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Intrauterine Fetal Death: A Study of Its Epidemiology, Causes & Methods of Termination

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ABSTRACT:
Background:
Fetal death is a tragedy that causes severe distress to parents and medical professionals. Some unfortunate events occur in utero leading to such an outcome. Present study was conducted to understand the incidence, epidemiological and etiological factors of intrauterine fetal death and to study the effects of various methods of termination of pregnancy, especially – Misoprostol & Dinoprostone.
Methods: Misoprostol & Dinoprostone were used to terminate such pregnancies with intrauterine death in the Department of Obstetrics &Gynaecology, NHL Medical college & the associated SVP Hospital (formerly VS General Hospital), Ahmedabad, Gujarat.
Pregnancies diagnosed with IUFD were studied from May 2018 to January 2020. A total of 100 cases were studied. Events occurring during the antenatal period leading to intrauterine death, sociodemographic conditions and clinical features were taken into account. Different inducing agents & their induction to delivery time were considered.
Results: Incidence of IUFD at our centre was found to be 50 per 1000 deliveries. The incidence was high in low socioeconomic strata, unbooked cases, primigravidas & placental abruption necessitating preterm delivery were the leading causes. Misoprostol was found to be more effective in termination of pregnancy in these cases .The induction delivery interval with Misoprostol was 9.88 hrs and that of dinoprostone was 12.80 hrs.

Conclusions: Socio-economic factors factors like poor socioeconomic class leading to malnutrition, teenage pregnancy, lack of reproductive health knowledge need to be taken into consideration as predisposing factor for intrauterine deaths. Many preventable causes of IUDs like abruption due to hypertensive disorders of pregnancy can be avoided with routine antenatal care. Misoprostol is less expensive and has a less induction to delivery interval than Dinoprostone; it can be safely used in cases of IUFD.

Keywords: Intrauterine fetal death, IUFD, Dinoprostone, Misoprostol

I. INTRODUCTION

The absolute objective of obstetrics is that every pregnancy that is wanted to the couple results in a healthy mother & a healthy baby, with minimal complications. Pregnancy loss is a dreadful problem for both the couple & the obstetrician.

The loss of a fetus at any stage is a fetal demise. According to the 2003 revision of the Procedures for Coding Cause of Fetal Death Under ICD-10, the National Center for Health Statistics defines fetal death as "death prior to the complete expulsion or extraction from its mother of a product of human conception, irrespective of the duration of pregnancy and which is not an induced termination of pregnancy.[1] The gestational age at which intrauterine fetal demise is considered a still birth varies from county to country, depending on the availability of obstetric & neonatal care. Some countries consider fetal death at 16 weeks as IUFD while others consider fetal demise as late as 28 weeks as IUFD. In a recent RCPI (Recent clinical practice

investigation guideline), stillbirth is taken as a baby delivered without signs of life from 24 weeks gestation and IUFD is taken to refer to death in utero after 24 weeks gestation.[2] ACOG refers to IUFD as the demise occurring at or later than 20 weeks.[3]

In 2009, the estimated global number of stillbirths was 2.64 million (uncertainty range, 2.14-3.82 million).[4] The worldwide stillbirth rate declined by 14.5% from 22.1 stillbirths per 1000 births in 1995 to 18.9 stillbirths per 1000 births in 2009. Range of incidence varies in different countries, ranging from 5 in 1000 births in high income countries and 36 in 1000 births in developing countries. The still birth rates in India is 9 per thousand births, (9:1000 births in rural India and 8 in 1000 births urban India), according to the Indian census of 2006.5 According to census 2010 the estimate of still birth rate for the year 2010, at the National level is 7 per 1000.

Several maternal factors are related with an increased risk of intrauterine fetal demise. Higher incidences of fetal deaths were associated with factors like age group >35 yrs, obese patients, patients not getting routine antenatal care, poor socioeconomic status. Several medical disorders like hypertension , diabetes, thrombophilias, kidney disease, thyroid disorders have association with intrauterine deaths.

In developed countries, unexplained antepartum fetal deaths form a large chunk of contributing to perinatal mortalitiy. In contradiction , preventable factors like asphyxia, infection, intracranial damage from difficult delivery are responsible for majority of still births in developing nations.

Maternal causes include CPD, rupture uterus, trauma to mother, anaemia, hepatic encephalopathy, jaundice, Rh incompatibility, epilepsy, diabetes, hypertensive disorders of pregnancy & many iothers. Fetal causes include malpresentations like breech, transverse lie; multiple pregnancy, congenital malformation, birth trauma, MSL, oligohydroamnios, polyhydroamniose among many others. Placental causes include placenta previa, premature separation of placenta, coiling of umbilical cord, prolapse of cord, true knot in umbilical cord and short cord.

