Determinants of stillbirths in sub-Saharan Africa: A systematic review

Ankita Mukherjee^{1,2} | Lydia Di Stefano³ | Hannah Blencowe⁴ Paul Mee^{4,5} ¹Faculty of Public Health and Policy, London Abstract School of Hygiene and Tropical Medicine, London, UK Background: Sub-Saharan African (SSA) countries have high stillbirth rates com-²Monitoring, Evaluation and Research, New Delhi, India remain scant. ³Mercy Hospital for Women, Heidelberg, Victoria, Australia gate their strength of association using a systematic review. ⁴Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK were searched for literature. ⁵Lincoln International Institute for Rural Selection Criteria: Observational population- and facility-level studies exploring Health, College of Social Science, University stillbirth risk factors, published in 2013–2019 were included. of Lincoln, Lincoln, UK Correspondence

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pared with high-income countries, yet research on risk factors for stillbirth in SSA

Objectives: To identify the modifiable risk factors of stillbirths in SSA and investi-

Search Strategy: CINAHL Plus, EMBASE, Global Health and MEDLINE databases

Data Collection and Analysis: A narrative synthesis of data was undertaken and the potential risk factors were classified into subgroups.

Main Results: Thirty-seven studies were included, encompassing 20264 stillbirths. The risk factors were categorised as: maternal antepartum factors (0-4 antenatal care visits, multiple gestations, hypertension, birth interval of >3 years, history of perinatal death); socio-economic factors (maternal lower wealth index and basic education, advanced maternal age, grand multiparity of ≥ 5); intrapartum factors (direct obstetric complication); fetal factors (low birthweight and gestational age of <37 weeks) and health systems factors (poor quality of antenatal care, emergency referrals, illequipped facility). The proportion of unexplained stillbirths remained very high. No association was found between stillbirths and body mass index, diabetes, distance from the facility or HIV.

Conclusions: The overall quality of evidence was low, as many studies were facility based and did not adjust for confounding factors. This review identified preventable risk factors for stillbirth. Focused programmatic strategies to improve antenatal care, emergency obstetric care, maternal perinatal education, referral and outreach systems, and birth attendant training should be developed. More population-based, high-quality research is needed.

KEYWORDS

fetal death, preventable factors, risk factors, stillbirth, sub-Saharan Africa, systematic review

INTRODUCTION 1

Sub-Saharan Africa (SSA) accounts for 44% of the global late-gestation stillbirths (defined as a birthweight of \geq 1000 g or a gestational age of \geq 28 weeks),¹ contributing to roughly 2300 stillbirths every day.² Stillbirth rates (SBRs)

are substantially higher in SSA (SBR 21.7, range 19.9-24.8), compared with those in high-income regions such as North America (SBR 3.0, range 2.9–3.0).² Eight of the 10 countries with the highest burden of stillbirths globally are found in SSA.³ Although the SBRs vary across the SSA countries as a result of economic and cultural diversity, conflict-affected

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countries experience the highest rates of stillbirth.³ Hence, there is an urgent need for SSA to accelerate current progress to achieve the WHO's Every Newborn Action Plan 2030 target SBR of \leq 12 per 1000 total births in every country.⁴

Quantifying the true numbers of stillbirth and identifying their causes is challenging in SSA. This is because of the inadequate health facility infrastructure, underskilled healthcare workers and suboptimal emergency obstetric care found in low-resourced SSA countries.^{4–6} Inequitable access to health care for women from rural areas and their lower socio-economic status further complicates estimates of stillbirth burden. The low reporting of home-delivered stillbirths,^{7–9} superstition, shame,^{7,9} and stigma^{10,11} in some SSA countries contribute to the challenge.

Despite high SBRs in SSA, research evidence on the SSAspecific contextual risk factors of stillbirth is limited, highlighting the need for an SSA-centred review. A previous review on stillbirth risk factors in low- and middle-income countries (LMICs) across the globe identified advanced maternal age, higher parity, lower wealth index and education, poor antenatal care, history of stillbirth, low birthweight and gestational age as major factors.¹² However, as it focused on all LMICs, the findings may not apply to all SSA countries because of notable contextual variations between SSA and other regions. Since this review, there has been a growing body of literature focused on determining stillbirth risk factors in SSA; but no systematic review has yet pooled this evidence. There is also a gap in understanding the impact of health facility factors on stillbirths in SSA. Addressing these knowledge gaps could inform improved SBR reduction policies.⁴

We undertook a systematic review to provide an updated summary of the evidence on the determinants of stillbirths in SSA. We aimed to identify modifiable risk factors for stillbirths in SSA, factors that potentially could be addressed through individual or public health interventions, and investigate their strength of association using observational studies.

2 | METHODS

2.1 | Search strategy

The CINAHL Plus, EMBASE, Global Health and MEDLINE databases were searched for the period 2013–2019. The year 2013 was selected as the lower limit as the previous LMIC review only included studies up to the year 2013. The search terms used were 'stillb*' AND 'Africa*' AND 'determinant*' (Appendix S1).

