



STUDY OF ETIOLOGICAL FACTOR RESPONSIBLE FOR STILLBIRTH AND IUFD

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ABSTRACT

Aims & objective : Intrauterine fetal death (IUFD) and still birth is a major tragic event for the parents and a great cause of stress for the doctor. Present study was conducted to understand the prevalence and etiological factors of stillbirths and to study the complications, and finally suggest some remedies to minimize the incidence.

Methodology: Retrospective record based multivariable analytical study was done in Department of Obstetrics and Gynaecology of PCMS and RC Bhopal from 1 July 2015 to 31 August 2017. Ante partum and intra partum events leading to fetal demise were recorded, socio-demographic and clinical characters were noted. Cases of stillbirth were identified from a computerized hospital database, and pathological, clinical, and biochemical data were reviewed for all cases. Trends were analyzed using the Cusick test for trend. Categorical data were analyzed using the Fisher's exact test, with the 5% level considered significant.

Results: The incidence of intrauterine fetal demise at term was 1.8 per 1000 at-risk pregnancies. Stillbirths were unexplained in 51% of cases, although in many cases a possible etiological factor was identified but not necessarily proven. Almost 50% of term stillbirths occurred in women who registered late or had no antenatal care

Conclusion: Despite advances in diagnostic and therapeutic modalities the rate of still birth is unacceptably high. Socio-cultural background, poverty, illiteracy, lack of adequate antenatal care and inaccessible health care are some of the reasons that predispose women to IUFD and stillbirth. Majority of fetal wastage can be prevented with universal and improved antenatal care. It is imperative that a complete diagnostic work-up is performed in cases of term stillbirth, to minimize the incidence of unexplained stillbirth.

KEYWORDS : Intrauterine fetal death, stillbirth, incidence, epidemiology.**INTRODUCTION:-**

A stillbirth is a baby born with no signs of life at or after 28 weeks' gestation. IUFD is a preventable cause provided we know the etiological factor responsible for this condition. There is a marked chance of recurrent IUFD in next pregnancy which is preventable. There are different conditions in labour and pregnancy which are responsible for fresh stillbirth. So present study is planned to explore the etiological factor for IUFD in hospital based population in PCMS & RC BHOPAL.

Although three million stillbirths occur annually worldwide, almost as high as postnatal deaths, they have not been addressed as much. The developing countries in Asia and sub-Saharan Africa together constitute 70% of the world's stillbirth burden. Lack of prenatal care, inaccessible or limited health care facility is the major factor responsible for high perinatal deaths in these regions. Many times these mortalities are due to preventable causes. Multitudes of factors are recognized as the causes of IUFD and stillbirth. Despite the method of categorizing the causative factors, majority of the intrauterine deaths remain unexplained. Classifying fetal deaths helps in identifying the probable etiology and the series of events that eventually led to fetal demise. It also helps in formulating prevention policies and protocols. Identification of cause of IUFD will be helpful in counseling and consoling the grieving parents. Bereavement counseling in the event of death of a viable child is the most difficult job for the obstetrician. Parents need to have closure with the tragedy and allay their fear regarding future pregnancies.

METHODOLOGY

In the present study incidence of total delivery were 1870 out of which IUFD occur in 81. Incidence rate of IUFD is 63 per 1000 deliveries. Patients who were attending antenatal clinic and were admitted in obstetric unit of Department of Obstetrics and Gynaecology in Peoples Hospital, Bhopal. They were investigated for 2 years from 1 July 2015 to 31 August 2017.

On admission, history of the patients was taken regarding her age, address and occupation, Menstrual history and detailed obstetrical history was taken regarding gravidity, parity, abortion, history of

D&C, following abortion and number of living term and preterm issues. Any history of neonatal jaundice in previous children and if present type of treatment if required and outcome of such a neonate : number of stillbirths and at gestation age at which last delivery occurred, and history of hydrops foetalis in previous pregnancies. Inquiry is made regarding any history of bleeding per vaginum the present pregnancy which included threatened abortion and APH. Any history of blood transfusion was taken into consideration.

A total of 81 cases of IUFD and stillbirths in 1870 deliveries over a period of two years were studied retrospectively, in the department of obstetrics and gynecology of a tertiary care hospital in Bhopal, India. Diagnosed cases of pregnancies with IUFD and stillbirths were included. Criteria for diagnosis were absent fetal heart sounds and an ultrasonographic confirmation. Ante partum and intra partum events leading to fetal demise were noted. Data collected to note the following parameters. Socio-demographic factors: Women's age, religion, parity, education level, socio-economic status, level of antenatal care, immunization, and Iron and calcium intake noted.

