

# Maternal and Fetal Risk Factors Associated with Stillbirth: A Scoping Review

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## Abstract

Stillbirth is most commonly caused by problems that arise during pregnancy. Some of the major causes of stillbirth include infections within the uterus, lack of oxygen during birth, high blood pressure, eclampsia, premature labor, and inadequate prenatal care. The study aimed to examine whether Maternal and Fetal Risk Factors are associated with stillbirth. A six-stage scoping review framework was utilized by the Saudi Digital Library SDL, which includes a variety of databases such as ScienceDirect, EBSCO, PUBMED, BIOMED CENTRAL, CINAHL, and Google Scholar, and was searched for studies examining the association of Maternal Risk Factors and Fetal Risk Factors associated with stillbirth. The studies addressed maternal and fetal risk factors for stillbirth and conditions among pregnant women with dead fetuses. There was a spectrum of risks; Obesity, maternal medical history, anemia, hypertension, and diabetes mellitus, placentas, and pathology of the placenta were the most common risks of stillbirth. Further research attempts to conceptualize stillbirth risk factors and explore them. perspective is needed to help inform stillbirth reduction strategies and efforts to prevent and reduce the scale of stillbirth. 19 studies met the inclusion criteria for this review, Pregnancy complications are the main cause of stillbirth. Maternal health conditions, birth asphyxia, eclampsia, preterm labor, and insufficient prenatal care are significant contributors to stillbirth.

**Keywords:** Fetal death, Fetal outcome, Maternal outcome, pregnancy, Risk factors, and Stillbirth.

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## INTRODUCTION

The scoping review will assist us in covering and summarizing several studies on the maternal and fetal risk factors associated with stillbirth. The data search was done using the Saudi Digital Library SDL, which includes a variety of databases such as (ScienceDirect, EBSCO, PUBMED, BIOMED CENTRAL, CINAHL, and Google Scholar, and only the English language was used. Pregnancy complications are the main cause of stillbirth. Intrauterine infection, birth asphyxia, hypertension, eclampsia, preterm labor, and insufficient prenatal care are significant contributors to stillbirth (Shakeel *et al.*, 2023).

The most common causes of stillbirth include bleeding before or during labor, placental abruption, infections, birth defects, poor lifestyle choices, lupus, clotting disorders, trauma, intrahepatic cholestasis of pregnancy (ICP), or obstetric cholestasis (Obiegbusi *et al.*, 2023; NHS, 2018). In Hamad Women's Hospital,

Doha, Qatar, the stillbirth rate for the multiethnic population is 7.81 per 1000 births. Maternal medical factors comprised 52.4%, while the rates of hypertensive disorders, diabetes, and other medical disorders were 22.5%, 20.8%, and 8.3%, respectively. The most common fetal factor was intrauterine growth restriction (IUGR) (22.5%), followed by congenital anomalies (21.6%) (Afzal, Saleh, & Lindow, 2017).

Compared with other causes of death, an accurate cause cannot often be identified through verbal autopsy or clinical observation, and, in some settings, more than 75% of all stillbirths have unknown causes (Patterson *et al.*, 2019). These gaps in understanding the causes of stillbirth have probably contributed to the slow progress in reducing stillbirth incidence. In most developing countries, in the absence of cost-recovery mechanisms, stillbirth is a significant health and economic loss, largely due to direct healthcare costs incurred during medical investigations; long-term mental health impacts on grieving parents, and adverse health

consequences on surviving siblings. Stillbirth has become a visible maternal and child health agenda in the era of the Sustainable Development Goal (SDG) (Poudel *et al*, 2020). The use of appropriate charts to assess fetal growth in pregnancy is essential for recognizing risk factors and prompting timely management for prevention (Gardosi, & Hugh, 2023).

Asia is home to over half of the estimated global stillborn babies; and the burden of stillbirth is inequitably distributed across Asia: the reported rate is as high as 26 per 1000 births in South Asia, and as low as 7 per 1000 births in East Asia (Poudel *et al*, 2020; Lawn *et al*, 2016). In the Poudel *et al* 2020 study, a lack of fetal movement and fetal complications were found to be associated with stillbirth. Several socio-demographic variables were found to be the determining factors for stillbirth in South Asia. The association between lower socioeconomic status and higher stillbirth in this review is in agreement with a previous study conducted in other developing countries by Giang *et al*, (2019).

Poudel, *et al* 2020 highlighted that preterm labor, maternal hypertensive disorder, advanced maternal age, poor household wealth status, lower or no educational status, and lack of antenatal care were associated with stillbirth in countries in South Asia such as Nepal, Bhutan, India, Maldives, Bangladesh, Sri Lanka, Pakistan, Afghanistan. To address the problem of stillbirth and achieve maternal, neonatal, and child health outcomes. There is a greater need for scoping reviews to find more possible fetal risk factors associated with stillbirth.

**Purpose**

The scoping review aimed to identify the Maternal and Fetal Risk Factors associated with stillbirth

**The following are specific research objectives**

This scoping review set out to compile and analyze all of the existing literature on the topic of maternal and fetal risk factors associated with stillbirth,

and then present the findings. The major goal of this evaluation was to assess the state of knowledge about the potential links between maternal and fetal risk factors and stillbirth to gather relevant data on this subject.