2.2 Inclusion criteria

Observational studies performed at the population or health facility level assessing at least one risk factor for stillbirth were included, regardless of the stillbirth definition used. Studies focusing solely on subpopulations, such as mothers with comorbidity and multiple gestations, were excluded. We also excluded animal studies, trials, reviews, studies outside SSA, and languages other than English and French (Table S1). All studies assessed as being of high or medium quality using the Joanna Briggs Institute Critical Appraisal Tool were included (Table S2),¹³ with the scoring adapted from Ho et al. 2016.¹⁴ We report our findings using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁵

2.3 | Data extraction and analysis

Data were double extracted in standard MS Excel for all included articles by two reviewers (AM, LD or HB) (Table S3) and disagreements were addressed by one of the senior authors (HB). In some instances, authors of the articles were contacted to obtain full access to the articles and to gain clarity on the SBR definition used. All analyses were undertaken using STATA 13.¹⁶

2.4 Data synthesis and presentation

An SSA-specific conceptual model was developed to categorise the findings (Figure 1).^{17–19} The potential risk factors were classified into subgroups: maternal, sociodemographic and lifestyle, fetal, obstetric and delivery complications, health system and unexplained/miscellaneous factors, and further into antepartum and intrapartum factors, wherever appropriate. When two or more studies reported a risk factor, their mean and confidence intervals were used to describe the proportion of total stillbirths with that given factor. The mean SBR of population-based studies and their country-specific point difference from the 2015 estimated rates were also calculated.⁹

As a result of variations in effect-estimate measurements, study context, and definition of stillbirths and risk factors, a narrative synthesis was undertaken. The median and interquartile range (IQR) of the adjusted effect estimate were calculated for studies reporting similar risk factors. Vote counting was used to present the data.²⁰ The adjusted estimate was presented where available, whereas in its absence crude estimates were shown. The findings were prioritised on the hierarchy of evidence. Adjusted effect estimates are displayed using forest plots. This review is registered with the PROSPERO database (CRD42020145574).²¹

3 | RESULTS

3.1 | Description of studies

Thirty-seven studies met the inclusion criteria, which examined 20264 stillbirths in 19 out of 46 SSA countries (Figure 2). Twelve high-quality and 25 medium-quality studies were included. Studies with robust methodologies



FIGURE 1 Conceptual model for potential risk factors of stillbirths. Adapted from Blencowe, et al.⁸ and Di Stefano, et al.¹⁷

assessing exposures, outcomes, confounding factors and statistical analysis were considered high quality.

The included studies were obtained from Angola, Botswana, Burundi, Democratic Republic of Congo, Ethiopia, Ghana, Kenya, Liberia, Malawi, Mozambique, Namibia, Nigeria, Rwanda, Sierra Leone, South Africa, Tanzania, Uganda, Zambia and Zimbabwe (Figure 3). The mean SBRs of included population studies were considerably higher in Angola, Ethiopia and Kenya, as compared with their SBR estimates in 2015 (point difference > 15; Table S4).

Twelve studies were performed at population level, whereas the remainder were hospital based, with 15 studies conducted in at least one referral hospital. There were 17 cross-sectional studies (including two audits),^{22–37} nine cohort studies,^{38–46} eight case–control studies,^{47–54} and three case series that collected data from medical records and household surveys.^{55–57} Twenty-three studies used the International Classification of Diseases 10th Revision (ICD-10) definition of stillbirth (babies born dead at ≥28 weeks of gestation/1000 g),¹ whereas the rest used various definitions, including babies born dead at ≥20 weeks of gestation and/or with a birthweight of ≥500 g. Stillbirth was not defined in nine studies (Table S5).

3.2 | Main findings

The risk factors were classified into five categories: maternal; sociodemographic and lifestyle; fetal; obstetric and delivery; and health system and unexplained/miscellaneous factors. Figure 4 and Table S6 display the distribution and mean proportion of risk-factor attributed stillbirths reported by studies. These factors include maternal hypertension, ^{23,24,46,55,57} pre-eclampsia, ^{31,43} infection, ^{23,25,46,56,57} malaria, ^{43,56} HIV, ^{30,43} diabetes, ^{31,43,55,57} prematurity, ^{31,55,56} asphyxia,^{23,55,57} congenital abnormality,^{23-25,31,46,55-57} intrauterine fetal growth restriction (IUFGR),^{23,30,43} ruptured uterus,^{25,47,48,55} cord prolapse,^{31,43,56,57} premature rupture of membranes (PROM),^{24,50} antepartum haemorrhage placental abruption, ^{24,31,55–57} and unex-(APH),^{23,30,46,56} plained factors.^{24,25,43,55-57} The results of the forest plots are presented in Figure S7, and where studies reported the numbers of antepartum and intrapartum stillbirths separately, these are shown under the 'Remarks' in Table S3. Only 10 studies categorised factors by the time of death, with a similar proportion of stillbirths occurring antepartum (53%) and intrapartum (47%).

3.2.1 | Maternal factors

Antepartum factors

Hypertension was more prevalent in antepartum stillbirths than in intrapartum stillbirths (21% vs. 4%).⁴⁶ Three hospitalbased studies reported women with gestational hypertension having a higher likelihood of stillbirth (median aOR9.53, IQR2.10–12.83)^{22,38,50}; however, two studies demonstrated no effect.^{45,47} Similarly, a greater stillbirth risk in women with hypertensive disorders in hospital settings was observed.^{36,54} One study reported a fourfold increased aOR of stillbirth to mothers with pre-eclampsia in referral hospitals,⁴⁵ whereas another study showed no association.⁵⁰ Eclampsia showed no effect on



FIGURE 2 PRISMA chart for study selection.

stillbirths in the aOR.^{45,50,51,56} The distinction between hypertensive disorders and pre-existing and gestational hypertension was unclear in many studies; only one study clearly defined pre-eclampsia/eclampsia.

