based on the study of KC et al[1]. Intrapartum stillbirth and pregnancies with either hypertensive disease of pregnancy or other medical diseases were excluded. Informed consent was obtained from each patient included in the study. Data collected was analysed.

#### RESULTS

A total of 1375 delivery, 854 live births and 119 antepartum stillbirths occurred in the institute during the study period, giving a stillbirth rate of 86.5 per 1000 births. Four hundred and two deliveries were excluded due to anaemia, chronic hypertension or hypertensive disease of pregnancy, thyroid disease, heart disease or intrapartum stillbirths.The mean age was 22.3 years.

In the study, 7.5 % women were diabetic.The difference in the diabetes status of women with still birth and those with live birth was found to be statistically significant(p=0.026).Odds ratio 11.286 (1.271 to 100.202)Table 1

Among women with antepartum stillbirth, 5% had pre existing diabetes and gestational diabetes developed in 10%.These women were diagnosed as diabetics in the last month or on admission at the time of delivery. Comparing to this, 3.75% women with live birth were diabetic but their sugar levels were controlled either by medical nutritional therapy or were on insulin therapy. Table 2.

Four women with antepartum stillbirth had Glycosylated Haemoglobin (HbA1c) > 6.5.These women had not attended any antenatal clinic and were diagnosed as diabetes at the time of admission.Table 3.

Postpartum morbidity was more in diabetic women with uncontrolled sugar levels. They had poorer wound healing and their average hospital stay was also longer.

However, due to lack of followup, long term follow up could not be done to comment about the late postpartum complications and future pregnancy outcome of these women.

#### DISCUSSION

Our stillbirth rate was high, 86.5 per 1000 births as compared to other studies (17 per 1000 births) [6] as it is a tertiary care referral centre. Proportion of stillbirth was found more in diabetes women, p =0.026. As compared to non diabetic women, there was higher risk of antepartum stillbirth in women with pre existing diabetic (odds ratio=4.53[0.4 – 51.67]) and gestational diabetic (odds ratio=4.53 [0.79-25.93]). A study by Hutcheon et al, in which national data on GDM and stillbirth was recategorized and then reanalyzed, the risk for stillbirth among women with GDM was significant.[7]

Women who have uncontrolled diabetes (pre gestational diabetes) in first trimester are more prone to congenital anomalies, mainly cardiovascular and neural tube defects.[8,9] Gestational diabetes manifests in the second half of pregnancy so it is not associated with any anomalies. A study by Tennant et al ,compared the risk of stillbirth for gravidas with pregestational diabetes with and without a congenitally anomalous fetus and found a 4.5 fold stillbirth risk even in the absence of fetal malformation.[10]

Diabetes is also associated with polyhydramnios, macrosomia and placental insufficiency. Preeclampsia also occurs in around 10 % women with diabetes[11]. Intrauterine growth retardation occurs in long uncontrolled diabetes with vasculopathy. All these complications lead to poor fetal outcome. Similar to our study, studies from different parts of world [12,13] also show that gestational diabetes is an independent risk factor for stillbirth .

Efforts are required to better understand the biological mechanisms associated with stillbirth risk. One hypothesis postulated is that there is failure of the uterine vasculature and placental aging in older women to adapt sufficiently to the increased

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hemodynamic demands of pregnancy and this was responsible for the stillbirth.

Diabetes remained an independent risk factor for stillbirth, even after accounting for medical conditions that are more likely to occur in them, such as hypertension, abortion and abruptio placenta, all of which are associated with higher rates of stillbirth. Recommendations to attempt strict glycaemic control among antepartum women that include those with gestational diabetes mellitus are reasonable [14]

#### CONCLUSION

Diabetic women are at highest risk of antepartum stillbirth and increased morbidity due to puerperal sepsis, poor wound healing and longer hospital stay as compared to women with live birth. Women with diabetes should be kept under increased antenatal surveillance to prevent antepartum stillbirth. These visits would provide an opportunity to timely detect and manage the specific complications and to establish a future care plan.

#### **CONFLICTS OF INTEREST-**Nil

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Glycaemic state	Total		Antepartum Stillbirth (N=40)		Live Birth (N=80)		Odds ratio
	No.	%	No.	%	No.	%	
Diabetes	9	7.5	6	15	3	3.7	11.286
							(1.271 to 100.202)
Euglycaemic	111	92.5	34	85	77	96.3	1

 Table 1: Diabetes as a variable of risk of antepartum stillbirth

Chi-square = 4.934 with 1 degree of freedom; P = 0.026 (Significant)

 Table 2: Type of Diabetes as a variable of risk of antepartum stillbirth

Glycaemic state	Antepartum		Live Birth		Odds ratio
	Still	birth	(N	=80)	
	(N=40)				
	No.	%	No.	%	
Pre-existing DM	2	5	1	1.3	4.53 (0.4 -51.67)
Gestational DM	4	10	2	2.5	4.53 (0.79-25.93)
Euglycaemic	34	85	77	96.3	1

Chi-square = 4.865 with 2 degrees of freedom; P = 0.088 (Not Significant)

<b>Table 3.Correlation</b>	of stillbirths v	with Glycosylated	Haemoglobin Levels

HbA1c Level	Total		Antepartum Stillbirth (N=40)		Live Birth (N=80)	
	No.	%	No.	%	No.	%
< 6.5	115	95.8	36	90	79	98.75
6.5-8.0	4	3.33	3	7.5	1	1.25
>8.0	1	0.83	1	2.5	-	-

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 $\dot{P}_{age}515$ 

#### Post partum Antepartum Live Birth Non Diabetic condition n=111 Stillbirth (N=3) (N=6) Puerperal sepsis 3 1 1 4 PPH 2 1 Poor wound 4 1 5 healing Average hospital 7.4 3.5 4.2 stay (in days)

### **Table 4: Maternal Morbidity in Diabetic Women**