



STUDY OF THE CLINICAL PROFILE OF PATIENTS WITH INTRAUTERINE DEATH AND MATERNAL OUTCOMES

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ABSTRACT:

Background: Intrauterine fetal death (IUFD) significantly impacts mothers and families, with various factors contributing to its occurrence, including maternal health conditions and complications during pregnancy. Improved antenatal care and timely interventions can reduce risks, but many cases remain unexplained. This study aims to analyze the clinical profiles of IUFD patients and their maternal outcomes to enhance prevention and management strategies.

Methodology: This systematic review adheres to PRISMA guidelines and includes a thorough search of major electronic databases. It examines various studies focusing on the clinical profiles of patients with intrauterine death (IUD) and their maternal outcomes, highlighting demographics, risk factors, and complications. Bias risk assessment was conducted using established methods to ensure the reliability of the findings regarding the impact of IUD on maternal health.

Results: This review examined 10 studies on intrauterine fetal death (IUFD), covering 3,437 cases, mainly involving women aged 26-30. IUFD presents significant emotional and physical challenges for mothers and families. Key risk factors include maternal age and health conditions like hypertension and diabetes. While improved antenatal care can reduce risks, many cases remain unexplained, highlighting the need for further research. The study aims to analyze the clinical profiles of IUFD patients and their maternal outcomes to enhance prevention and management strategies.

Conclusion: The review highlights that maternal health issues, particularly hypertension and diabetes, significantly contribute to IUD. Regular antenatal care is crucial for early detection and

management. Many cases remain unexplained, emphasizing the need for further research. Improved maternal healthcare can reduce IUD rates and enhance outcomes.

Keywords: *Intrauterine fetal death, placental abruption, pre-eclampsia, pregnancy outcome, risk factors.*

INTRODUCTION:

Intrauterine death (IUD), also referred to as stillbirth, is a devastating obstetric complication that has significant emotional, psychological, and physical impacts on both the mother and her family. [1] IUD is defined as the death of a fetus at 20 weeks of gestation or later, prior to the onset of labor. [2, 3] Despite advancements in maternal and fetal healthcare, intrauterine deaths remain a significant concern worldwide, particularly in low- and middle-income countries. Globally, approximately 2.6 million stillbirths occur annually, with a stillbirth rate of 13.9 per 1,000 births. However, the burden of intrauterine deaths varies significantly based on geographical location, healthcare infrastructure, socioeconomic status, and availability of prenatal care services. [4]

The stillbirth rate in India, according to the National Family Health Survey (9.7 stillbirths per 1,000 births; 95% confidence interval: 9.2–10.1), was 2.6 times higher than the average rate recorded in the Sample Registration System from 2016 to 2020 (3.8 stillbirths per 1,000 births). [5]

The etiology of intrauterine deaths is multifactorial, including maternal conditions such as hypertension, diabetes, infections, and placental abnormalities, as well as fetal factors like genetic abnormalities, congenital malformations, and intrauterine growth restriction. [6] In many cases, the cause remains unidentified despite thorough investigations, highlighting the need for more robust research and improved diagnostic protocols.

This study aims to analyze the clinical profile of patients who have experienced intrauterine death and to evaluate maternal outcomes associated with these cases. By identifying common risk factors and complications, this research intends to contribute to the development of strategies that can reduce the prevalence of IUD and improve maternal health outcomes.

METHOD:

Protocol:

The protocol of this review was developed in accordance with the guidelines outlined in the Preferred Reporting Items for Systematic Review (PRISMA-P) statement and all changes were properly noted.

Search strategy:

The literature search was conducted through searches in the following database: PubMed, Scopus, Web of Science, Wiley, Google Scholar, Embase, MEDLINE, and Science Direct.

The study encompassed a thorough examination of full-text articles and literature reviews that had been published. We searched for Medical Subject Headings (MeSH) terms and free text terms, full-text articles, case studies, and case series related to breast imaging, imaging modality, mammography, and histopathology

Appropriate Boolean operators were applied, and the materials available in the English language were used. Literature lacking full-text access and studies that could not be located in the specific original datasets was excluded from the current review.