Absence or delayed antenatal care (ANC) visits (after 28 weeks of gestation) had a stillbirth prevalence of 12%-17%.³⁰ Compared with no ANC visits, according to four studies ANC visits reduced the risk of stillbirths (median aOR0.45, IQR0.30–0.60)^{34,44,48,58}; however, three studies showed no effect.^{28,35,50} Further, fewer than four ANC visits increased the odds of stillbirth,^{37,45} compared with four or more ANC visits. Not registering the pregnancy with the health facility also increased the stillbirth risk.^{51,54}

A birth interval of >33 months between the analysed and previous pregnancy substantially reduced the odds after adjusting for sociodemographic, obstetric factors and birth outcomes, compared with birth intervals of <24 months and <33 months.^{27,33} However, one study observed no effect of birth interval (<24 months) on stillbirth.⁴⁷

Only one study showed an independent association of sexually transmitted infections (STIs) with stillbirths

(aOR 5.74, 95% CI 1.10–29.70).⁴⁹ However, no effect of HIV or syphilis was evidenced with crude estimates.^{45,48,54,58} Maternal febrile illness raised the unadjusted odds of stillbirth.⁵¹ Although maternal infection was common in antepartum stillbirths compared with intrapartum stillbirths (50% vs. 11%),⁴⁶ infections (including malaria) showed no effect.^{29,50}

Pregnant women who were overweight (with body mass index, BMI > 25 kg/m²) had a higher prevalence of stillbirths than women who were underweight (BMI < 18.50 kg/m²) (11.20% vs. 4.20%),³⁰ but no direct effect of BMI was observed,^{39,50} and neither was a direct effect of diabetes observed.^{45,50,54} The type of diabetes (pre-existing or gestational) was unclear in four of seven studies that studied diabetes as a risk factor. Maternal anaemia increased the stillbirth risk in one study,⁴⁵ but showed no effect in two studies reporting adjusted estimates.^{29,48}

Multiple gestations increased the stillbirth risk, compared with singleton pregnancies (median aOR 2.57, IQR 3.75–4.93).^{33,37} Compared with no history, a history of perinatal death (median aOR 10.40, IQR 6.16–13.90),^{22,33,49}



FIGURE 3 Geographical distribution of included studies and stillbirth rates: (a) distribution of included studies; (b) stillbirth rate estimates of included studies.



Proportion of stillbirths linked to risk factors

FIGURE 4 Distribution of risk factors for stillbirths in included studies. Abbreviations: APH, antepartum haemorrhage; IUFGR, intrauterine fetal growth restriction; PROM, premature rupture of membranes. Preterm defined as gestational age below 37 weeks. IUFGR defined as birthweight less than 10th percentile for the gestational age.

or a history of stillbirth (median aOR 3.62, IQR 3.46–3.79),^{32,37} acted as a determinant of a subsequent stillbirth. Some studies reporting aORs observed no effect of multiple gestation,⁴⁸ history of abortion,⁴⁹ or history of perinatal death on stillbirths.^{26,37}

3.2.2 | Sociodemographic and lifestyle factors

An advanced maternal age (AMA) of \geq 35 years acted as an independent stillbirth risk factor, compared with women aged <35 years.^{27,45} Further, the stillbirth risk doubled for women aged over 30 years, as noted by one study comparing against women aged under 30 years,²⁸ and another study comparing against women aged under 20 years.²⁶ Conversely, young women aged <20 years had higher odds of stillbirth than women aged >35 years in one study.²⁷ Stillbirth risk increased fourfold when mothers were aged 40–49 years, relative to mothers aged <30 years.²⁸ Some studies, however, observed no effect of advanced maternal age on stillbirths.^{25,32,51,52,58}

Women with no schooling had higher adjusted odds of stillbirths relative to women with primary education,²⁷ at least secondary education,²⁶ and tertiary education.⁴⁹ Further, in one study, women with primary education had an aOR of 1.64 (95% CI 1.32–2.05), compared with women with a minimum of secondary education.²⁶ However, two studies showed no association of maternal education/literacy on stillbirths.^{34,47}

Unemployed or semi-skilled women had 50% higher adjusted odds of stillbirth compared with skilled women.³⁶ Compared with a farmer, protective effects were conferred to pregnant woman who were housewives.²² Further, although one study reported an increased stillbirth risk to women in rural residence compared with urban residence,²² two studies observed no effect of residence.^{35,45}

Compared with poorer women, women with the middle,²⁷ and with the highest,^{27,53} wealth indices had reduced odds of stillbirths, after adjusting for sociodemographic, economic, obstetrics and antenatal factors. However, one study showed no effect of wealth index.³⁷ Maternal alcohol consumption,^{45,50} and smoking and unsafe drinking water acted as independent stressors for stillbirths.²⁶

Compared with women of parity 0–4, grand multiparous women (\geq 5) had a median adjusted effect estimate of 0.95 (IQR 0.27–3.00) for stillbirth^{28,32,36}; however, one study showed no association with parity.⁵⁸ Grand multiparous women with advanced age (35–49 years) had twice the adjusted odds of stillbirth in comparison with young women with parity 1–4.^{33,58}

3.2.3 | Fetal factors

Antepartum factors

Gestational age of <37 weeks increased the risk of stillbirth compared with term births in hospitals (median aOR3.54, IQR2.02–4.81).^{32,36,45,50} Compared with term births, postterm births (>42 weeks of gestation) also increased the adjusted odds by twofold,⁴⁵ but another study showed no effect.⁴⁸

Multiple studies reported that low birthweight (<2.50 kg) increased the odds of stillbirths, compared with normal birthweight (≥ 2.50 kg) (median aOR 5.63, IQR 5.60–9.98).^{22,32,45,47,48,58} Similarly, very low birthweight (<1.50 kg) increased the crude risk in two studies.^{40,54} Relative to normal weight, macrosomia (birthweight>4 kg) increased the aOR of stillbirth^{45,58}; however, one study showed no effect.⁴⁷

Congenital abnormality was more prevalent in antepartum stillbirths.^{24,46} One hospital-based study reporting adjusted odds observed an adverse association between congenital abnormality and stillbirth,⁴⁹ whereas one study found no association.⁴⁵ A large-scale study reported an independent association between male sex and stillbirth.³³

Intrapartum factors

Fetal distress (e.g. fetal bradycardia) showed no association with stillbirths,⁴⁰ whereas polyhydramnios independently increased the adjusted odds by 13-fold.⁵⁰ Madhi and colleagues attributed 16% of stillbirths to fetal bacterial infections with Group B Streptococcus, *Enterococcus faecalis, Escherichia coli* or *Staphylococcus aureus*.⁵⁵ A higher stillbirth risk was observed in fetuses with abnormal or no heartbeat and in fetuses with chorioamnionitis, reported with crude odds,^{40,54} and with meconium-stained amniotic fluid (aOR 3.15, 95% CI 1.73–8.18).^{50,54}