Clinical parameters: Gestational age at the time of diagnosis, obstetric history, past and present medical history, history of pregnancy related and aggravated conditions noted. Complete investigations like hemoglobin levels, blood group, urine examination, HIV, HbsAg, VDRL, blood sugar, Thyroid profile, LFT, KFT was noted. Special investigations were done relevant to the case. Recorded data analyzed to identify probable cause of IUFD. Rh antibody titre of the patients was done at first visit and were repeated accordingly at 28 weeks and 32 weeks. Patients whose husbands were Rh positive and negative antibody titre were offered antepartum RhIG immunoprophylaxis.

Ultrasonography was done to know the gestational age, foetal wellbeing, amount of liquor, placental grading, maturation and to rule out any congenital malformations. The USG was repeated at regular intervals as per the patient. The labor was monitored carefully and the mode of delivery and the outcome of labor was studied in detail. Inj. methergin was not given after delivery and the

placenta was examined for hyperplacentosis. Cold blood was collected and was sent for ABO/Rh typing, Hb% serum bilirubin (total, direct and indirect) and direct Coomb's test to know the neonatal status. Baby was thoroughly examined for any obvious congenital anomaly and weight, sex and condition was noted particularly for hydrops foetalis. If neonate was Rh positive then the mother was given postpartum immunoprophylaxis within 24 hours of delivery.

OBSERVATION TABLES

TABLE -1: DEMOGRAPHIC PARAMETERS

Age group (years)	Number %	Parity	Number %	G.A. (in weeks)	Number (%)
16-20	5 (4.76)	G1	47(44.76)	24-30	29(27.62)
21-25	48(45.71)	G2	23(21.90)	31-45	35(33.33)
26-30	38(36.19)	G3	16(15.24)	36.40	29(27.62)
31-35	13(12.38)	G4	14(13.33)	40+	12(11.43)
40-	1(0.95)	G5	5(4.76)		

TABLE -2: KEY CLINICAL RISK FACTORS

Key factor	Sub factor	Number (%)	Additional risk in maternal	Additional risk in fetal	Additional risk in Placental
Maternal	1 PIH and complication	30(28.75)	3	0	10
	2 Severe anemia	16(15.24)	1	0	5
	3 Medical disorder	6(5.71)	1	0	0
	4 Infection	8(7.62)	0	1	0
	5 Labor Complications	4(3.81)	1	0	0
Fetal	1 Congenital anomalies	11(10.48)	0	0	0
	2 Rh isoimmunization	1(0.95)	0	0	0
	3 Non Immune hydrops	2(1.90)	0	0	0
	4 Multiple pregnancy	2(1.90)	1	0	1
	5 PROM	3(2.86)	0	0	0
Placental	1 Placental previa	4(3.81)	3	0	0
	2 Accidental hemorrhage	11(10.48)	7	0	0
	3 IUGR	8(7.62)	5	1	0
	4 Cord accidents	2(1.90)	0	0	0
	5 Postdatism	4(3.81)	0	0	0

In many cases there were more than one risk factor

TABLE 3: ETIOLOGICAL FACTORS OF STILL BIRTH

S. No	CAUSES	SERIES
1	ABRUPTION PLACENTAE	10
2	GDM	6
3	RH NEGATIVE	5
4	PROM	5
5	PLACENTA PREVIA	4

TABLE 4: SIDE EFFECTS AND COMPLICATIONS

S. No	RETAINED PLACENTA	12	2.4	2
1	PSYCHOTIC DISORDER	18	4.4	2
2	DIC	14	1.8	3
3	HELLP SYNDROME	9	2.8	5
4	BREAST ENGORGEMENT	7		

Statistical analysis:

Data was analyzed using SPSS 20 statistical package. A descriptive analysis was done on all variables to obtain a frequency distribution.

The mean ± SD and ranges were calculated for quantitative variables. Continuous variables were compared by the Student t test. Proportions were analyzed with the chi-square test. A P value of 0.05 or less was considered statistically significant

DISCUSSION

Death of a viable fetus is a distress to the family and the obstetrician. Despite advances in medical science, diagnostic and therapeutic modalities, pregnancy wastage still occurs, at an unacceptably high rate. Although the perinatal mortality has reduced over last few decades the fetal deaths still remain high. Our facility is tertiary referral centre and many women are referred for further management after IUFD has already been diagnosed. Rate of stillbirths vary greatly in different studies and regions.