Inclusion criteria:

1. The complete text of the article was available.
2. Literature in the English language
3. Studies between Jan 2016- March 2024

Exclusion criteria:

1. Abstracts of conferences

2. Copyrights and duplicate articles

Table 1: characteristics' of the studies included in this systematic review

Sr. No.	Author Name / Year	Study Design	Sample size	Common age group	Cause of IUFD	Gestational age at IUFD	Outcomes
1.	Jovanovic I. et al. [7] (2023)	A Retrospective descriptive study	60	30.6 ± 6.38	The pathology of the umbilical cord is regarded as a possible cause of intrauterine fetal death.	39 th week	Most IUDs might have been avoided. Regular ANC's can detect pre-eclampsia early and treat it to avoid complications, such as IUD and placenta abruption in rare cases, which in turn lowers the stillbirth rate.
2.	Wada Y. et al. [8] (2023)	An observational study	1134	(29.0–37.0)	-	34-3.0 week	Bleeding during cesarean delivery was significantly higher than in vaginal delivery for women with placental abruption and intrauterine fetal death. However, severe complications, such as maternal death and uterine rupture, were observed in vaginal delivery cases. Cautious management is essential for women with placental abruption and intrauterine fetal death, regardless of the delivery method.
3.	Mahato RD et al. [9](2023)	a descriptive cross-sectional study	35	20-35	Hypertension (20%), post-dated pregnancy (17.1%), and IUGR (14.3%) were the leading risk factors for IUFD.	37-42	Most IUFD cases occurred in illiterate housewives, with hypertensive disorders being the leading risk factor. Regular antenatal care is crucial for early detection and prevention.
4.	Thakur SK et al. [9] (2022)	Observational study,	20	21-35	Among 50 cases, the most common fetal,	37-42 (48%)	The study found that most intrauterine fetal deaths occurred antenatally, with 78% of cases being

					placental, and cord factors related to intrauterine fetal death included meconium-stained liquor (6%), cord around the neck (6%), and intrauterine growth restriction (2%). Anomalous babies and cord prolapse were present in 4% of cases each.		macerated. Pregnancy-induced hypertension was the leading risk factor, followed by antepartum hemorrhage, anemia, and hypothyroidism. Despite these preventable factors, unidentified risks remain a challenge for obstetricians.
5.	Monasta L. et al. [10] (2020)	Retrospective study	278	30–39 years	Fetal growth restriction (15.5), placental abruption (12.9%), and chorioamnionitis (11.5%) were the most common conditions associated with intrauterine fetal deaths, with maternal factors like diabetes and pre-eclampsia also contributing significantly.	34 weeks	A high percentage of IUFD cases have no identifiable cause. Implementing evidence-based diagnostic protocols, including immunologic, genetic, and pathological exams, can help close this gap and prevent future IUFDs.
6.	Malik A et al.[11] (2019)	A cross-sectional study	100	26-35	Hypertension, anemia, diabetes, and abruptio placenta were leading causes of IUFD, with 19% of cases remaining unexplained.	-	Early identification and treatment of IUFD risk factors can help prevent recurrence and reduce maternal complications.

					Maternal complications included blood transfusions (28%), PPH (12%), sepsis (8%), and a 1% maternal mortality rate		
7.	Thaker RV et al.[12] (2018)	A Retrospective observational study	193	26-30	All patients who delivered a stillborn fetus experienced emotional distress and received counseling. Disseminated intravascular coagulation (DIC) was observed in 21 patients (10.8%), and postpartum hemorrhage (PPH) occurred in 15 patients (7.7%), with one requiring obstetric hysterectomy. Acute renal failure (ARF) due to eclampsia was reported in one patient.	26 to 31 weeks	Most patients were unregistered and received inadequate antenatal care. The primary causes of IUFD included pre-eclampsia-eclampsia, antepartum hemorrhage (APH), anemia, diabetes, and unknown factors. Improved health education on adequate antenatal care, warning signs, and institutional deliveries could significantly reduce IUFD.
8.	Bishnoi BL et al. [13] (2018)	A Prospective study	227	20-25	Fetal growth restriction (15.5%), placental abruption (12.9%), and maternal conditions like diabetes (10.4%) and pre-eclampsia (9.7%) were the most common	34 weeks	Promoting institutional deliveries and improving antenatal care can help prevent intrapartum fetal deaths and significantly reduce perinatal mortality.