3.2.4 | Maternal obstetric and delivery factors

In Liberia, 14% of total stillbirths had obstructed labour.⁵⁶ Verbal autopsies of 2104 stillbirths suggested intrapartum stillbirths being more common in women with complicated labour than antepartum stillbirths (69% vs. 5%).⁴⁶ Although two studies reported an increased adjusted relative risk of obstructed labour on stillbirths in hospital,^{29,51} another study found no association.^{46,48} Likewise, obstetric complications,⁵³ and a prolonged labour of >12 and >24 h (relative to ≤12 h),^{39,47} increased the adjusted risk by six- and fourfold respectively.^{47,51,53} Prolonged membrane rupture also had higher crude estimates for stillbirths.⁵¹

Uterine rupture significantly increased the stillbirth risk (aOR 4.9, 95% CI 1.67–14.35).⁴⁸ Although cord accidents accounted for 0.70%–17.00% of the total stillbirths,^{24,31,43,56,57} cord prolapse raised the crude odds of stillbirths in the hospital setting.⁴⁰

Placental abruption was considerably higher in intrapartum stillbirths than in antepartum stillbirths (12% vs. 2%).²⁴ Although one study reported placental abruption significantly increasing the adjusted odds of stillbirth,⁴⁵ another study observed no effect.⁵⁰ A fivefold higher risk was seen in women with placenta praevia and placental abruption.⁴⁸ Women with APH,^{22,40} in hospital settings,⁵² had a higher stillbirth risk^{22,40,52}; however, another study observed no effect (it should be noted that this study adjusted for important confounding factors, such as anaemia, hypertension and eclampsia).⁵⁰ Women with PROM had higher odds of having stillbirths (median aOR 2.18, IQR 0.32, 4.03).^{45,49,54}

A large cohort study observed non-cephalic fetal presentation to have an aOR of 5.64 (95% CI 4.42–7.19), compared with cephalic presentation.⁴⁵ Two studies observed caesarean section as an independent stillbirth risk factor, compared with vaginal deliveries^{34,58}; however, one of these studies did not adjust for potential confounding factors (such as referral and labour complications). Two studies saw no effect of caesarean section on stillbirths.^{32,47} Compared

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with spontaneous vaginal deliveries, assisted vaginal deliveries had a higher stillbirth risk.^{32,40,47,58}

3.2.5 | Health system factors

Antepartum factors

Macerated stillbirths were more prevalent in women with delays in help seeking and decision making (74%).²⁴ Receiving high-quality ANC visits (>7 ANC visits, as recommended by the World Health Organization) reduced the adjusted odds of stillbirth by 50% in one study.³⁷ Distance of maternal residence from the health facility had no association in one study.³⁵

Intrapartum factors

Fresh stillbirths were more common in women with delays in reaching hospital and obtaining optimal care (68%).²⁴ A delay in admission of >24 h had a higher stillbirth risk among vaginal deliveries (cOR 16.13, 95% CI 4.18–62.17).³⁵ Giving birth at clinics, private facilities, maternity homes and government health centres reduced the stillbirth risk by 70%, compared with hospitals (including government) in Zambia, Kenya,⁴⁴ and Tanzania.³⁷ Compared with home deliveries, one study reporting crude estimates showed protective effects in the risk of institutional delivery,²⁷ whereas findings from another study contradicted this result.⁴⁴ In hospital settings, patients referred from other facilities had higher stillbirth risk (median aOR 3.20, IQR 0.30–3.47).^{32,34,53} Using a partograph reduced the aOR by 80% in a referral hospital.⁴⁹

3.2.6 Unexplained/miscellaneous factors

Macerated stillbirths, a proxy for antepartum stillbirths, had a high rate of no identified risk factors in Rwanda (75% vs. 26% of fresh stillbirths).²⁴ The presence of herb use,⁴³ trauma,^{23,24,46} amniotic concern (oligo- or polyhydramnios),⁵⁷ and other maternal- and fetal-associated factors accounted for <7% of the reported stillbirths.^{25,46}

4 | DISCUSSION

4.1 | Main findings

This review identified modifiable antepartum and intrapartum maternal, fetal, obstetric and health system-level factors. Using varying stillbirth definitions and facility-based studies limits the generalisability of these findings; nevertheless, we identified a wider range of risk factors that can be further researched. The included articles were concentrated on Kenya, Ghana, Tanzania and Ethiopia, and had less representation from other SSA countries, particularly those with high SBRs,⁹ such as Guinea-Bissau, Central African Republic and South Sudan. Some factors were extensively reported, such as maternal age, hypertension, ANC visits, gestational age, birthweight and education, whereas obstetric factors, BMI, maternal infection, syphilis, malaria, endemic diseases and health facility preparedness had limited reporting. The type of maternal infections was often not specified. In 2018, Ahmed et al. reported a higher prevalence of maternal infection and APH in population-based studies, implying their higher plausible prevalence at population levels.⁴⁶ While it could be argued that preterm births are stillbirth characteristics as opposed to risk factor, it was a commonly cited factor. Further, factors such as emergency referrals and assisted vaginal deliveries may be secondary consequences of other risk factors or may indicate the suboptimal levels of care provided; nonetheless, these necessitate further research.

These findings build on the previous 2014 review by Aminu et al., which identified maternal factors of wealth, education, age and high parity, and fetal factors of low gestational age and birthweight, as well as previous stillbirth, as key risk factors, by examining associations not explored in the past review, such as obstetrics and health systems factors.¹² The health systems and obstetric factors identified in this review include emergency referrals, poor ANC quality, failure to use partograph, ill-equipped hospitals, delayed decision making and direct obstetric complications. Focusing on a more holistic set of potentially modifiable associated factors in a sub-Saharan context can provide more contextspecific information for policymakers and programmes to target interventions for stillbirth prevention.