**METHODS (SEARCH STRATEGY)**

The scoping review helps to discuss and summarize several types of research that have looked at the Maternal and Fetal Risk Factors Associated with Stillbirth. The data search was done using the Web of six electronic databases there are ScienceDirect, EBSCO, PUBMED, BIOMED CENTRAL, CINAHL, and Google Scholar, and only the English language was used. PRISMA, an add-on for conducting scoping reviews, was used to search. Also, the relevant terms used to search were identified, and then the searches were conducted based on the research question. The PRISMA guides systematic searches for relevant papers for reviews and meta-analyses. This involves choosing search phrases and databases.

**Search Terms**

The relevant terms used to search were identified (Table 1), and then the searches were conducted based on the research question. The specific search terms for the database search are listed in the following:

1. The following MeSH terms and words were combined to construct systemic searches:
2. ‘Maternal OR Mom OR Mother, OR Motherhood OR Motronly OR Motherly AND fetal OR Fetal-stage OR Antenatal OR Embryonal AND ‘Association OR Connection OR Relationship OR Correlation OR Affiliation OR Relation OR Interaction AND risks OR risk OR Hazards OR Dangers AND Stillbirth OR Fetal demise OR Fetal mortality OR Antepartum death OR Intrauterine death OR Perinatal death’. Also, manually searching the reference lists of the included studies and relevant reviews was done to identify additional studies. please see Table 1.

**Table 1: Search methods**

|   |
|---|
| Maternal [Mesh]   |
| ‘Maternal OR Intrapartum stage OR Antenatal’  |
| ‘fetal OR Fetal-stage OR Antenatal OR Embryonal’  |
| ‘Association OR Connection OR Relationship OR Correlation OR Affiliation OR Relation OR Interaction’        |
| Stillbirth OR Fetal demise OR Fetal mortality OR Antepartum death OR Intrauterine death OR Perinatal death’ |

They were used in the search engines that were identified through a series of brainstorming and searching a thesaurus, the database, and preexisting knowledge on the topic. The thesaurus helped in finding and using the control terms to ensure accurate and high-level coherency among the terms. Furthermore, the thesaurus helped control the narrowing and broadening of the search. The search was restricted to the English language. Following the studies’ selection, some references in the studies were also selected.

Subsequently, the results were screened based on the inclusion and exclusion criteria. These criteria allowed a broad search to be conducted while keeping the scope as precise as possible. the year of publication was restricted from 2010 to 2023. However, the rationale was used to exclude papers in these spread hits to maintain the chain of evidence.

**Inclusion Criteria**

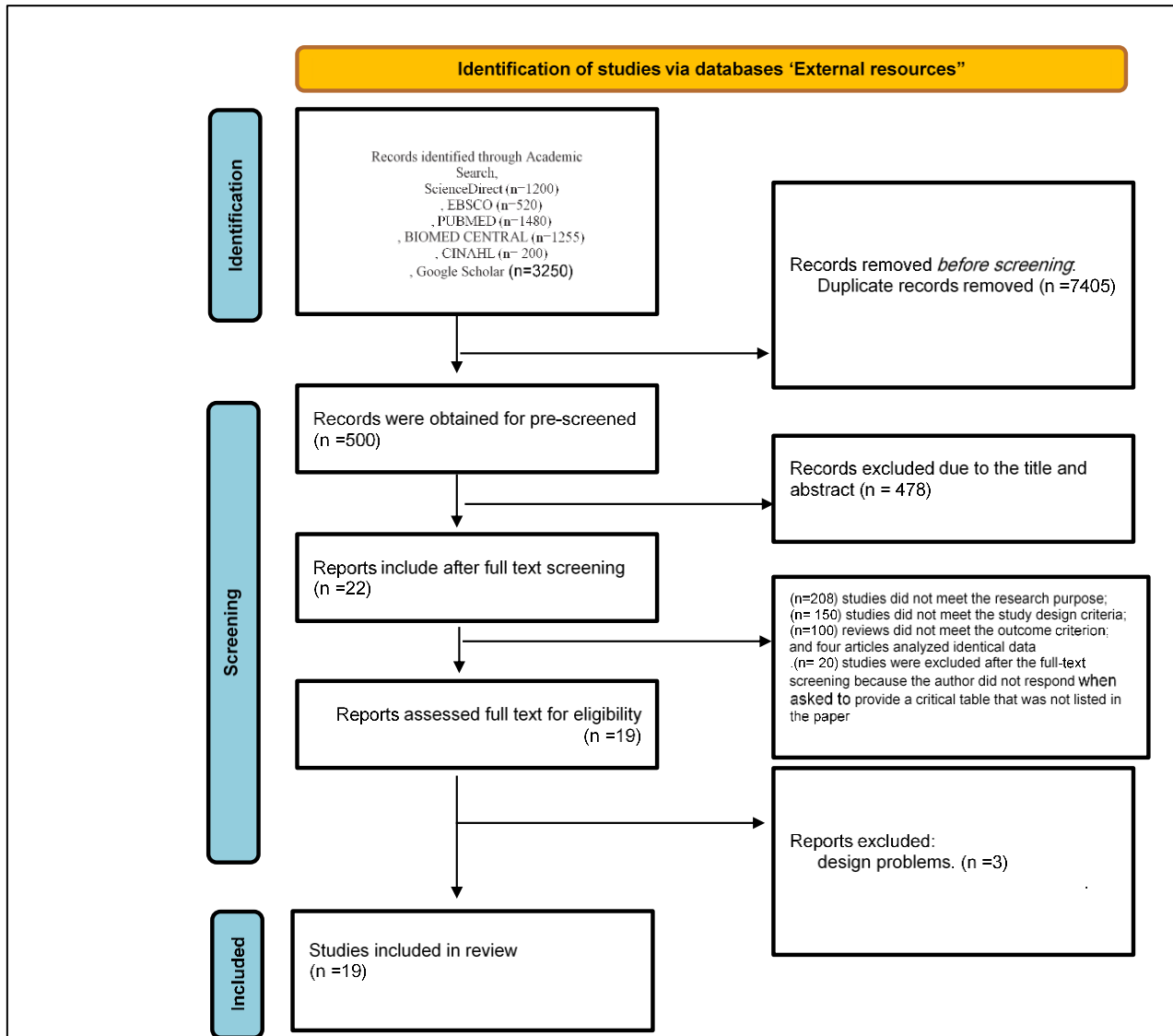
- Articles related to search terms that influence artificial intelligence and nursing practice.
- Published from 2010 to 2023
- Full-text studies
- English language papers

