IUFD (IUD) Among Different Gestational Age Groups

Kishore Kumar R[1,2*], Padmini Isaac[3] and Anuradha S[3]

[1]*Neonatology & Pediatrics, Cloud nine Hospital, Jayanagar, Bangalore, India*

[2]*Neonatology & Pediatrics, Notre Dame University, Australia*

[3]*Senior Obstetrician & Gynecologist, Cloud nine, Jayanagar, Bangalore*

[*]**Corresponding author**

Kishore Kumar R, Neonatology & Pediatrics, Cloud nine Hospital, Jayanagar, Bangalore, India.

ABSTRACT

Purpose of the study: To compare the occurrence of Unexplained IUFD among different gestational age groups and to find if any possible association with seasonal variation in the occurrence of IUFD.

Methodology: A retrospective multicentric study was performed. Secondary data regarding unexplained or uncomplicated IUFD that occurred between January 2008 and December 2019 was collected from hospital records. Gestational age, Date of occurrence and fetal birth weight were obtained and subjected to statistical analysis using SPSS (version.22) software.

Results: During the study period a total of 318 IUFD occurred due to unexplained or uncomplicated reasons. The highest occurrence of IUFD (40.9%) was observed in 201 to 250 days gestational age group. The peak occurrence of IUFD was observed in the monsoon particularly in July.

Conclusion: Most of the IUFDs were noted during 28 weeks to 35 weeks gestation. We also found an increased incidence of IUFD during monsoon season and in the third trimester of pregnancy.

Keywords: IUFD, Stillbirths, Uncomplicated IUFD, Unexplained Fetal Demise, Fetal Death

Introduction

The World health organisation defines Intra Uterine Foetal Deaths (IUFD) as antepartum deaths beyond 20 weeks of gestation or birth weight >500gm. In 2015, there have been 2.6 million stillbirths globally, with more than 7178 deaths a day. The majority of these deaths occurred in developing countries. Ninety-eight percent of these are seen in low- and middle-income countries. About 50% of all stillbirths occur in the intrapartum period, which represents the greatest time of risk. An Estimated the proportion which varies from 10% in developed regions to 59% in South Asia [1]. Stillbirth and IUFD causes a severe psychological impact on the mother and the family. In 2014 'India New born Action Plan' (INAP) had adopted stillbirth prevention target of <10 stillbirths per 1,000 births by 2030 [2].

Maternal risk factors such as nulliparity or grand multiparity increased maternal body mass index (BMI), diabetes mellitus (DM), antenatal vaginal bleeding and women aged over 40 years had shown a highly significant risk of stillbirth in the previous studies [3-5]. Yet, certain studies in the past revealed a very high incidence of IUFD of about thirty to fifty percent which cannot be related to any known etiological or risk factors [6-9]. There are numerous risk factors enumerated in the literature oftentimes, risk of occurrence of IUFD seems to be inconsistently associated with increasing or decreasing gestational ages in the past research from India [10-12]. A recent study from WHO also exhibited similar result [13]. This demands further research in this aspect. Hence, the primary aim of this retrospective study was to compare the occurrences of Unexplained IUFD (due to unknown factors) among different Gestational age groups.

On the other hand, Environmental and meteorological factors are being evaluated as determinants of adverse birth outcomes in recent times. Looking for seasonal patterns is a method of investigating environmental determinants of birth outcomes [14]. Understanding seasonal fluctuations in disease patterns can help us to understand certain aspects of its aetiology. Earlier studies relating the seasonality with neonatal mortality among the historical European populations in Sweden and Italy observed a strong correlation of cold weather with a high occurrence of neonatal deaths [15,16]. There is a dearth of research when

it comes to the association of seasonal variations with IUFD. Studies done in the past in this regard at different places around the world obtained equivocal results [17,18]. Consequently, the secondary aim of this study was to find, if any, seasonal variations exist in the occurrences of IUFD.

Materials and Methods
This study was a retrospective multi-centric study, conducted at 14 different locations of Cloud nine chains of Hospitals across India. Secondary data comprising of gestational age, birth weight, and date of occurrence of IUFD were collected from the hospital records of female patients, who had the incidence of IUFD from January 2008 till December 2019 after obtaining permission from the ethical committee and the hospital administration. All IUFD resulted from uncomplicated pregnancy that occurred in the above-mentioned duration were included in the study whereas those due to known predisposing factors like gestational diabetes, chromosomal abnormalities, uterine abnormalities etc. were excluded.