4.2 Strengths and limitations

This study is the first systematic review to focus on identifying stillbirth determinants in SSA. The included studies have limitations that affect the external validity and the potential generalisability of the findings. Only 12 of the 37 included studies were population based, whereas the remaining hospital-based studies may be subject to biases, especially where these are referral facilities. There were few articles from Central or West Africa included, and the findings from the predominantly East and Southern African countries may not be generalisable to other African geographies. Using non-standardised definitions of stillbirth and risk factors across studies can result in misclassification and incorrect SBR estimation, leading to difficulty in comparison. As risk factors vary with gestational age, using disparate systems of definitions can result in inaccurate risk factor assessment. Most studies also did not categorise factors by time of death, which is crucial for identifying pregnancy stage-specific risk factors. The narrative synthesis used indicates the direction of the effect, not the magnitude of the effect. Articles such as case series, audits and select cross-sectional studies, despite not reporting effect estimates, were included to comprehensively account for all factors because of the limited high-quality evidence available. Exposure measurement from some papers was subject to disease seasonality or political climate

due to study periods being less than 1 year. The lack of reliable exposure measurement, identification and adjustment of confounding factors, and appropriate matching of cases with controls, severely affected the quality of the included studies. Although many studies did not adjust for confounding factors, some failed to show associations between known risk factors (e.g. syphilis, HIV, infection or malaria),⁵⁹⁻⁶¹ which calls into question the sampling strategies. The poor readiness of a facility to conduct ANC (e.g. syphilis testing) may have also impacted exposure measurement. In addition, few studies sought to differentiate between antepartum and intrapartum death, despite probable differences in the pathways to and risk factors for these deaths. Future research should seek to disaggregate stillbirth by timing to better inform programmatic action. Despite these limitations, this review provides timely evidence of stillbirth determinants in SSA.

4.3 | Interpretation

The maternal antepartum and socio-economic factors identified in this review are consistent with the literature from other countries within SSA.^{12,62-68} AMA was identified as a risk factor in several included studies, although these were not adjusted for similar confounding factors, and is supported by studies in high- and middle-income countries.^{69–71} Notably, women in our studies had higher parity compared with women in high- and middle-income countries, who were more likely to be nulliparous. This could imply a potential interplay of parity or past pregnancy-related complications interfering with the independent risk of AMA.

Limited evidence supported an increased risk with prolonged labour, uterine rupture, abruptio placenta and placenta praevia, consistent with previous literature.^{66,72} The impact of PROM on stillbirths was mixed: whereas one study in Tanzania reported a reduced stillbirth risk,⁴⁵ another study in Ethiopia noted it as a risk factor.⁴⁹ The increased risk could be attributed to fetal hypoxia,⁷³ and it is plausible that where women are alerted by PROM to potential pregnancy complications and are able to access high-quality obstetric care, the stillbirth risk could be reduced. However, caution is required in interpreting these findings as neither study adjusted for all potential confounding factors. Further, emergency referrals increased the institutional stillbirth risk, which could be linked to referral delays and a lack of timely transportation.⁵³ In our review, women underwent home deliveries and visited facilities mainly during emergencies, causing an increase in stillbirth incidence. Many articles studying obstetric factors grouped factors impacting the quality of evidence and individual risk assessment.

The major fetal factors observed were low birthweight and preterm birth, which are corroborated by previous studies.^{66,74,75} Weak evidence of macrosomia as a stillbirth risk factor was observed, as studies did not adjust for confounding factors. Limited studies observed independent associations between congenital abnormality and stillbirths, despite being widely reported as a prevalence factor.

Limited evidence suggests greater stillbirth risk with having no partograph, delivery in a government hospital, meconium-stained fluid, STIs, and smoking. Although these risk factors have been demonstrated by studies in other countries,^{76–78} more research is needed in SSA.

The high proportion of unexplained stillbirths could be linked to a lack of fetal autopsies in all studies except one,⁵⁵ and inadequacies in laboratory tools at the facilities.^{23,43,51,54,79}

5 | CONCLUSION

We identified modifiable stillbirth risk factors in SSA that operate at individual, community, and facility levels that can be easily prevented with timely interventions. To achieve substantial reductions in SBRs, SSA countries need to focus investments and strengthen maternal and newborn health policies with a focus on stillbirths. However, in view of the gaps identified, there remains an urgent need to conduct high-quality population-based studies and use standardised definitions to understand regional risk factors in these settings. The following programmatic actions should be prioritised: improving ANC and institutional birth uptake, supported by counselling women on danger signs and the quality of intrapartum care provided in facilities; improving the availability of diagnostic kits at facilities and outreach centres; upskilling health workers; and improving laboratory set-ups.²⁷ Future studies seeking to understand the interplay between underlying individual-level risk factors and the health systems, especially timely access to high-quality care, are needed to inform interventions to close these gaps and target action towards ending preventable stillbirths.

AUTHOR CONTRIBUTIONS

AM conceived the study, designed the protocol, searched the databases, selected the studies meeting the inclusion and quality criteria, and conducted the analysis in consultation with HB. LS and AM abstracted the data. AM prepared the drafts and LS reviewed and edited the drafts for coherence and structure. HB retrieved full-access versions for some articles and abstracted data for three articles. HB and PM were the senior authors who critically reviewed the drafts and checked for clarity and inconsistencies.

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CONFLICT OF INTEREST STATEMENT None declared.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

Not applicable.