- Systematic reviews.

A total of 12 studies were included in the full-text screening. 19 studies met the inclusion criteria and were incorporated into the study (Figure 2).

### Prisma diagram

#### Exclusion criteria



## RESULTS

### Findings and results

A total of 19 studies were found: 1 case study, 8 retrospective cohort studies, 1 retrospective cross-sectional study, 1 qualitative semi-structured interview, 5 case-control studies, 1 cross-sectional study, 1 prospective study, and 1 systematic review. This research focused on the following locations: 3 studies in the KSA, 3 in Australia, 2 in the United States, 3 studies in the UK, and one study each in Ghana, Iran, Netherlands, France, Greece, Sweden, India, and Jordan. The distribution of these studies was then mapped according to the data extraction table in Appendix 3.

The study's findings were presented and obtained through the analysis, comparison, and contrast of the information from the studies. The researcher found 8 studies that have assessed maternal risk (appendix III). Additionally, 2 studies have investigated the fetal risk factors (Turner *et al.*, 2021; Heinke *et al.*, 2020), 3 studies have mentioned the placental risk factors (Åmark *et al.*, 2021; Patel *et al.*, 2023; Konstantinidou *et al.*, 2022), 2 studies have mentioned the pre-pregnancy risk factors (Hajipour *et al.*, 2019; Ikedionwu *et al.*, 2020), only one study stated mothers' experiences and knowledge about behavioral risk factors for stillbirth (Escañuela *et al.*, 2023), and finally 4 studies have mentioned rate and risks of stillbirth (Widdows *et al.*,

2021; Mathieu *et al.*, 2023; Mohamed *et al.*, 2021, and Shattnawi *et al.*, 2020).

### 1. Rate and risk factors of stillbirth

Four studies have mentioned the rate and risks of stillbirth (Widdows *et al.*, 2021; Mathieu *et al.*, 2023; Mohamed *et al.*, 2021, and Shattnawi *et al.*, 2020). In England, the total stillbirth rate declined from 4.2 to 3.4 per 1,000 births between the two time points. There was a contemporaneous increase in the induction of labor and emergency Caesarean section. The number of ultrasound scans performed and the proportion of small for gestational age infants detected also increased. The rate of fetal death varied between 1.3 % and 2.1 %, with an average of 1.8 % over the 6 years (Mathieu *et al.*, 2023). Poor antenatal care, obesity  $\geq 30$  kg/m<sup>2</sup>, and preeclampsia were the main risk factors associated with fetal death in this group. Four hypertensive crises were reported. The main causes of fetal death were obstetric complications, particularly intrapartum fetal death with labor-associated asphyxia under 26 weeks, and placental abruption. Maternal-fetal infections were common, particularly mosquito-borne diseases (e.g., Zika virus, dengue, and malaria), re-emerging infectious agents such as syphilis, and severe maternal infections. 19.3 % of fetal deaths remained unexplained (Mathieu *et al.*, 2023). According to a Saudi study in Hail Maternity and Children Hospital, the perinatal mortality rate at Hail Maternity and Children Hospital was 24.9/1000 by 2019 in which Intrauterine growth retardation (IUGR) was the most distinguishable cause, followed by unexplained death (Mohamed *et al.*, 2021). In Jordan, the rate of stillbirth was 9.9 per 1000 total births. Although the rate of stillbirth is lower than that in other countries in the region, there is an opportunity to prevent such deaths. While the majority of stillbirths occurred during the antepartum period (Shattnawi *et al.*, 2020)

### 2. Maternal Risks

Follow-up analysis identified that Saudi women had a high prevalence of gestational and pregestational diabetes. This increased the risk of macrosomia, preterm delivery, stillbirth, and neonatal intensive care unit admission (Dallak *et al.*, 2022). Maternal prenatal mental health disorders appear to be associated with a moderate increase in the risk of stillbirth and infant mortality, although the mechanisms are unclear (Adane *et al.*, 2021).

A history of stillbirth remains an important risk for recurrent stillbirth, especially in early gestation (22–28 weeks). Women with a previous stillbirth should be counseled for elective induction in the subsequent pregnancy at 37–38 weeks of gestation to decrease the risk of perinatal death (Nijkamp *et al.*, 2022). Approximately one-fourth of the effect of obesity on the risk of stillbirth in term pregnancies is explained by umbilical cord-associated pathology (Åmark *et al.*, 2021). The rate of stillbirth was higher among macrocosmic infants born to mothers with obesity

compared to those without. After controlling for confounding, women with obesity types II and III were at increased risk for stillbirth (Ikedionwu *et al.*, 2020).