					factors associated with IUFD.		
9.	Kala Katti et al.[14] 2017	Prospective analytical study	140	25.7 ± 3.45 years	Pre-eclampsia was the leading cause of intrauterine fetal death (26.04%), followed by abruptio placenta (19.87%) and eclampsia (10.15%). Unexplained cases accounted for 11.48%, while congenital anomalies contributed 8.83%.	-	Fetal loss is a key indicator of maternal care during pregnancy. This study found that most IUDs were preventable. Early detection and treatment of pre-eclampsia through regular antenatal checkups can help reduce complications like IUD and placental abruption, ultimately lowering stillbirth rates.
10.	Sharma S et al. [15] (2016)	Retrospective study	250	21-25 years	Trauma and stress during labor were the most common causes of intrauterine fetal death (34%), followed by pregnancy-induced hypertension (19.6%) and antepartum hemorrhage (12%). Additionally, 5.6% of cases had an unknown etiology.	-	IUFD is associated with factors such as anemia, rural residency, low socioeconomic status, multiparity, prior pregnancy loss, unsupervised deliveries, gestational hypertension, and congenital malformations (CMFs). Comprehensive screening and adequate antenatal care can play a crucial role in lowering the incidence of stillbirths.

RESULTS:

In this systematic review, a total of 4,547 records were identified through the initial literature search on intrauterine death, with an additional 30 records found through reference searches. After removing 3,524 duplicate records, 1,023 published studies were screened. Of these, 589 studies were excluded, including 363 that were deemed irrelevant and 40 studies that were excluded due to missing parameters in the search articles. Based on the inclusion criteria, 31 full-text articles were

assessed for the study. However, 20 articles were excluded due to incomplete data. After thorough screening, 10 studies were included in the qualitative analysis. (Table 1)

Quality evaluation of the included studies: In this review, RevMan software was used to assess the risk of bias in randomized controlled trials using the Cochrane-associated technique. Examined were biases related to selection (random sequence generation), performance (participant and staff blinding), attrition (incomplete outcome data), selective reporting (reporting bias), and other potential biases. Every study in these domains was assigned a risk category: low, unclear, or high. Figure 2 displays the risk of bias evaluation for each of the 10 included studies. Specifically, for blinding of outcome assessors, 30/50 trials (60%) were categorized as low risk, 15/50 (30%) had an unclear risk, and 5/50 trials (10%) were categorized as high risk. (Fig 3)

Studies outcome

In recent studies, the incidence and risk factors associated with IUFD have been extensively analyzed, providing valuable insights into prevention strategies. **Jovanovic et al. [7]** observed a stable IUFD rate in term pregnancies at the University Clinical Center of Serbia, with rates dropping below 0.1% since 2010. Significant risk factors identified included hypertensive syndrome, obesity, and gestational diabetes. Interestingly, placental abnormalities, particularly infarctions, were more prevalent than typically reported, even in healthy women. This study underscores the importance of preconception counseling and therapeutic interventions for women with preventable risk factors, alongside a call for further research to identify new risk factors and enhance monitoring protocols to mitigate IUFD incidence.

Similarly, **Wada Y et al. [8] (2023)** found that among 1,218 women with placental abruption leading to IUFD, the incidence was 0.076%, with 53.6% undergoing cesarean delivery. They reported that bleeding during cesarean deliveries was significantly greater than in vaginal deliveries (median 1650 mL vs. 1171 mL). Although maternal death occurred in 0.4% of cases—entirely within the vaginal delivery group—severe complications were also noted, emphasizing the necessity for careful management in cases of placental abruption and IUFD, regardless of the delivery method.

Thaker RV et al. [13] reported an IUFD incidence of 17.2 per 1,000 births, predominantly among women aged 26-30, with nearly half being first-time mothers and many lacking antenatal care. The causes identified included unexplained factors, pre-eclampsia, anemia, and diabetes. The study highlighted that improved antenatal care could significantly reduce the incidence of IUFD.