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REFERENCES

- 1. ICD-10 version: 2016 [Internet]. [cited 2020 Jul 11]. Available from: https://icd.who.int/browse10/2016/en
- Hug L, You D, Blencowe H, Mishra A, Wang Z, Fix MJ, et al. Global, regional, and national estimates and trends in stillbirths from 2000 to 2019: a systematic assessment. Lancet. 2021;398(10302):772–85.
- United Nations Children's Fund. A neglected tragedy: the global burden of stillbirths-UNICEF DATA [Internet]. 2020 [cited 2022 Oct 1]. Available from: https://data.unicef.org/resources/a-neglected-trage dy-stillbirth-estimates-report/
- 4. World Health Organization. UNICEF. Every newborn: an action plan to end preventable deaths. Geneva: World Health Organization; 2014.
- De Bernis L, Kinney MV, Stones W, Ten Hoope-Bender P, Vivio D, Leisher SH, et al. Stillbirths: ending preventable deaths by 2030. Lancet. 2016;387(10019):703–16.
- Lawn JE, Lee ACC, Kinney M, Sibley L, Carlo WA, Paul VK, et al. Two million intrapartum-related stillbirths and neonatal deaths: where, why, and what can be done? Int J Gynecol Obstet. 2009;107:S5–S19.
- McClure EM, Goldenberg RL. Understanding causes of stillbirth: moving in the right direction. Lancet Glob Health. 2019;7(4):e400–1.
- Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet. 2016;387(10018):587–603.
- Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. Lancet Glob Health. 2016;4(2):e98–108.
- Haws RA, Mashasi I, Mrisho M, Schellenberg JA, Darmstadt GL, Winch PJ, et al. "These are not good things for other people to know": how rural Tanzanian women's experiences of pregnancy loss and early neonatal death may impact survey data quality. Soc Sci Med. 2010;71(10):1764–72.
- Heazell AEPP, Siassakos D, Blencowe H, Burden C, Bhutta ZA, Cacciatore J, et al. Stillbirths: economic and psychosocial consequences. Lancet. 2016;387(10018):604–16.
- Aminu M, Unkels R, Mdegela M, Utz B, Adaji S, van den Broek N. Causes of and factors associated with stillbirth in low- and middleincome countries: a systematic literature review. BJOG. 2014;121:141–53.
- Joanna Briggs Institute. Critical appraisal tools [Internet]. [cited 2020 May 30]. Available from: https://joannabriggs.org/ebp/critical_appra isal_tools
- Ho YF, Li IC. The influence of different dialysis modalities on the quality of life of patients with end-stage renal disease: a systematic literature review. Psychol Health. 2016;31(12):1435–65.
- 15. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6:e1000097.
- StataCorp. Stata statistical software: release 13. College Station: StataCorp LP; 2013.
- Di Stefano L, Bottecchia M, Yargawa J, Akuze J, Haider MM, Galiwango E, et al. Stillbirth maternity care measurement and associated factors in population-based surveys: EN-INDEPTH study. Popul Health Metr. 2021;19(1):1–16.
- Blencowe H, Chou VB, Lawn JE, Bhutta ZA. Modelling stillbirth mortality reduction with the Lives Saved Tool. BMC Public Health. 2017;17(Suppl 4):784.
- Honkavuo L. Women's experiences of cultural and traditional health beliefs about pregnancy and childbirth in Zambia: an ethnographic study. Health Care Women Int. 2021;42(4–6):374–89. https://doi. org/10.1080/07399332.2021.1898613

- Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. BMJ. 2020;368:1–6.
- National Institute for Health Research. PROSPERO [Internet]. [cited 2020 Jul 11]. Available from: https://www.crd.york.ac.uk/prospero/ display_record.php?ID=CRD42020145574
- 22. Adane AA, Ayele TA, Ararsa LG, Bitew BD, Zeleke BM. Adverse birth outcomes among deliveries at Gondar University Hospital, Northwest Ethiopia. BMC Pregnancy Childbirth. 2014;14(1):90.
- Allanson ER, Muller M, Pattinson RC. Causes of perinatal mortality and associated maternal complications in a South African province: challenges in predicting poor outcomes. BMC Pregnancy Childbirth. 2015;15(1):37.
- Musafili A, Persson LÅA, Baribwira C, Påfs J, Mulindwa PA, Essén B. Case review of perinatal deaths at hospitals in Kigali, Rwanda: perinatal audit with application of a three-delays analysis. BMC Pregnancy Childbirth. 2017;17(1):85.
- Demise A, Gebrehiwot Y, Worku B, Spector JM. Prospective audit of avoidable factors in institutional stillbirths and early neonatal deaths at Tikur Anbessa Hospital in Addis Ababa, Ethiopia. Afr J Reprod Health. 2015;19(4):78–86.
- Akombi BJ, Ghimire PR, Agho KE, Renzaho AM. Stillbirth in the African Great Lakes region: a pooled analysis of demographic and health surveys. PLoS One. 2018;13(8):e0202603.
- Lakew D, Tesfaye D, Mekonnen H. Determinants of stillbirth among women deliveries at Amhara region, Ethiopia. BMC Pregnancy Childbirth. 2017;17(1):1–7.
- Asiki G, Baisley K, Newton R, Marions L, Seeley J, Kamali A, et al. Adverse pregnancy outcomes in rural Uganda (1996–2013): trends and associated factors from serial cross sectional surveys. BMC Pregnancy Childbirth. 2015;15(1):1–12.
- Pires G, Rosa M, Zangarote M, Chicumbe S. Determinants of stillbirths occurred in health facilities in Zambezia province, Mozambique (2013–2014). Rev Bras Saude Materno Infant. 2016;16(4):415–20.
- Tshibumbu DD, Blitz J. Modifiable antenatal risk factors for stillbirth amongst pregnant women in the Omusati region, Namibia. Afr J Prim Health Care Fam Med. 2016;8(1):e1-6.
- Ngwenya S. Stillbirth rate and causes in a low-resource setting, Mpilo Central Hospital, Bulawayo, Zimbabwe. Trop Doct. 2018;48(4):310–3.
- 32. Okonofua FE, Ntoimo LFC, Ogu R, Galadanci H, Mohammed G, Adetoye D, et al. Prevalence and determinants of stillbirth in Nigerian referral hospitals: a multicentre study. BMC Pregnancy Childbirth. 2019;19(1):533. https://doi.org/10.1186/s12884-019-2682-z
- 33. Kujala S, Waiswa P, Kadobera D, Akuze J, Pariyo G, Hanson C. Trends and risk factors of stillbirths and neonatal deaths in Eastern Uganda (1982–2011): a cross-sectional, population-based study. Trop Med Int Health. 2017;22(1):63–73.
- Tilahun D, Assefa T. Incidence and determinants of stillbirth among women who gave birth in jimma university specialized hospital, Ethiopia. Pan Afr Med J. 2017;28:299.
- 35. Rosario EVN, Gomes MC, Brito M, Costa D, Rosário EVN, Gomes MC, et al. Determinants of maternal health care and birth outcome in the Dande Health and Demographic Surveillance System area, Angola. PLoS One. 2019;14(8):e0221280.
- Dassah ET, Odoi AT, Opoku BK. Stillbirths and very low Apgar scores among vaginal births in a tertiary hospital in Ghana: a retrospective cross-sectional analysis. BMC Pregnancy Childbirth. 2014;14(1):289.
- 37. Afulani P. Determinants of stillbirths in Ghana: does quality of antenatal care matter? BMC Pregnancy Childbirth. 2016;16(1):132.
- Johnson KM, Zash R, Haviland MJ, Hacker MR, Luckett R, Diseko M, et al. Hypertensive disease in pregnancy in Botswana: prevalence and impact on perinatal outcomes. Pregnancy Hypertens. 2016;6(4):418–22.
- Anzaku AS, Idikwu OG, Emmanuel OA, Kingsley O. Impacts of obesity on maternal and fetal outcomes in women with singleton pregnancy at a Nigerian clinical setting. Br J Med Med Res. 2015;6(12):1159–65.