Advanced maternal age, absence of antenatal visits, low level of education, tobacco addiction, pre-eclampsia/eclampsia, APH, and PROM in pregnancy were the major risk factors associated with stillbirth. Uteroplacental vascular pathology, chorioamnionitis, chronic inflammation, retroplacental hematoma, and calcific changes were the most significant placental lesions associated with stillbirth (Patel *et al.*, 2023).

In Saudi Arabia, it was shown that COVID-19 directly impacts pregnancy and its results, there is evidence that the pandemic and its impact on healthcare systems have had serious consequences on pregnancy outcomes, including an increase in stillbirths and maternal death (Al-Zahrani *et al.*, 2022) These patterns might signify growing gaps and a worrisome reversal of recent advancements in mother and newborn health. Preterm birth is significantly associated with old age, multiparity, and a history of preterm delivery. Preterm birth is not significantly associated with having a confirmed COVID-19 infection at delivery (Alhumaidan *et al.*, 2023).

In the UK, Khalil *et al.*, (2020) demonstrated a rise in the incidence of stillbirths during the pandemic. Possible direct result of SARS-CoV-2 infection. Surveillance studies in pregnant women found that up to 90% of SARS-CoV-2 positive cases were asymptomatic, even though no women with COVID-19 had stillbirths during the pandemic era. Additionally, national policy in the UK restricted testing to those with severe symptoms necessitating hospitalization until very recently. The rise in stillbirths could have been the consequence of a combination of factors, including a reluctance to seek medical attention when it was warranted (such as in the case of diminished fetal movements), fear of infection, or a desire to avoid adding to the National Health Service's workload. Because of staffing constraints or decreased antenatal visits, ultrasound scans, and/or screening, changes in obstetric services may have had an impact. Even though there were noticeable demographic variations between the two time periods, a lower proportion of nulliparous and hypertensive women during the pandemic period should have been associated with a decreased incidence of stillbirth. However, as women may have had fewer in-person antenatal appointments due to the pandemic, hypertension during pregnancy may have been underdiagnosed.

### 3. Placental Risks

Three studies have mentioned the placental risk factors (Åmark *et al.*, 2021; Patel *et al.*, 2023; Konstantinidou *et al.*, 2022). A long and hypercoiled cord, cord thrombosis, and velamentous cord insertion were stronger risk factors for stillbirth in obese women compared to normal-weight women. When these



variables were adjusted for in the logistic regression analysis, also adjusted for potential confounders (Åmark *et al.*, 2021). A prospective multicenter study of non-vaccinated pregnant women affected by coronavirus disease 2019 in Greece from April 2020 to August 2021 found that placentas of all six stillborn cases showed severe and extensive histological changes typical of SARS-CoV-2 placentas, characterized by a combination of marked interventions with a mixed inflammatory infiltrate and massive perilous fibrinoid deposition with trophoblast damage, associated with intensely positive immunostaining for SARS-CoV-2 spike protein, the presence of virions on electron microscopy and positive reverse-transcription polymerase chain reaction test of placental tissues. The histological lesions obliterated over 75% of the maternal intervillous space, accounting for intrauterine fetal death (Konstantinidou *et al.*, 2022).

#### 4. Mothers' experiences and knowledge about lifestyle risk factors

Only one study stated mothers' experiences and knowledge about behavioral risk factors for stillbirth (Escalañuela *et al.*, 2023). Women spoke about behavior change in terms of outcomes, and most changes (e.g., ceasing alcohol consumption) were perceived as easy to manage. Awareness of stillbirth was limited among the women interviewed, and the association between risk behaviours and stillbirth was not known to any woman. Results suggest that there is a silence around stillbirth, including in antenatal care, which hinders information provision. However, most women highlighted the value of receiving information and extra education about modifiable risk factors and stillbirth.

Nonterah *et al.* (2020) found that there is a modest decline in the stillbirth rate, but the stillbirth rate is still relatively high. Primiparous women and preterm deliveries leading to low birth weight are identified factors that result in increased stillbirths. Women should be informed that consumption of caffeine during pregnancy is associated with an increased risk of stillbirth, particularly at levels greater than recommended by the WHO (more than 300mg/day). Recommendations from midwives and internet-based resources are likely to be 51 the most effective means to influence maternal behavior (Heazell *et al.*, 2021). Sleeping more than 9 hours per night in the last month of pregnancy was associated with stillbirth, as was waking on the right side. No restless sleep in the last month was also found to be associated with stillbirth, with good sleep quality in the last month approaching significance. On the last night of pregnancy, not waking more than one time was associated with stillbirth (O'Brien *et al.*, 2019).

#### 5. Pre-pregnancy maternal risks

Two studies have mentioned the pre-pregnancy risk factors (Hajipour *et al.*, 2019; Ikedionwu *et al.*, 2020). The rate of stillbirth was higher among macrosomic infants born to mothers with obesity in pre-pregnancy compared to those without. After controlling

for confounding, women with obesity types II and III were at increased risk for stillbirth (Hajipour *et al.*, 2019). There are several risk factors for stillbirth, including a previous history of stillbirth, miscarriage, or irregular menstrual cycle, most of which can be controlled through pre-pregnancy training. Educational interventions are, therefore, required to improve the knowledge of women of childbearing age, and preventive measures should be taken to reduce the number of stillbirths in pregnant (Ikedionwu *et al.*, 2020).