After the diagnosis of intrauterine fetal death, induction for delivery of the fetus is started. It is mentally stressful for the patient as well as relatives so it is important to offer both the options of delivery and expectant management to women experiencing fetal death. The mode and timing of delivery after a fetal death and the type of indction- pharmaceutical or mechanical - depends on the gestational age at which the death occurred, on the maternal history of a previous uterine scar and maternal preference.

Derivatives of prostaglandins are used for induction of labour in cases of IUFD; of which, misoprostol, a synthetic analogue of PGE1 is widely used because of it is cost effective, stable at room temperature, has a long shelf life and ease to administer. Dinoprostone (PGE2) gel can also be used to induce labour in IUFD but it is expensive. Misoprostol can be used in preference to prostaglandin E2 because of equivalent safety and efficacy with lower cost. The Royal College of Obstetricians and Gynaecologists' (RCOG) guideline on the management of late IUFD (after 24 completed weeks of pregnancy) and stillbirth advises that the dose of misoprostol should be adjusted according to gestational age (100 micrograms 6hourly before 26 weeks; 25 to 50 micrograms 4-hourly at 27 weeks or more.

The aim of the present study is to understand various socioeconomic and demographic factors related to IUFD and the methods of termination and to compare the efficacy of misoprostol and dinoprostone in induction.

II. METHODS

It was a prospective study conducted in the Department of Obstetrics & Gynaecology, NHL medical college and the associated VS General & SVP hospital, Ahmedabad. All pregnancies diagnosed with IUFD in cases admitted in the Department were studied from May 2018 to January 2020. A total of 100 cases were studied.

Selection criteria

Inclusion criteria

All those cases who were diagnosed as intrauterine dead fetus at the time of admission with gestational age >28 weeks pregnancy were included in the study.

Exclusion criteria

All cases of intrapartum IUFD were excluded and all the cases <28 weeks were also excluded from the study.

Maternal factors like age, parity, gestational age, socioeconomic status, antenatal care, associated complicating factors like hypertensive disorders of pregnancy, diabetes, Rh isoimmunization, severe anaemia were taken into account. Fetal characteristics were studied with respect to sex, birth weight, gross congenital anomalies. Risk factors related to placenta and cord (true knot, cord prolapse and tight cord around neck) were also analysed. Laboratory investigations were studied. Method of induction in these cases was studied and the efficacy of misoprostol was compared with dinoprostone in induction.

III. RESULTS

Total number of deliveries during this period was 8129. Among this, total number of IUFD >28 wks of gestation were 100. Incidence of IUFD at our centre was found to be 12.30 per 1000 deliveries. In our study that maximum number of still birth occurred between the age group of
21 to 25 years (50%). 2nd in the age group >30 (21%).

Maximum numbers of cases studied were unbooked (87%) as compared to 13% cases, which were booked. The IUFD occurred mainly in low socioeconiomic class V and IV (84%) it was minimum in class I. Maximum number of intrauterine deaths occurred in primi (44%) followed by second gravida (37%) 3rd gravida showed 10% still birth and in 4th and 5th gravida it was 5% & 4% respectively.

Distribution of cases according to demographic variables

1. Maternal age

Serial Number	Maternal age (in years)	Number of still birth
1	15-20	14
2	21-25	50
3	26-30	15
4	>30	21
Total		100

2. PARITY

Serial Number	Parity	Number of still birth
1	Primi	44
2	Second gravida	37
3	Third gravida	10
4	Fourth gravida	5
5	Fifth gravida	4
Total		100

3. SOCIOECONOMIC CLASS

Serial Number	SOCIOECONOMIC CLASS	Number of still birth
1	I	2
2	II	5
3	III	9
4	IV	39
5	V	45
		100

4. BOOKED/UNBOOKED CASES

Serial Number	BOOKED/UNBOOKED	Number of still birth
1	Booked case	13
2	Unbooked case	87
Total		100

Distribution of cases according to fetal variables

1. SEX

Serial number	Fetal sex	Number of still birth
1	Male	61
2	Female	39
Total		100

2. BIRTH WEIGHT

Serial number	Birth weight (in grams)	Number of still birth
1	500-1000	23
2	1001-1500	19
3	1501-2000	20
4	2001-2500	22
5	2501-3000	13
6	3001 & more	3
Total		100

3. GESTATIONAL AGE

Serial number	Gestational age (in weeks)	Number of still birth
1	28-31	36
2	32-36	38
3	>37	26
Total		100

IUFD was found to be more in male fetuses i.e. 61% v/s females fetuses 39%.and more in preterm fetus as compared to term fetuses. 36% was found in fetuses less than 32 weeks and 38% was found in gestational age 32-36 weeks whereas it was 26% in term babies.
62% IUFD were found among fetuses weighing 2000 grams or less due to prematurity. Still birth was most common in fetuses of 1 Kg. or less (23%). It was least with birth at 3.5 Kg or more (1.55%).