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- Kidanto H, Msemo G, Mmbando D, Rusibamayila N, Ersdal H, Perlman J. Predisposing factors associated with stillbirth in Tanzania. Int J Gynecol Obstet. 2015;130(1):70–3.
- 41. Harrison MS, Ali S, Pasha O, Saleem S, Althabe F, Berrueta M, et al. A prospective population-based study of maternal, fetal, and neonatal outcomes in the setting of prolonged labor, obstructed labor and failure to progress in low- and middle-income countries. Reprod Health. 2015;12(2):S9.
- 42. Harrison MS, Pasha O, Saleem S, Ali S, Chomba E, Carlo WA, et al. A prospective study of maternal, fetal and neonatal outcomes in the setting of cesarean section in low- and middle-income countries. Acta Obstet Gynecol Scand. 2017;96(4):410–20.
- Alhassan A, Ayikai LA, Alidu H, Yakong VN. Stillbirths and associated factors in a peri-urban District in Ghana. J Medical Biomed Sci. 2016;5(1):23–31.
- 44. Saleem S, Tikmani SS, McClure EM, Moore JL, Azam SI, Dhaded SM, et al. Trends and determinants of stillbirth in developing countries: results from the Global Network's Population-Based Birth Registry. Reprod Health. 2018;15(Supplement 1):100. https://doi.org/10.1186/ s12978-018-0526-3
- 45. Chuwa FS, Mwanamsangu AH, Brown BG, Msuya SE, Senkoro EE, Mnali OP, et al. Maternal and fetal risk factors for stillbirth in Northern Tanzania: a registry-based retrospective cohort study. PLoS One. 2017;12(8):e0182250.
- 46. Ahmed I, Ali SM, Amenga-Etego S, Ariff S, Bahl R, Baqui AH, et al. Population-based rates, timing, and causes of maternal deaths, stillbirths, and neonatal deaths in south Asia and sub-Saharan Africa: a multi-country prospective cohort study. Lancet Glob Health. 2018;6(12):e1297–308.
- Badimsuguru AB, Nyarko KM, Afari EA, Sackey SO, Kubio C. Determinants of stillbirths in Northern Ghana: a case control study. Pan Afr Med J. 2016;25(Suppl 1):18.
- Welegebriel TK, Dadi TL, Mihrete KM. Determinants of stillbirth in Bonga General and Mizan Tepi University Teaching Hospitals southwestern Ethiopia, 2016: a case-control study. BMC Res Notes. 2017;10(1):713.
- Worede DT, Dagnew GW. Determinants of stillbirth in Felege-Hiwot comprehensive specialized referral hospital, North-west, Ethiopia, 2019. BMC Res Notes. 2019;12(1):579.
- 50. Tasew H, Zemicheal M, Teklay G, Mariye T. Risk factors of stillbirth among mothers delivered in public hospitals of central zone, Tigray, Ethiopia. Afr Health Sci. 2019;19(2):1930–7.
- Mbachu II, Achigbu KI, Odinaka KK, Eleje GU, Osuagwu IK, Osim VO. Tracking stillbirths by referral pattern and causes in a rural tertiary hospital in Southern Nigeria. Niger Postgrad Med J. 2018;25(2):87–93.
- 52. Maaloe N, Housseine N, Bygbjerg IC, Meguid T, Khamis RS, Mohamed AG, et al. Stillbirths and quality of care during labour at the low resource referral hospital of Zanzibar: a case-control study. BMC Pregnancy Childbirth. 2016;16(1):351.
- Geelhoed D, Stokx J, Mariano X, Mosse Lázaro C, Roelens K. Risk factors for stillbirths in Tete, Mozambique. Int J Gynecol Obstet. 2015;130(2):148–52.
- Suleiman BM, Ibrahim HM, Abdulkarim N. Determinants of stillbirths in Katsina, Nigeria: a hospital-based study. Pediatr Rep. 2015;7(1):7–12.
- 55. Madhi SA, Briner C, Maswime S, Mose S, Mlandu P, Chawana R, et al. Causes of stillbirths among women from South Africa: a prospective, observational study. Lancet Glob Health. 2019;7(4):e503–12.
- Lori J, Rominski S, Osher B, Boyd C. A case series study of perinatal deaths at one referral center in rural post-conflict Liberia. Matern Child Health J. 2014;18(1):45–51.
- Aminu M, Bar-Zeev S, White S, Mathai M, Van Den Broek N. Understanding cause of stillbirth: a prospective observational multicountry study from sub-Saharan Africa. BMC Pregnancy Childbirth. 2019;19(1):470.
- 58. Agbozo F, Abubakari A, Der J, Jahn A. Prevalence of low birth weight, macrosomia and stillbirth and their relationship to associated