#### 6. Fetal risks

Two studies have investigated fetal risk factors (Turner *et al.*, 2021; Heinke *et al.*, 2020). Decreased fetal movements (DFM) were not associated with higher odds of stillbirth after 28 weeks of gestation. Turner *et al.*, 2021 finding was consistent regardless of several presentations or gestational age at the first presentation with DFM. However, these results suggest that the risk of stillbirth may be increased among women with 2 or more presentations of DFM compared with women with 1 presentation. These results reiterate the importance of recognition of DFM as a surrogate associated with placental dysfunction and possible fetal growth restriction (Turner *et al.*, 2021). Birth defect-specific stillbirth risk was high compared with the U.S. stillbirth risk (6/1,000 fetuses), even for isolated cases of oral clefts and limb defects; elective termination may appreciably bias some estimates (Heinke *et al.*, 2020).

### DISCUSSION

The primary objective of this review is to synthesize the results of the study that posed the topic of how maternal and fetal risk factors are associated with stillbirth over the next decade and beyond. The next sections will talk more about how the results affect clinical practice, policy, administration, education, and research.

Four studies with our results about the rate and risks of stillbirth (Widdows *et al.*, 2021; Mathieu *et al.*, 2023; Mohamed *et al.*, 2021, and Shattnawi *et al.*, 2020). Most of these papers also agreed that the main causes of fetal death were obstetric complications, particularly intrapartum fetal death with labor-associated asphyxia under 26 weeks, and placental abruption. Maternal-fetal infections were common, particularly mosquito-borne diseases (e.g., Zika virus, dengue, and malaria), re-emerging infectious agents such as syphilis, and severe maternal infections. 19.3 % of fetal deaths remained unexplained. Changes in lifestyle, as well as social deprivation and isolation, adversely affect pregnancy in Western French Guiana, in the context of a poor healthcare system that is similar to what is found in the Amazonian basin. Particular attention must be paid to emerging infectious agents in pregnant women and travelers returning from the Amazon region.

Nine studies conducted by (Al-Zahrani *et al.*, 2022; Alhumaidan *et al.*, 2023; Dallak *et al.*, 2022; Khalil *et al.*, (2020); Patel *et al.*, 2023; Ikedionwu *et al.*, 2020; Åmark *et al.*, 2021; Nijkamp *et al.*, 2022; Adane *et al.*, 2021) agree with our findings about maternal risks and most of them agree that In Saudi Arabia, it was shown that COVID-19 directly impacts pregnancy and its results, there is evidence that the pandemic and its impact on healthcare systems have had serious consequences on pregnancy outcomes, including an increase in stillbirths and maternal death. These patterns might signify growing gaps and a worrisome reversal of recent advancements in mother and newborn health. Preterm birth is significantly associated with old age, multiparity, and a history of preterm delivery.

Preterm birth is not significantly associated with having a confirmed COVID-19 infection at delivery. Advanced maternal age, absence of antenatal visits, low level of education, tobacco addiction, pre-eclampsia/eclampsia, APH, and PROM in pregnancy were the major risk factors associated with stillbirth. Uteroplacental vascular pathology, chorioamnionitis, chronic inflammation, retroplacental hematoma, and calcific changes were the most significant placental lesions associated with stillbirth. In addition, 2 studies have investigated fetal risk factors (Turner *et al.*, 2021; Heinke *et al.*, 2020) and agree with our findings and show that regardless of several presentations or gestational age at the first presentation with DFM. However, these results suggest that the risk of stillbirth may be increased among women with 2 or more presentations of DFM compared with women with 1 presentation, and this mentioned the importance of recognition of DFM as a surrogate associated with placental dysfunction and possible fetal growth restriction.

Three studies have mentioned the placental risk factors (Åmark *et al.*, 2021; Patel *et al.*, 2023; Konstantinidou *et al.*, 2022) and show that inflammation tended to be a mediator on the pathway from BMI to stillbirth. Obesity is associated with increased levels of inflammatory markers. This, in turn, contributes to the increased risk of hypertensive disorders and other common complications in pregnancies with obesity. It is also possible that inflammation associated with obesity contributes to the increased risk of stillbirth. In an animal model, it was demonstrated that a high-fat diet during pregnancy increased placental inflammation and decreased uteroplacental perfusion, regardless of obesity. SARS-CoV-2 placentas occurred uncommonly in COVID-19-affected pregnancies of non-vaccinated mothers, appeared to evolve rapidly, and, when extensive, caused fetal demise, with no evidence of transplacental fetal infection. Thrombophilia and prenatally detected FGR emerged as independent predisposing factors for the potentially lethal SARS-CoV-2 placentas. advanced maternal age, absence of antenatal visits, low level of education, tobacco

addiction, pre-eclampsia/eclampsia, APH, and PROM in pregnancy were the major risk factors associated with stillbirth. Uteroplacental vascular pathology, chorioamnionitis, chronic inflammation, retroplacental hematoma, and calcific changes were the most significant placental lesions associated with stillbirth.

Only one study stated mothers' experiences and knowledge about behavioral risk factors for stillbirth (Escañuela *et al.*, 2023), and the study shows that there is a general lack of understanding of the link between behavioral risk factors and potential pregnancy outcomes such as stillbirth. Providing further information to women about stillbirth and providing additional support with behavior change might contribute to enhancing preventive efforts.