Distribution of cases based on cause of IUFD

Causes of IUFD	No. of still-birth
Abruption	14
Placenta Previa	3
Pre-eclamptic toxemia	13
Eclampsia	9
Severe Anemia	4
Rh incompatibility	1
IUGR	3
Polyhydroamnios	2
Post-maturity	3
Jaundice	1
Oligohydroamnios	8
PROM	2
Congenital Anomaly	6
Cord causes	4
Hepatic encephalopathy	2
Hand prolapse	2
Epilepsy	1
Gestational Hypertension	3
Diabetes	2
Rupture uterus	3
Unidentified	12
MSL	3
Total	100

The leading reason for IUFD was abruption (14%) followed by hypertensive toxaemia (13%).Next incidence was of the IUD whose reason could not be identified (12%). Other reasons were eclampsia (9%), oligohydramnios (8%), congenital anomalies (6%), severe anaemia (4%), cord abnormalities (4%), gestational hypertension (3%), MSL (3%) post maturity (3%), ruptured uterus (3%), placenta previa (3%) IUGR (3%),

hand prolapsed (2%), polyhydramnios (2%), PROM (2%), diabetes (2 %), hepatic encephalopathy (2%), jaundice (1%), Rh incompatibility (1%), epilepsy (1%).

The termination of pregnancy was attempted by various methods but mainly by use of 2 drugs. 28 cases were induced with dinoprostone, 30 cases with misoprostol, 18 underwent operative intervention and 24 were augmented with oxytocin drip.

Mean induction delivery interval of misoprostol was found to be 9.60 hrs and mean induction delivery interval of dinoprostone was found to be 12.65 hrs.

The induction delivery interval was more in primigravida as compared to multigravida in both the groups. The mean interval in term pts was less as compared to preterm pts in both the groups thus both are more effective in term patients.[2] Maternal deaths occurred due to hepatic encephalopathy and eclampsia.

The indication for operative intervention was previous 1 casearan section, previous 2 casearan section, rupture uterus, oligohydramnios.

Distribution of cases according to method of termination

Method of termination	Total number
Dinoprostone	**28**
Misoprostol	**30**
Oxytocin	**24**
Operative	**18**
Total	**100**

Induction-Delivery interval

Method of induction	Mean Induction-Delivery interval (In hour)
Dinoprostone	**12.65**
Misoprostol	**9.60**

Induction-Delivery interval according to gravity & gestational age

Gravidity	Mean induction-delivery Interval (MISOPROSTOL)	Mean induction-delivery Interval (DINOPROSTONE)
Primigravida	**9.8 hrs**	**14.15 hrs**
Multigravida	**9.28 hrs**	**9.42 hrs**
Gestational age		
Preterm	**9.6 hrs**	**12.75 hrs**
Term	**8.33 hrs**	**12.33 hrs**

IV. DISCUSSION

Incidence of IUFD at our centre was found to be 12.30 per 1000 deliveries.

Various causes of IUFD need to be identified in order to prevent them and reduce the burden.

In our study that maximum number of still birth occurred between the age group of 21 to 25 years (50%). 2nd in the age group >30 year age group. Pregnancy in extremes of age group and obesity in reproductive age group is uncommon in our setup. Out of total 200 cases 87 were unbooked as compared to 13 booked cases showing the importance of proper antenatal care so that the high risk patients could be identified earlier and timely referred so that IUFD can be prevented. Maximum number of IUFD occurred in primi (44%) , followed by second gravida (37%) 3rd gravida10% and in 4th and 5th gravida it was 5% and 4% respectively. In the study by neetu singh et al[7] it was found that the incidence was maximum in primigravida (25%) followed in order 17%, 18% and 24% in grandmultiparity according toc increase in parity.

We included only the antepartum intrauterine deaths in which the leading reason for IUD was abruption (14%) followed by Hypertensive toxemia (13%). Then in the order are IUFD whose reason could not be identified Idiopathic (12%). Other maternal factors were eclampsia, oligohydramnios, severe anaemia, gestational hypertension , post maturity, rupture uterus, PROM, polyhydramnios, hepatic encephalopathy, jaundice, RH incompatibility, epilepsy, diabetes.

In study by Choudhary A et al[6] similar findings were there, hypertensive disorder to be complicating 28.7% pregnancies and Diabetis in 4.2% women. A total of 17.2% cases presented with Ante partum hemorrhage out of which 3.9% were placenta previa, and 11.7% placental abruption. Mild anemia was found in 19.4% cases, moderate in 6.3% cases and15.9% were severely anemic. There was one case of road traffic accident. Severe IUGR was found to be responsible for the death of 8.5%babies, 11.5% fetuses had congenital anomalies. Maternal infections were found to be complicating eight pregnancies out of which there were two cases of jaundice (infective hepatitis) five cases of clinically proven malaria and one case of pneumonia. There

were 19.5% women where no causative factor was found for intrauterine fetal demise. Singh Neetu et al[7] found 33% unexplained fetal deaths in their study of 296 cases of IUFD.