maternal risk factors in Hohoe Municipality, Ghana. Midwifery. 2016;40:200-6.

- Duan CC, Zhang XH, Li SS, Wu W, Qiu LQ, Xu J. Risk factors for stillbirth among pregnant women infected with syphilis in the Zhejiang Province of China, 2010–2016. Can J Infect Dis Med Microbiol. 2021;2021:8877962.
- 60. Korenromp EL, Rowley J, Alonso M, Mello MB, Saman Wijesooriya N, Guy Mahiané S, et al. Global burden of maternal and congenital syphilis and associated adverse birth outcomes—estimates for 2016 and progress since 2012. PLoS One. 2019;14(2):e0211720. https://doi.org/10.1371/journal.pone.0211720
- Moore KA, Simpson JA, Scoullar MJL, McGready R, Fowkes FJI. Quantification of the association between malaria in pregnancy and stillbirth: a systematic review and meta-analysis. Lancet Glob Health. 2017;5(11):e1101–12.
- Isaacson A, Diseko M, Mayondi G, Mabuta J, Davey S, Mmalane M, et al. Prevalence and outcomes of twin pregnancies in Botswana: a national birth outcomes surveillance study. BMJ Open. 2021;11:e047553.
- Neogi SB, Negandhi P, Chopra S, Das AM, Zodpey S, Gupta RK, et al. Risk factors for stillbirth: findings from a population-based case-control study, Haryana, India. Paediatr Perinat Epidemiol. 2016;30(1):56–66.
- Williams EK, Hossain MB, Sharma RK, Kumar V, Pandey CM, Baqui AH. Birth interval and risk of stillbirth or neonatal death: findings from rural North India. J Trop Pediatr. 2008;54(5):321–7.
- Ashish KC, Nelin V, Wrammert J, Ewald U, Vitrakoti R, Baral GN, et al. Risk factors for antepartum stillbirth: a case-control study in Nepal. BMC Pregnancy Childbirth. 2015;15(1):146. https://doi. org/10.1186/s12884-015-0567-3
- Poudel S, Ghimire PR, Upadhaya N, Rawal L. Factors associated with stillbirth in selected countries of South Asia: a systematic review of observational studies. PLoS One. 2020;15(9):e0238938.
- 67. McClure EM, Saleem S, Goudar SS, Moore JL, Garces A, Esamai F, et al. Stillbirth rates in low-middle income countries 2010–2013: a population-based, multi-country study from the Global Network. Reprod Health. 2015;12(2):S7.
- Ghimire PR, Agho KE, Renzaho A, Christou A, Nisha MK, Dibley M, et al. Socio-economic predictors of stillbirths in Nepal (2001– 2011). PLoS One. 2017;12(7):e0181332. https://doi.org/10.1371/journ al.pone.0181332.g001
- McClure EM, Saleem S, Pasha O, Goldenberg RL. Stillbirth in developing countries: a review of causes, risk factors and prevention strategies. J Matern-Fetal Neonatal Med. 2009;22(3):183–90.
- Nahar S, Rahman A, Nasreen HE. Factors influencing stillbirth in Bangladesh: a casecontrol study. Paediatr Perinat Epidemiol. 2013;27(2):158–64.
- Stringer EM, Vwalika B, Killam WP, Giganti MJ, Mbewe R, Benjamin BH, et al. Determinants of stillbirth in Zambia. Obstet Gynecol. 2011;117(5):1151–9.
- Hossain N, Khan N, Khan NH. Obstetric causes of stillbirth at low socioeconomic settings. J Pak Med Assoc. 2009;59(11):744–7.
- Liyew AD, Molla M, Azene ZN. Risk factors of stillbirth among women who gave birth in Amhara region referral hospitals, Ethiopia, in 2019: a case-control study. Int J Womens Health. 2021;13:557–67.
- 74. Lavin T, Preen DB, Pattinson R. Timing and cause of perinatal mortality for small-for-gestational-age babies in South Africa: critical periods and challenges with detection. Matern Health Neonatol Perinatol. 2016;2(1):11.
- Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller A, et al. Born too soon: the global epidemiology of 15 million preterm births. Reprod Health. 2013;10(Suppl 1):S2. https://doi. org/10.1186/1742-4755-10-S1-S2
- Frey HA, Odibo AO, Dicke JM, Shanks AL, MacOnes GA, Cahill AG. Stillbirth risk among fetuses with ultrasound-detected isolated congenital anomalies. Obstet Gynecol. 2014;124(1):91–8.
- Marufu TC, Ahankari A, Coleman T, Lewis S. Maternal smoking and the risk of still birth: systematic review and meta-analysis. BMC Public Health. 2015;15(1):239.
- 78. Ashish AC, Wrammert J, Clark RB, Ewald U, Målqvist M. Inadequate fetal heart rate monitoring and poor use of partogram associated

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with intrapartum stillbirth: a case-referent study in Nepal. BMC Pregnancy Childbirth. 2016;16(1):233.

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

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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