All statistical analysis was performed with SPSS (Statistical package for social sciences) version 22. Chi-square Test, Kruskal-Wallis and Post Hoc analysis were performed.

Results
There was a total of 318 IUFD as per the inclusion and exclusion criteria, from January 2008 till December 2019 across all the centres of the study. There were 92,680 babies born during the said period – with IUDs accounting for 0.34% of all pregnancies. The median gestational age at the time of IUFD occurrence was 32 weeks (224 days) with a range of 20 weeks to 40 weeks 5 days. The mean fetal birth weight was 1.57+1.01 Kg (range: 0.12 - 4.70 Kg).

In our study, the highest occurrence of IUFD of about 40.9% was seen in the gestational age group of 201 to 250 days (28.7 to 35.7 weeks) as shown in Table 1. One sample chi-square test yielded a statistically significant difference compared to other gestational age groups. (p=0.000). Month-wise distribution of IUFD (in number and percentage) is depicted in Table 2. A total of thirty-six IUFD (11.3%) were recorded in July which was the highest, while February had the least incidence of 16 (5%) which is depicted in Figure 1a.

Occurrences of IUFD was observed to be highest in the monsoon (121 deaths) compared to other seasons of the year which was statistically highly significant (p=0.000) as shown in Figure 1b. Kruskal-Walli's test was performed to observe any substantial effect of seasonal variation on the birth weights and gestational ages which did not yield statistically significant difference (p =0.621 and p= 0.397, respectively).

**Table 1: Frequency of occurrence of IUFD among different gestational age groups**

Gestational Age	IUFD (Frequency)	Percentage
101-150 days	12	3.8
151-200 days	85	26.7
201-250 days	130	40.9
252-300 days	91	28.6

Table 2: Month wise distribution of IUFD

Month	IUFD (Number)	Percentage
January	28	8.8
February	16	5.0
March	30	9.4
April	21	6.6
May	20	6.3
June	27	8.5
July	36	11.3
August	25	7.9
September	33	10.4
October	26	8.2
November	28	8.8
December	28	8.8
Total	318	100.0
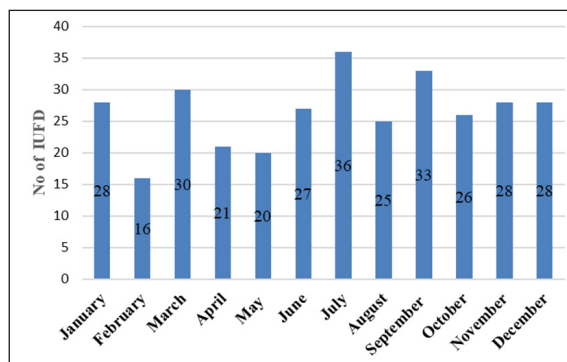
Figure 1a: Month wise incidence of IUFD (In Number)
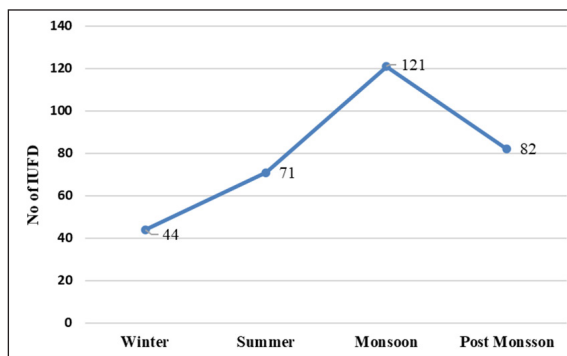
Figure 1b: Seasonal variation in the incidence of IUFD

Discussion
Despite the availability of modern interventions like non-stress test, ultrasonography etc. the majority of causes of IUFD could not be linked to any definite aetiology. There were 92,680 babies born during the said period – with IUDs accounting for 0.34% of all pregnancies, which is probably one of the lowest in the country suggesting regular antenatal check-ups does lead to healthy pregnancy. In our study, the highest occurrence of IUFD (40.9%) was in between 201 to 250 days of gestational age (28.7 to 35.7 weeks). Similar results were obtained in a recent study done at Taiwan, with 55.4% of stillbirths occurring at second trimester out of which 29% cannot be associated with any causative factor; While 44.6% of the stillbirths occurred at the third trimester in which 14% could not be linked to any cause [7]. secondary analysis of the WHO antenatal care trial found

that both high- and low-risk women within the intervention group had an increased relative risk of fetal death between 32-36 weeks of gestation [13]. In our study, the aim was to compare the occurrences of the uncomplicated and unexplained IUFD among different gestational age groups. Yet, such comparisons were not reported in many of the past studies. Nevertheless, it is worth mentioning the studies which reported the incidences of IUFD due to both known and unknown factors among different Gestational age groups.