In addition, two studies agree with our findings and have mentioned the pre-pregnancy risk factors (Hajipour *et al.*, 2019; Ikedionwu *et al.*, 2020) and show that increased maternal age is an independent risk factor for stillbirth even after controlling the effect of maternal morbidities. They did not find a significant relationship between higher maternal age and the risk of stillbirth, which is attributed to the elimination and exclusion of congenital anomalies. Since a higher maternal age increases the risk of congenital anomalies, the relationship between maternal age and stillbirth remains unidentified after eliminating and excluding these factors. Obesity-related fetal overgrowth is a significant risk factor for stillbirth, especially among women with type II and type III obesity. This finding highlights the need for more effective clinical and public health strategies to address pre-pregnancy obesity and to optimize gestational weight gain.

### Implications

Educating pregnant women and their families about the identified risk factors can empower them to make informed decisions and adopt appropriate lifestyle changes. This could include educating women about the importance of prenatal care, healthy lifestyle choices, and recognizing warning signs during pregnancy. Healthcare administrators may need to allocate resources to support the implementation of screening protocols, risk reduction strategies, and enhanced prenatal care services as recommended by the study findings. (Nonterah *et al.*, 2020).

Policymakers may use the study findings to inform public health policies aimed at reducing stillbirth rates. This could involve allocating resources for research, developing guidelines for prenatal care, implementing quality improvement initiatives in healthcare facilities, and promoting community-based interventions targeting at-risk populations (Brackett *et al.*, 2020). The study findings may prompt healthcare systems to enhance prenatal care services, ensuring timely access to healthcare facilities, specialist consultations, and diagnostic tests for high-risk

pregnancies. This may involve multidisciplinary approaches involving obstetricians, neonatologists, midwives, and other healthcare professionals (Dube *et al.*, 2021).

The study may highlight gaps in current knowledge and areas requiring further research. This could include investigating the mechanisms underlying the identified risk factors, evaluating the effectiveness of interventions aimed at reducing stillbirth rates, and conducting longitudinal studies to monitor trends in stillbirth rates over time (Ashoor *et al.*, 2022).

### Limitations

This scoping review has some limitations. For example, to make the review practical, only data were used, despite the stillbirth risk factors are an emerging healthcare issue. Furthermore, the quality of the results was not assessed. The pressure to share information rapidly might impact the quality of studies published, as some of them might overlap.

## SCOPING REVIEW CONCLUSION AND RECOMMENDATION

This scoping review identified 19 studies that addressed maternal and fetal risk factors for stillbirth and conditions among pregnant women with dead fetuses across various healthcare settings. In summary, there was a spectrum of the risks. Obesity, diabetes mellitus, placentas, and the pathology of placental history to stillbirth were the most common risks of stillbirth. Unexpected decreased fetal movements weren't a risk factor to stillbirth according to our review. Care should be taken for the early identification of high-risk pregnancies, and stillbirth risk factors including the early detection of risks, and ensuring adequate antenatal obstetric interventions to reduce the rate of stillbirth.

Data were also collected on vertical transmission and potential vertical transmission. Efforts aimed at impacting stillbirths should include the elimination of outmoded cultural practices. Health systems strengthening especially in the utilization of antenatal care services and skilled attendants at delivery are essential in improving fetal-maternal outcomes.

There is a need for developing and implementing effective interventions that minimize the modifiable risk factors of stillbirth, such as improving the health and nutritional status of pregnant women, antenatal care, healthy behavior during pregnancy, control of overweight/ obesity, and smoking cessation. The interventions need a greater focus on timely management of preterm labor, maternal hypertension, and provision of financial support for quality antenatal and delivery care and should be targeted for women living in remote areas, who are less educated, and those with low socioeconomic status. Further, the quality of maternal and child health care services should be

improved with assurance of access to and availability of trained health care providers, quality equipment and medication, and emergency neonatal care services at health facilities around the clock

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## Appendix 2

### Literature search strategy

The following databases were searched:

- Cochrane Library
- Medline
- Embase
- The official journal of the Saudi Society of hematology
- CINAHL
- Science Direct

|  |  |
|--|--|
| <b>The search strategy was to combine searches of:</b><br>"Maternal" related terms<br>"Fetal" related terms<br>"Risk Factors" related terms<br>"Stillbirth" related terms<br>"Associated with" related terms<br>"A retrospective cohort study, 2023" related terms | <b>Maternal terms</b><br>Pregnant women<br>Mothering<br>The mother's<br>Mother<br>Maternity<br>Women's<br>Maternal<br>Mama<br>The maternal<br>Motherhood                         |
| <b>Fetal terms</b><br>Infant<br>Fetus<br>Baby<br>Pregnancy product   | <b>Risk Factors Terms</b><br>Risk elements<br>Danger Factors<br>Hazard Factors<br>Risk signs<br>Potential Factors<br>Threat Factors<br>Potential danger Factors<br>Risky Factors |
| <b>Stillbirth terms</b><br>Stillbirth<br>Death before 28 weeks of gestation<br>Death of pregnancy product<br>The stillbirth<br>Having a dead fetus<br>Pregnancy outcome<br>fetal stillbirth<br>Being stillborn<br>A stillborn baby                                 | <b>Associated with terms</b><br>Connected with<br>Related to<br>Linked to<br>Connected to<br>Concerned with<br>Relevant to<br>In relation to                                     |