There is a need for retrospection and introspection to figure out probable causes of fetal deaths and devise strategies to reduce the burden. Although chromosomal abnormalities and congenital malformations are unavoidable, routine screening and selective termination of pregnancies would reduce these deaths. Other causes of fetal demise like PIH, Diabetes, IUGR, placental abruption, maternal infection, post-datism, Rh isoimmunization are preventable causes of IUFD. Proper antenatal care, recognition of risk factors appropriate management, judiciously timed delivery, intra partum monitoring and timely intervention has reduced the incidence deaths resulting from these factors. [1]

It is a well established fact that adequate prenatal care is associated with better pregnancy outcome. However implementation of universal prenatal care is dependent on lot of factors like availability of health care facilities, skilled personnel, infrastructure and transport. Government of Uttarakhand with the help of USAID has adapted Health and Population Policy to upgrade health care in the area since 2002. The policy specified certain goals to achieve by year 2010. Achieving fertility rate of 2.1 children per woman, increasing contraceptive use, reduce maternal and infant mortality, implementing antenatal care and promoting institutional deliveries were few of the goals. Since inception of the policy prenatal care increased from 20 % to 45% and institutional deliveries increased from 21 % to 36 % from year 1989 to 2006. Despite these efforts a lot more needs to be done to bring down IUFD rate to a minimum acceptable figure.

Walsh CA, Vallerie AM et al studied the etiology of stillbirth at term. This was a 10-year cohort study. The objective was to examine etiological factors contributing to cases of intrauterine fetal demise in term pregnancies. Cases of stillbirth were identified from a computerized hospital database, and pathological, clinical, and biochemical data were reviewed for all cases. Trends were analyzed using the Cusick test for trend. Categorical data were analyzed using the Fisher's exact test, with the 5% level considered significant. The incidence of intrauterine fetal demise at term was 1.8 per 1000 at-risk pregnancies. Almost 50% of term stillbirths occurred in women who registered late or had no antenatal care. However, suboptimal antenatal care was not predictive of differences in either acceptance of perinatal postmortem or successful identification of stillbirth etiology. The incidence of stillbirth at term is 2 per 1000 term pregnancies and has not changed significantly in the past 10 years. Almost 50% of term stillbirths occurred in women with suboptimal antenatal care. More than half of cases are unexplained, often resulting from an incomplete diagnostic work-up. Despite this, there has been a significant downward trend in the rates of unexplained stillbirth at term. It is imperative that a complete diagnostic work-up is performed in cases of term stillbirth, to minimize the incidence of unexplained stillbirth. [2]

In a very similar study as ours, Choudhary A, Gupta V et al worked on epidemiology of intrauterine fetal deaths, this was a study in tertiary referral centre in Uttarakhand. Over the years the causative factors responsible for IUFD have changed. There was an observation that not only the incidence of stillbirth reducing in developed countries, but the pattern of etiologies are also changing

.Some causes incriminated in fetal wastage like syphilis, Rh isoimmunization thirty years ago, are no longer significant . Since the introduction of Rh immune prophylaxis, still births resulting from Rh isoimmunization have largely been reduced, accounting for less than 1%. Still births occurring during labor as a result of fetal hypoxia, are lesser due to electronic fetal monitoring However newer entities like thrombophillias, intrahepatic cholestasis of pregnancy have only recently been recognized as significant contributor to prenatal mortality. Despite extensive research and treatment modalities available many of the stillbirths remain unexplained. The percentage of unexplained fetal demise has stayed constant over the years. The authors concluded that socio-cultural background, poverty, illiteracy, unawareness and inaccessible health care are some of the reasons that predispose women to IUFD and stillbirth. Majority of fetal wastage can be prevented with health education, universal and improved antenatal care.[3]