In a study from India, 57.69% of IUFD could not be related to any maternal and fetal risk factors. The maximum number of IUFD was among the gestational age group between 28 and 32 weeks which was almost similar to our study [8]. A study from tertiary care hospital from India reported 35.8% IUFD cases which were due to unidentified reasons. Highest IUFD cases were found in the gestational age groups between 20-28 weeks followed by 28-30 weeks in their study [9].

In a prospective study from India, 10.57% of IUFD were due to unexplained reasons, 35.86% of deaths occurred at term [11]. In another study from India, 19.05% of IUFD had no causative factor and the highest occurrence of IUFD (35%) was between 31 – 35 weeks of gestational age [12]. Similar results were seen in another study from India where 28.5% of IUFD was due to unidentified causes and the highest incidence was between 31-35 weeks of gestational age [19]. In contrast to our study, few studies observed the highest incidences of IUFD at term (>36 weeks). Similar contrast results were also seen in another study from India where 16% of IUFD had no identified causes and highest occurrence of IUFD (33%) was at term (38-41 weeks) [20].

Warlandetal in 2014, proposed a 'triple-risk model' which could explain the late unexplained stillbirth [21]. According to this model death occurs due to the intersection of 1) maternal factors 2) fetal/placental factors, and 3) a fetal stressor. They put forth the concept of the vulnerable fetus which is susceptible to specific maternal conditions and stressors leading to fetal death. Some of the previous studies also observed high incidences of IUFD at an early gestational age. One such study from India reported 32.1% of fetal death at 20-24 weeks of gestation with no explainable cause found in 12.5% of the total cases. Pregnancies with early IUFD had Congenital anomalies as the most common factor according to this study [10].

There is a popular belief among Obstetricians in India that babies in India are more mature than our western counterparts and IUDs are more common in 39 to 41 weeks, hence induction of labour and caesarean sections are usually done in many high-risk pregnancies at around 37 weeks to prevent possible IUFD. We found in our study, that the peak occurrences of IUFD were between 28 to 35 weeks and with highest incidence in July (11.3%) and the least in February (5%). It is possible our peak in July may be coinciding with our peak incidence of seasonal flu and reduction in IUFD might be due to routine flu vaccination in pregnant women prior to this season.

In a historical study among Swedish population, the cold ambient temperature in utero preceded an increased risk of stillbirth and preterm birth but did not influence birth weight similar to our study where the season of birth did not have any statistically significant association with birth weight [17]. In contrast to our study, previous research done at Brisbane, Australia reported an Increase in temperature increased the risk of stillbirth with a mean gestational age of 27.7 weeks. The risk of stillbirth was greater when using the last 4 weeks of temperature exposure compared with the last week only. Though in our study, the temperature gradient was not considered in describing the various seasons [22].

Again, in our study, IUFD due to uncomplicated or unexplained reasons only were included. Hence, our study results cannot be extrapolated with others since most of the earlier research associated foetal factors with seasonal variations in the occurrences of IUFD. Further exploration is required in this aspect in future research.

The results of our retrospective study showed that the highest occurrence of unexplained IUFD was in the gestational age group of 201 to 250 days, contrary to the "belief" of most Obstetricians in India who are worried about the maturity of Indian babies and try to induce at early term rather than late term for the fear of IUFD. The highest peak of IUFD was observed in the monsoon, particularly in July month. We also noticed the variation due to seasonality, was not evident in terms of birth weight and gestational age. Most of the IUFD is preventable, and the knowledge of the direct or indirect effect of risk factors like seasonal variation will help in improving the health care for those at risk and thereby improving the overall outcome of live births.