## Appendix 3

### Literature review Matrix

| Author Year | Aim of the Study | Research Design | Participants | Key Finding and Implications |
|-------------|------------------|-----------------|--------------|------------------------------|
|-------------|------------------|-----------------|--------------|------------------------------|

|  |  |  |   |   |
|--|--|--|---|---|
| Escañuela Sánchez <i>et al.</i> , 2021 | to explore women's experiences of modifiable factors during pregnancy and their awareness of stillbirth.                             | qualitative semistructured interview study | Eligible women were primiparous, >18 years of age and had an uncomplicated pregnancy and delivery. Eighteen women who consented to be followed up were interviewed at 3–5 months postpartum | There is a general lack of understanding of the link between behavioural risk factors and potential pregnancy outcomes such as stillbirth.  |
| Heinke <i>et al.</i> , 2020            | To estimate the risk of stillbirth (fetal death at 20 weeks of gestation or more) associated with specific birth defects.            | retrospective cohort                       | neonates and fetuses  | Birth defect-specific stillbirth risk was high compared with the U.S. stillbirth risk (6/1,000 fetuses), even for isolated cases of oral clefts and limb defects; elective termination may appreciably bias some estimates. These data can inform clinical care and counseling after prenatal diagnosis.  |
| Mohammed <i>et al.</i> , 2021          | to identify the perinatal mortality rate in Hail Maternity and Children Hospital and to find the underlying causes and risk factors. | retrospective analytic study               | whole perinatal deaths in Hail Maternity and Children Hospital, from 1st of January to 31st of December 2019  | The perinatal mortality rate at Hail Maternity and Children Hospital was 24.9/1000 by 2019 in which IUGR was the most distinguishable cause, followed by unexplained death. Due to the lack of such a study in this hospital, we couldn't find if our results considered as an improvement or deterioration of PMR comparing with past years.   |
| Alhumaidan <i>et al.</i> , 2023        | to investigate the effects of COVID-19 infection on preterm birth in pregnant women in the Al-Qassim region of Saudi Arabia.         | retrospective cohort study                 | pregnant women  | It was shown that preterm birth is evident among women with COVID-19 infection. Preterm birth is significantly associated with old age, multiparity, and a history of preterm delivery. Preterm birth is not significantly associated with having a confirmed COVID-19 infection at delivery. More research regarding infection-related adverse effects is advised and should be highlighted. |
| Dallak, <i>et al.</i> , 2022           | to measure the prevalence of adverse birth outcomes and associated factors among mothers from the Jazan region in Saudi, Arabia.     | cross-sectional investigation              | women who'd had a history of pregnancy and resided in Jazan   | this study found a relatively high prevalence of adverse birth outcomes, with the most frequently reported being miscarriage.   |
| Adane <i>et al.</i> , 2021             | To examine whether maternal prenatal mental health disorders are   | Systematic reviews and Meta-Analyses       | MEDLINE, Embase, PsycINFO, and Scopus were searched for studies examining the   | We found no significant evidence of publication bias. Maternal prenatal mental health disorders appear to be  |



|                                      |  |                               |   |   |
|--------------------------------------|--|-------------------------------|---|---|
|                                      | associated with stillbirth and/or infant mortality.  |                               | association of any maternal prenatal (occurring before or during pregnancy) mental health disorder(s) and stillbirth or infant mortality. | associated with a moderate increase in the risk of stillbirth and infant mortality, although the mechanisms are unclear. Efforts to prevent and treat these disorders may reduce the scale of stillbirth/infant deaths.   |
| O'Brien, <i>et al.</i> , 2019        | To investigate and an international call heart with the maternal is the practice are Related to late stillbirth  | case-control study            | women who had a stillbirth $\geq 28$ weeks' gestation within 30 days  | Long periods of undisturbed sleep are associated with late stillbirth. Physiological studies of how the neuroendocrine and autonomic system pathways are regulated during sleep in the context of late pregnancy are warranted.   |
| Heazell, <i>et al.</i> , 2021        | to investigate the degree of consumption of caffeinated drinks or soft drinks in the last four weeks of pregnancy in women who experienced a late stillbirth compared to women with ongoing live pregnancies at similar gestation. | case-control study            | pregnant women.   | Women should be informed that consumption of caffeine during pregnancy is associated with increased risk of stillbirth, particularly at levels greater than recommended by the WHO ( $>300$ mg/ day). Recommendations from midwives and internet-based resources are likely to be the most effective means to influence maternal behaviour.   |
| Patel, <i>et al.</i> , 2023          | to identify the placental pathologies and maternal factors associated with stillbirth.   | case-control study            | pregnant women with a gestational age of 28 weeks   | In our study, advanced maternal age, absence of antenatal visits, low level of education, tobacco addiction, pre-eclampsia/eclampsia, APH, and PROM in pregnancy were the major risk factors associated with stillbirth. Uteroplacental vascular pathology, chorioamnionitis, chronic inflammation, retroplacental hematoma, and calcific changes were the most significant placental lesions associated with stillbirth. |
| Åmark, <i>et al.</i> , 2021          | to explore the potential role of the placenta for the risk of stillbirth at term in pregnancies of obese women.  | case-control study            | pregnant women.   | Approximately one fourth of the effect of obesity on the risk of stillbirth in term pregnancies is explained by umbilical cord associated pathology.  |
| Konstantinidou, <i>et al.</i> , 2022 | To describe the placental pathology, fetal autopsy findings and clinical characteristics of pregnancies that resulted in stillbirth owing to severe  | prospective multicenter study | non-vaccinated pregnant women affected by coronavirus disease 2019 (COVID-19) in Greece from April 2020 to August 2021.                   | SARS-CoV-2 placentitis occurred uncommonly in COVID-19-affected pregnancies of non-vaccinated mothers and, when extensive, caused fetal demise, with no evidence of transplacental fetal infection. Thrombophilia and   |