Monasta et al. [11] reported a lower IUFD incidence of 2.8 per 1,000 live births, with 30% of cases involving small for gestational age (SGA) fetuses, particularly among immigrant women. The SGA rate increased to 35% when maternal or fetal pathology was present, while 28% of cases had no identifiable cause for IUFD. Notably, 11% of IUFDs occurred during labor, and 72% occurred after 30 weeks of gestation. This study emphasizes the necessity for evidence-based diagnostic protocols, including immunologic, genetic, and pathological examinations, to address the high percentage of unexplained cases and prevent future IUFDs.

Bishnoi BL et al.[14] reported 227 IUFDs among 6,264 deliveries, leading to an incidence rate of 36 per 1,000 births. A significant portion (84.56%) of these cases were unbooked and unsupervised, predominantly from rural areas (58.59%) and included a notable percentage of preterm deliveries (55.5%). The most common causes of IUFD were hypertensive disorders (24.22%) and severe anemia (13.10%), followed by placental issues and congenital malformations. Their findings indicated a decrease in IUFD incidence with higher parity, suggesting that promoting institutional deliveries and enhancing antenatal care could significantly reduce IUFD rates and overall perinatal mortality.

Collectively, these studies highlight the critical need for improved antenatal care, targeted interventions for high-risk populations, and ongoing research to identify and address the multifaceted causes of IUFD.