References

1. Maternal, newborn, child and adolescent health Stillbirths. Available at: https://www.who.int/maternal_child_adolescent/epidemiology/stillbirth/en/
2. India newborn action plan. Ministry of health and family welfare, Govt. of India. September 2014. Available at:https://nhm.gov.in/images/pdf/programmes/inap-final.pdf.
3. Manktelow BN, Smith LK, Evans TA, Hyman-Taylor P, Kurinczuk JJ, et al. MBRRACE-UK perinatal mortality surveillance report. UK perinatal death for births from January to December 2013. Supplementary report. UK Trusts and Health Boards. The Infant Mortality and Morbidity Studies Group, Department of Health Sciences, University of Leicester: Leicester, 2015. Available at:https://www.npeu.ox.ac.uk/downloads/files/mbrrace-uk/reports/MBRRACE-UK-PMS-Report-2014.pdf
4. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and foetal risk factors for stillbirth: population - based study. Br Med J. 2013. 346: 108.
5. Drysdale H, Ranasinha S, Kendall A, Knight M, Wallace EM. Ethnicity and the risk of late-pregnancy stillbirth. Med J Aust. 2012. 197: 278-281.
6. Singh N, Pandey K, Gupta N, Arya AK, Pratap C, et al. A retrospective study of 296 cases of Intrauterine fetal deaths at a tertiary care centre. Int J Reprod ContraceptObstet Gynecol. 2013. 2: 141-146.
7. Liu LC, Huang HB, Yu MH, Su HY. Analysis of intrauterine fetal demise. A hospital-based study in Taiwan over a decade. Taiwan J ObstetGynecol. 2013. 52: 546-550.

8. Desai S, Sawant V. Evaluation of clinical and aetiological factors for intrauterine fetal death. Online IntInterdiscipl Res J. 2014. 4: 250-259.

9. Saha D, Kurude VN, MundheS. A study of intrauterine fetal death in a tertiary care hospital. Int J ReprodContraceptObstet Gynecol. 2019. 8: 2647-2651.

10. Jamal S, Agarwal S. IUFD incidence, causes and complications: a retrospective study done at a tertiary care centre in greater Noida, India. Int J ReprodContraceptObstet Gynecol. 2017. 6: 5483-5487.

11. Gehlot H, Nagar GG, Sharma S, Yadav OP. A prospective analytical study of intrauterine fetal death cases and associated maternal condition at a tertiary centre.Int J ReprodContraceptObstet Gynecol. 2017. 6: 3392-3396.

12. Choudhary A, Gupta V. Epidemiology of Intrauterine Fetal Deaths: A Study In Tertiary Referral Centre In Uttarakhand. IOSR-Journal of Dental and Medical Sciences. 2014.13: 3-6.

13. Vogel JP, Habib NA, Souza JP, Gülmezoglu AM, Dowswell T, et al. Antenatal care packages with reduced visits and perinatal mortality: a secondary analysis of the WHO Antenatal Care Trial. Reprod Health. 2013. 10: 19.

14. Turabian JL. The Variation of Seasonal Diseases in Family Medicine Depends on Infectious Diseases and these are mainly RespiratoryDiseases. J Gen Pract (Los Angel). 2017. 5: 1-6.

15. Karlsson L, Lundevaller E, Schumann B. The association between cold extremes and neonatal mortality in Swedish Sápmi from 1800 to 1895. Glob. Health Action. 2019. 12: 1623609.

16. Scalone F, Samoggia A. Neonatal mortality, cold weather, and socioeconomic status in two northern Italian rural parishes 1820-1900. Demogr Res. 2018. 39: 525-560.

17. Bruckner TA, Modin B, Vågerö D. Cold ambient temperature in utero and birth outcomes in Uppsala, Sweden, 1915-1929. Ann Epidemiol. 2014. 24:116-122.

18. Karlsson L, Lundevaller EH, Schumann B. Season of birth, stillbirths, and neonatal mortality in Sweden: the Sami and non-Sami population, 1800-1899. Int J Circumpolar Health. 2019. 78: 1629784.

19. Ara S, Nisar S, Bashir U. Incidence and risk factors of intra uterine fetal death: a retrospective study at a tertiary care centre in Kashmir, India. Int J ReprodContraceptObstet Gynecol. 2019. 8: 1517-1519.

20. Shrestha J, Shrestha R, Gurung S. Stillbirths - Determining the associated factors and causes according to relevant condition at death: an experience from Pokhara, Nepal. J Nobel Med Coll. 2017. 6: 58-65.

21. Warland J, Mitchell EM. A triple risk model for unexplained late stillbirth. BMC Pregnancy Childbirth. 2014. 14: 142.

22. Strand LB Barnett AG, Tong S. Maternal Exposure to Ambient Temperature and the Risks of Preterm Birth and Stillbirth in Brisbane, Australia, Am J Epidemiol. 2012. 175: 99-107.