Goldenberg RL, Thompson C. et al in their study determined the relationship between various types of perinatal infections and stillbirths. Infection may cause stillbirth by a number of mechanisms, including direct infection, placental damage, and severe maternal illness. A large variety of organisms have been associated with stillbirth, including many bacteria, viruses, and protozoa. In developed countries, between 10% and 25% of stillbirths may be caused by an infection, whereas in developing countries, which often have much higher stillbirth rates, the contribution of infection is much greater. Ascending bacterial infection, both before and after membrane rupture, with organisms such as *Escherichia coli*, group B streptococci, and *Ureaplasma urealyticum* is usually the most common infectious cause of stillbirth. However, in areas where syphilis is very prevalent, up to half of all stillbirths may be caused by this infection alone. Malaria may be an important cause of stillbirth in women infected for the first time in pregnancy. Because infection-related stillbirth is relatively rare in developed countries, and those that do occur are caused by a wide variety of organisms, reducing this etiologic component of stillbirth much further will be difficult. However, in certain developing countries, the stillbirth rate is so high and the infection-related component so great that achieving a substantial reduction in stillbirth should be possible simply by reducing maternal infections.[4]

Ohana O, Holcberg G et al in a similar study worked on risk factors for intrauterine fetal death . *Objective. Was to determine risk factors for intrauterine fetal death (IUFD).* This was a retrospective population-based study, of all singleton deliveries between the years 1988–2009 was conducted. Intrapartum deaths, postpartum death, and multiple gestations were excluded. A multiple logistic regression model was used to determine independent risk factors. Several independent risk factors were identified, suggesting a possible cause of death. Other pathologic conditions that facilitate tighter pregnancy surveillance and active management were found protective, pointing the benefit of such management approaches in high-risk pregnancies.[4]

In the present investigation by Khashoggi TY on the epidemiological factors responsible for intrauterine fetal deaths after 26 week of gestation were studied. A retrospective study of 16882 pregnancies registered and managed in the Department of Obstetrics and Gynecology. One hundred and three cases of intrauterine fetal deaths were registered and treated expectantly out of 16882 total pregnancies registered during the four year study period. The stillbirth rate was 6.1 per 1000 total births. Antepartum fetal deaths were 87 (84.5%) while intrapartum fetal deaths were 16 (15.5%). The Saudi population accounted for 80 (77.6%), Asians 14 (13.6%) and Africans 9 (8.7%) cases of intrauterine fetal death. Most of the patients (80%) were being followed in the hospital for antenatal care, while 14% presented as un-booked emergencies and 6% were referred from other hospitals. The incidence of stillbirth in the Kingdom of Saudi Arabia is comparable to developed countries. The purpose of counting perinatal mortality is

to understand etiological factors and the ways of avoiding recurrence.[5]

To estimate incidence and risk factors for intrauterine fetal death (IUFD) in a Norwegian study-population ,Helgadóttir LB, Skjeldestad FE et al took a case-control study applying two different control groups. 377 women with IUFD. Controls: 1) all women delivering at the study-hospitals in the period (facility-based), and 2) 1 215 women with live births at one study-hospital in the period (selected). Data were analyzed using chi-squared test and logistic regression .The incidence was 4.1/1 000 deliveries. Small-for-gestational age (SGA) and placental abruption were the strongest risk factors for IUFD. Hypertensive disorders were of low risk if not associated with SGA. Low to moderate risk factors were pre-pregnancy diabetes mellitus, thyroid disease, placenta previa, gestational diabetes, smoking and twin pregnancy. Advanced maternal age was significant when compared with facility-based controls. Risk estimates pointed in the same direction independent of control-group. *The authors concluded that SGA has a strong association with IUFD, and the risk of hypertensive disorders is mediated through SGA.* The other risk factors, except placental abruption, are of low prevalence and of limited importance in the prevention of a relatively low incidence, although dramatic, event like IUFD.[6]

McClure EM, Goldenberg RL et al studied relation of infection and stillbirth. Infection may cause stillbirth by several mechanisms, including direct infection, placental damage, and severe maternal illness. Various organisms have been associated with stillbirth, including many bacteria, viruses, and protozoa. In developed countries, between 10% and 25% of stillbirths may be caused by an infection, whereas in developing countries, which have much higher stillbirth rates, the contribution of infection is much greater. In developed countries, ascending bacterial infection, both before and after membrane rupture, with organisms such as *Escherichia coli*, group B streptococci, and *Ureaplasma urealyticum* is usually the most common infectious cause of stillbirth. However, in areas where syphilis is prevalent, up to half of all stillbirths may be caused by this infection alone. Malaria may be an important cause of stillbirth in women infected for the first time in pregnancy. The two most important viral causes of stillbirth are parvovirus and Coxsackie virus, although a number of other viral infections appear to be causal. *Toxoplasma gondii*, *Listeria monocytogenes*, and the organisms that cause leptospirosis, Q fever, and Lyme disease have all been implicated as etiologic for stillbirth. In certain developing countries, the stillbirth rate is high and the infection-related component so great that achieving a substantial reduction in stillbirth should be possible by reducing maternal infections. However, because infection-related stillbirth is uncommon in developed countries, and because those that do occur are caused by a wide variety of organisms, reducing this etiologic component of stillbirth much further will be difficult.[7]