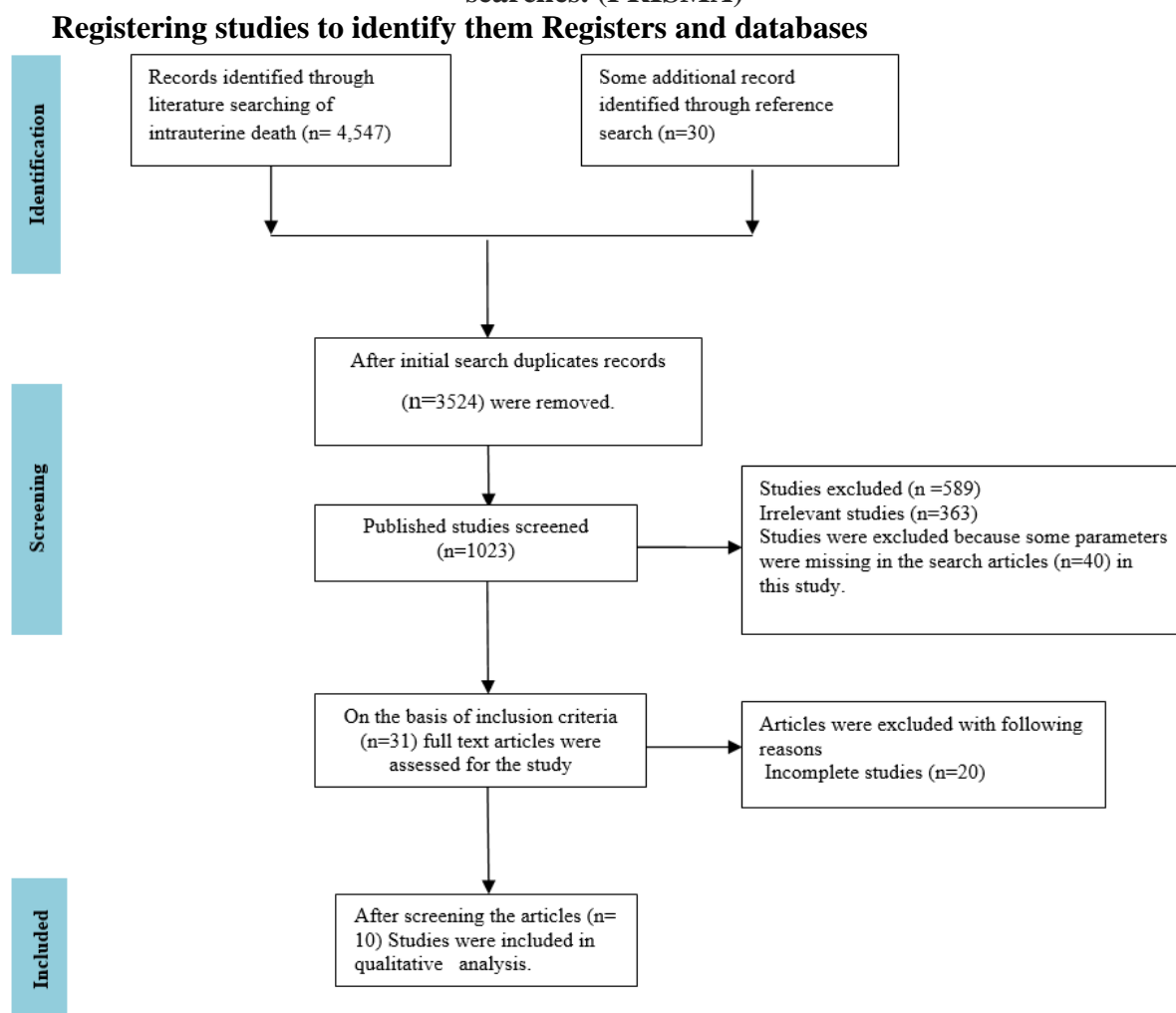
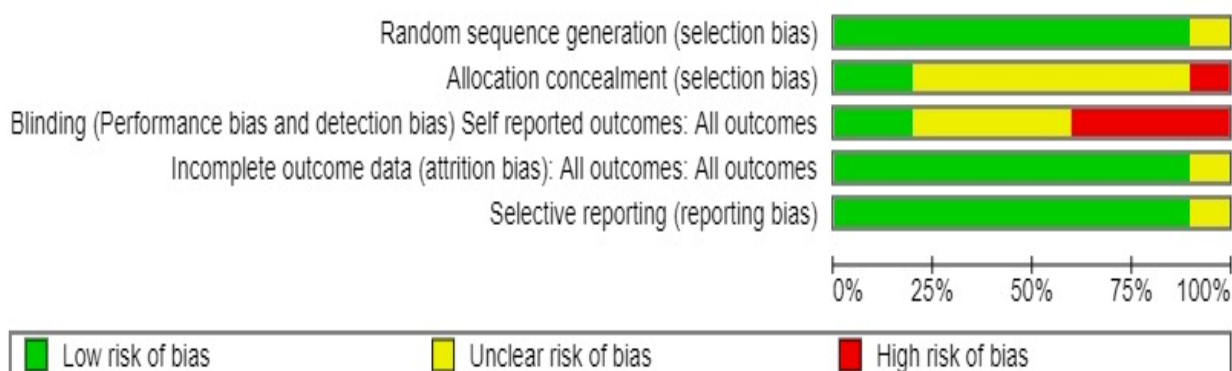
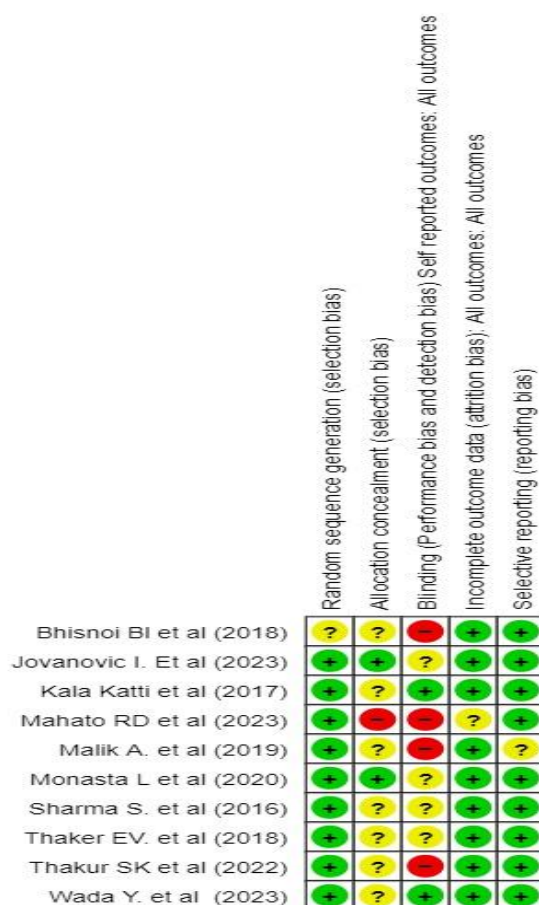
Fig1: A flowchart illustrates a systematic review that involved databases and registered searches. (PRISMA)**Fig 2: Risk of bias graph: Percentages demonstrating review authors' evaluation of each risk of bias item across all collected literatures.**