|                                 |   |                                     |  |  |
|---------------------------------|---|-------------------------------------|--|--|
|                                 | acute respiratory syndrome coronavirus 2 (SARS-CoV-2) placentitis, and to identify potential risk factors.  |                                     |  | prenatally detected FGR emerged as independent predisposing factors for the potentially lethal SARS-CoV-2 placentitis.   |
| Ikedionwu, <i>et al.</i> , 2020 | to determine the association between fetal macrosomia, maternal obesity, and the risk of stillbirth.  | retrospective cross-sectional study | DC's Birth Data and Fetal Death Data files for 2014–2017   | Obesity-related fetal overgrowth is a significant risk factor for stillbirth, especially among women with type II and type III obesity. This finding highlights the need for more effective clinical and public health strategies to address pre-pregnancy obesity and to optimize gestational weight gain.  |
| Widdows, <i>et al.</i> , 2021   | To assess implementation of the Saving Babies Lives (SBL) Care Bundle, a collection of practice recommendations in four key areas, to reduce stillbirth in England. | retrospective cohort study          | collected electronic data supplemented with case note audit (n = 1,658), and surveys of service users (n = 2,085) and health care professionals (n = 1,064). | Implementation of the SBL care bundle increased over time in the majority of sites. Implementation was associated with improvements in process outcomes. The reduction in still-birth rates in participating sites exceeded that reported nationally in the same timeframe. The intervention should be refined to identify women who are most likely to benefit and minimize unwarranted intervention. |
| Mathieu, <i>et al.</i> , 2023   | to describe the epidemiology of intrauterine fetal deaths in multiethnic western French Guiana and to assess its main causes and risk factors.                      | retrospective descriptive study     | 18,037 deliveries beyond 20 weeks of gestation.  | Change in lifestyle as well as social deprivation and isolation adversely affect pregnancy in western French Guiana, in the context of a poor health care system that is similar to what is found in the Amazonian basin. Particular attention must be paid to emerging infectious agents in pregnant women and travelers returning from the Amazon region.  |
| Turner, <i>et al.</i> , 2021    | to examine the Pregnancy outcome of women presenting with DFM in the third trimester at a tertiary Australian centre with a clinical management algorithm           | cohort study                        | All singleton births without a known congenital anomaly after 28 weeks' gestation were included.   | Prevalence of DFM was associated with increased risk for a fetus.  |
| Nijkamp, <i>et al.</i> , 2022   | to estimate gestational-age specific risks of recurrent stillbirth and to evaluate the effect of obstetrical  | retrospective cohort study          | women with two consecutive singleton pregnancies (1st and 2nd delivery) between 1999 and 2007.   | A history of stillbirth remains an important risk for recurrent stillbirth especially in early gestation (22– 28 weeks). Women with a previous stillbirth should be counselled   |

|                                |   |                            |  |  |
|--------------------------------|---|----------------------------|--|--|
|                                | management on perinatal outcome after previous stillbirth.  |                            |  | for elective induction in the subsequent pregnancy at 37–38 weeks of gestation to decrease the risk of perinatal death.  |
| Shattnawi <i>et al.</i> , 2020 | This study used the data from JSANDS to determine the rate, determinants, and contributing conditions of stillbirths in Jordan  | Retrospective cohort study | births, stillbirths and their contributing conditions, and other demographic and clinical characteristics in the period between August 2019 – January 2020                                   | Although the rate of stillbirth is lower than that in other countries in the region, there is an opportunity to prevent such deaths. While the majority of stillbirths occurred during the antepartum period, care should be taken for the early identification of high-risk pregnancies, including the early detection of SGA pregnancies, and ensuring adequate antenatal obstetric interventions.                               |
| Nonterah <i>et al.</i> , 2020  | This paper analysed the trends and the associated risk factors of stillbirths in a district hospital located in an impoverished and remote region of Ghana.   | Retrospective cohort study | All deliveries conducted in the Navrongo War Memorial hospital from 2003–2013 were retrieved and analysed.   | Despite the modest reduction in stillbirth rates over the study period, it is evident from the results that stillbirth rate is still relatively high. Primiparous women and preterm deliveries leading to low birth weight are identified factors that result in increased stillbirths. Efforts aimed at impacting on stillbirths should include the elimination of outmoded cultural practices such as Female genital mutilation. |
| Khalil et al., 2020            | evaluated the outcomes of pregnancies at St. George's University Hospital in London between two time periods: (i) October 1, 2019 through January 31, 2020 (before the first documented UK instances of COVID-19), and (ii) February 1, 2020 through June 14, 2020. | Comparative study          | Pregnancy woman between two time periods i) October 1, 2019 through January 31, 2020 (before the first documented UK instances of COVID-19), and (ii) February 1, 2020 through June 14, 2020 | The number of stillbirths during the pandemic period (n = 16 [9.31 per 1000 births]; none associated with COVID-19) was significantly higher than the number of stillbirths during the pre-pandemic period (n = 4 [2.38 per 1000 births]) (difference, 6.93 [95% CI, 1.83-12.0] per 1000 births; P = .01) (Table 2). This trend was also evident when late terminations for fetal abnormality were                                 |