Over the years the causative factors responsible for IUFD have changed. There was an observation that not only the incidence is reducing in developed countries, but the patterns of etiologies are also changing syphilis and other infections are no longer significant. In many studies hypertensive disorders complicated by abruption as found to be the main cause. Among the fetal causes, major congenital anomalies accounted for 5.5% cases. The main congenital malformations we found were anencephaly, congenital heart disease, renal agenesis, hydrocephalous multiple anomalies in placental causes abruption, placenta previa and cord abnormalities were important contributing factors. The IUFD in our series was more in male fetuses 61% than females' fetuses. In the study by SinghNeetu[7] et al it was 54%in males and 46%in females. Whereas in study by Choudhary A et al[6] there were 58 male babies v/s 47 female babies. 62% IUFD were found among fetuses weighing 2000 grams or less. It is obvious that prematurity is contributing factor. In developed countries maternal and fetal outcomes have been improved due to early arrival of the patient and timely intervention.

After the diagnosis of intrauterine death the patient may choose to wait for spontaneous labour which is not common and it becomes necessary to terminate the pregnancy. In our study 28 pts were induced with dinoprostone, 30 pts were induced with misoprostol, 18 underwent operative intervention and 24 were augmented with oxytocin drip.

Many clinical trials have demonstrated that misoprostol is effective for induction of labour at term, including prelabour rupture of membranes. In our study mean induction delivery interval of misoprostol was found to be 9.60 hrs and mean induction delivery interval of dinoprostone was found to be 12.65 hrs.

Various methods of induction of labour following IUFD have been tried and studied and most of the studies compared between combined method (mifepristone and misoprostol) and misoprostol only. No study has been undertaken to compare the role of dinoprostone gel vs. misoprostol in induction of labour in a case of IUFD however there are various randomized studies, which compared vaginal misoprostol with dinoprostone for induction of labour at term with living fetus. In those studies the incidence of vaginal delivery within 24 h of induction was found higher in the misoprostol group. In a study by Titol Biswaset al[8] the mean induction delivery interval in misoprostol was found to be 8.13 hrs whereas in dinoprostone was found to be 14.32hrs.

The Misoprostol was found to be more efficacious than dinoprostone in terms of induction delivery interval and the amount of doses required and less need of Oxytocin augmentation. In a study by Kriplani A et al[9] the efficacy at term induction delivery, interval was shorter in misoprostol; 12.8+/-6.4 h versus 18.53+/-8.5 h in dinoprostone. A 2010 Cochrane review10 concluded that vaginal misoprostol was also superior to other induction agents (vaginal prostaglandin, intracervical prostaglandin, and oxytocin), with less epidural use and fewer failures to achieve vaginal delivery within 24 hours, but more tachysystole with FHR changes. The indication for operative intervention was previous 1 section, previous 2 section rupture uterus hand prolapsed, placenta previa, oligohydramnios. The induction delivery interval was more in primigravida as compared to multigravida. In both the groups misoprostol was more effective in multigravida. In a study by Batool et al[11] oral misoprostol is effective for induction of labour in both primigravida and multigravidas. Induction to delivery was less than 18 hours in multigravida and it was more than 18 hours in primigravida. The study indicates that the mean induction delivery interval of misoprostol is less in term patients (8.33 hrs) as compared to preterm patients (9.6 hrs). Similiarly in dinoprostone the mean interval in term pts was less (12.33 hrs) as compared to preterm pts (12.75 hrs). Thus both are more effective in term patients.

V. CONCLUSIONS

The main aim of the study was to study the various risk factors and causes of intrauterine death to reduce the incidence. It can be concluded from the present study that Socio- demographic factors need to be considered as predisposing factor for prenatal deaths. Literacy, teenage pregnancies, unregulated reproduction, low socioeconomic states, poor nutrition, lack of health education and antenatal care all conspire against the women's health and predispose her to IUFD. Many of the causes of intrauterine death found out to be preventable like abruption hypertensive disorders which can be avoided by proper antenatal care. The use of folic can prevent neural tube defects. Training of dais can help in early diagnosing high risk pregnancies so that they can be timely referred.

After diagnosing intrauterine dead baby the method of termination is chosen accordingly. The labour can be augmented by pitocin or induction can be done by prostaglandins. In the study it was observed that misoprostol is more effective in induction of intrauterine death as compared to dinoprostone in terms of induction delivery interval and cost effectiveness.

Maternal and child health services are to be evaluated and improved. Health agencies, public health personnel social workers to & traditional birth attendants should be properly trained for proper antenatal care and timely diagnosis of intrauterine death.

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