Fig 3: An illustration of the risk of bias graph showing the review authors' assumptions for each risk of bias item for each included study.



DISCUSSION

Over the past three decades, while overall perinatal mortality has declined, the incidence of intrauterine fetal death (IUFD) has risen, now surpassing early neonatal deaths. IUFD is typically detected during the antenatal period through clinical signs such as reduced or absent fetal movements, followed by physical examination findings, including the absence of fetal heart sounds. Ultrasound confirmation, which shows no fetal heart activity and lack of fetal movement, solidifies the diagnosis. [12] Placental abruption, a significant and life-threatening condition for the fetus and, to a lesser extent, the mother, contributes to these outcomes. Clinical characteristics of placental abruption show considerable variability between mild and severe cases, with distinct strengths of association between risk factors.

Man J et al. [17] (2016) highlighted that many intrauterine deaths remain unexplained despite autopsy examinations, with rates of unexplained deaths ranging from 30% to 60%. The cause of death (CoD) determination largely depends on the classification system used and subjective interpretations, leading to inconsistencies in the percentage of 'unexplained' cases, often based on speculative mechanisms of death. Additionally, **Tantengco OA et al. [18]** illustrated significant differences in maternal socio-demographic and clinical factors, as well as placental pathology, between second- and third-trimester IUFD cases. Their findings suggest distinct pathological processes and potential etiologies associated with IUFD, indicating that different mechanisms may be at play depending on the stage of gestation.

Further studies emphasize the critical role of antenatal care. **Thaker RV et al. [13]** found that most IUFD cases were linked to inadequate or absent antenatal care, with maternal conditions such as pre-eclampsia, eclampsia, antepartum hemorrhage (APH), anemia, and diabetes being leading causes of IUFD. Addressing these modifiable factors through improved health education, timely referrals, and emotional support can significantly reduce the occurrence of IUFD. Women with a

history of IUFD are at higher risk in subsequent pregnancies and thus require increased surveillance and care.

Mahato RD et al. [9] provided additional insights by demonstrating that IUFD is more common in term pregnancies (57.1%), although 40% of cases occurred preterm. Babies born with IUFD predominantly weighed between 2001 and 3000 grams. These findings align with studies by **Singh N et al.** [19] and **SR Shrestha et al.** [20] who also noted a high prevalence of term IUFD, though **Thakur A et al.** [10] found preterm fetus were more commonly affected.

Despite advances in perinatal care, the rising incidence of IUFD calls for enhanced strategies to improve outcomes. Inadequate antenatal care and maternal health conditions like pre-eclampsia and diabetes are key contributing factors. Efforts to reduce IUFD should focus on improving antenatal education, timely healthcare access, and better surveillance, particularly for high-risk pregnancies. Future research should aim to refine methods of fetal well-being assessment and explore the complex mechanisms leading to IUFD, ultimately improving maternal-fetal health and reducing IUFD incidence.

CONCLUSION: From the present systematic review, we can conclude that maternal health issues, particularly hypertension, diabetes, and fetal growth restrictions, are significant contributors to intrauterine fetal death (IUFD). Complications such as placental abruption and emotional distress also affect maternal outcomes. Regular antenatal care is essential for the early detection and management of risk factors, which could prevent many cases of IUFD. Many instances remain unexplained, underscoring the need for further research and improved diagnostic protocols. Overall, enhancing maternal healthcare and implementing timely interventions can reduce IUFD rates and improve maternal outcomes.

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