Helgadóttir LB, Turowski G et al did a case-control study for classification of stillbirths and risk factors by cause of death. In their study ,socio-demographic, clinical and thrombophilic risk factors for stillbirths were assessed by cause of death in univariate and multivariable logistic regression analyses. Stillbirths were classified according to CODAC based on information from medical records and validated placenta histology. Causes of stillbirths in percentages, prevalence, odds ratios and adjusted odds ratios for potential risk factors. Approximately half of the women (n = 190) had placental and 19.4% (n = 73) unknown cause of stillbirth. Placental-associated conditions were registered in 18% (n = 68) of cases with a non-placental or an unknown cause. Smoking and small-for-gestational age were more prevalent in all causal groups, compared with controls, whereas twin pregnancy, hypertension and diabetes were more prevalent only among women with placental and unknown causes of stillbirth. Two-thirds of all stillbirths (68%) were caused by or associated with placental pathology. Risk factors differed somewhat according to cause, apart from smoking and small-for-gestational age, which were significant risk factors across the causal groups.[8]

In a study done by Fretts RC and American Kirkley-Best E, Kellner KR et al on etiology and prevention of stillbirth. Both studies were a systematic review of the literature on the causes of stillbirth and clinical opinion regarding strategies for its prevention. Both studies reviewed the causes of stillbirth by performing a Medline search limited to articles in English published in core clinical journals from January 1, 1995, to January 1, 2005. Fifteen risk factors for stillbirths were identified and the prevalence of these conditions and associated risks are presented. The most prevalent risk factors for stillbirth are prepregnancy obesity, socioeconomic factors, and advanced maternal age. Biologic markers associated with increased stillbirth risk are also reviewed, and strategies for its prevention identified. Identification of risk factors for stillbirth assists the clinician in performing a risk assessment for each patient. Unexplained stillbirths and stillbirths related to growth restriction are the 2 categories of death that contribute the most to late fetal losses. Late pregnancy is associated with an increasing risk of stillbirth, and clinicians should have a low threshold to evaluate fetal growth. The value of antepartum testing is related to the underlying risk of stillbirth and, although the strategy of antepartum testing in patients with increased risk will decrease the risk of late fetal loss, it is of necessity associated with higher intervention rates.[9,10]

Duke CW, Correa A et al did a study on challenges and priorities for surveillance of stillbirths. They did this by studying a report on two workshops. Both workshops explored the challenges of conducting surveillance of stillbirths. Workshop participants considered an approach that added the surveillance of stillbirths, those with and without birth defects, as part of existing population-based birth defects surveillance programs in Iowa and Atlanta. The workshops addressed three key aspects for expanding birth defects programs to conduct active, population-based surveillance on stillbirths: (1) case identification and ascertainment, (2) data collection, and (3) data use and project evaluation. Participants included experts in pediatrics, obstetrics, epidemiology, maternal-fetal medicine, perinatology and pediatric pathology, midwifery, as well as practicing clinicians and pathologists. This helped in expanding existing birth defects surveillance programs to include information of stillbirths could potentially enhance the data available on fetal death reports and also could benefit such programs by improving the ascertainment of birth defects.[11]

CONCLUSION

Nothing is as sad and depressing as intrauterine death of a fetus for both parents and the obstetrician. Congenital fetal malformations and anuploidies are unavoidable but IUFD due to these causes can be prevented by routine prenatal screening. Hypertensive disorders, Diabetes ante partum hemorrhage, IUGR, maternal infections are the common factors causing fetal demise which are preventable. Despite advances in diagnostic and therapeutic modalities a large number of fetal deaths remain unexplained, even with proper antenatal care. Socio-cultural background, poverty, illiteracy, unawareness and inaccessible health care are some of the reasons that predispose women to IUFD and stillbirth. Majority of fetal wastage can be prevented with health education, universal and improved antenatal care.

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