Predictor of Adverse Pregnancy Outcome: A Scoping Review

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Abstract. Neonatal mortality are mostly preventable. It specifically occurs due to adverse pregnancy outcome (APO) that can be detected during pregnancy and handle it properly. However, it remains problem in low and middle income country such as Indonesia. This scooping review aims to identify the measurement, prevalence, and risk factors that related to APO and impacted to neonatal mortality. We used Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to conduct Scoping Review. A systematic search was carried out in Pubmed, Science Direct, Springerlink, and Embace. Articles published from 2012–2021 were screened with inclusion criteria such as the population are pregnant women, include risk factor and pregnancy outcome. Twenty-two articles were eligible to be reviewed. The data were extracted to summarize and write the narrative finding. Mostly, the measurement of APO were low birthweight, preterm birth, and stillbirth. Low birthweight was found as the APO for 14.6% of total newborns in the world. Furthermore, other APO that is preterm birth, 9.8% occur in low-income countries. The risk factors for APO are socio-demographic, general morbidity episodic illness, infections and environment, behavior, infant characteristics and obstetrical. This scoping review focused on APO which contribute to high neonatal mortality in low-middle income countries. The overview of this issue is expected to be used as the analysis for planning program that might decrease the neonatal mortality.

Keywords: adverse pregnancy outcome · risk factor · neonatal mortality · low birthweight · preterm birth · stillbirth

1 Introduction

One of the Sustainable Development Goals (SDGs) targets is to end preventable deaths of newborns and under-five children. Globally there were 2.4 million (46%) child mortality in the first month of life [1]. In Indonesia, the data by the Ministry of Health's Family Health Report in 2020 showed that 72.0% of under-five children mortality occurred in the

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neonatal period, mostly caused by adverse pregnancy outcomes, such as low birth weight (LBW) 35.2%, asphyxia 27.4%, other causes of death 22.5%, congenital abnormalities 11.4% and infections 3.4% [2]. The SDGs aim to reduce the neonatal mortality rate to 12 per 1000 live births and the under-five mortality rate to 25 per 1000 live births by 2030 [3].

Indonesia is in the 7th rank of countries with highest newborn mortality rate in the world, and the first rank in Southeast Asia [4]. Based on the Indonesia Demographic Health Survey (IDHS), neonatal mortality rate in Indonesia is not much decreased within 26 years period. It was 32 per 1,000 live births in 1991 to 15 per 1,000 live births in 2017. The most common causes of neonatal death in the world and Indonesia are almost similar. It is due to adverse pregnancy outcomes, especially complications of premature birth 36.1%, intrapartum-related events 23.9%, other causes 18.8%, infection (11.5%), and congenital abnormalities (9.7%) [5].

Adverse pregnancy outcomes is a problem because it may reduce the opportunity of mother to have a healthy baby and increase the possibility to have several condition such as premature birth, low birth weight (LBW), stillbirth and neonatal death which are the main causes of morbidity, mortality, long-term physical and psychological problems of mothers [6, 7]. However, it is not yet clear what measurements, levels and risk factors of adverse pregnancy outcomes as the leading cause of neonatal mortality. Thus, the adverse pregnancy outcomes should be reviewed comprehensively. This scoping review aims to identify the measurement, prevalence, and risk factors that related to adverse pregnancy outcome (APO) which impacted to neonatal mortality.

2 Methods

A. *Study Design*

We conducted a scoping review which include studies related to risk factor pregnancy outcomes worldwide and published within the last 10 years, from January 2012 to December 2021. This scoping review used the methodological framework of Arksey and O'Malley (2005) and the selection of journals based on Preferred Reporting Items for Scoping review and Meta-Analysis (PRISMA ScR) [8]. Using the recommendations by Arksey and O'Malley (2005) and Levac et al. (2010) [9], this scoping review was conducted with the following stages: (1) Identify research questions; (2) Identify relevant studies; (3) Study selection, by setting inclusion/exclusion criteria; (4) Screening, charting, and sorting information according to the main issues and themes; and (5) compiling, summarizing, and reporting results. We used Participant, Concept and Context (PCC) formula. In this study, the participant refers to pregnant women, while concept is risk factor and context is pregnancy outcomes.

B. *Research Flow*

To find out relevant studies in the last 10 years comprehensively, we carried out three-step search strategies. First, we searched peer-review journal articles in English using four electronic database: PubMed, Science Direct, SpingerLink and Embase. For terms, we referred to Medical Subject Titles (MeSH) and using one or combination of " pregnant women OR Post partum mother OR Babies" AND "risk factor", AND "pregnancy

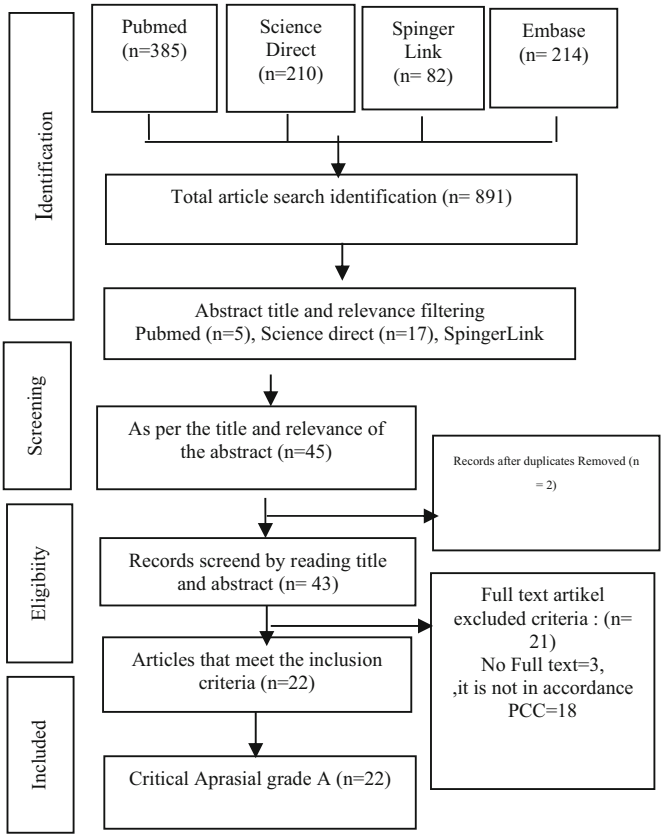

Fig. 1. Study Selection using PRISMA Scoping Review

outcome OR birth weight OR low birth weight OR preterm birth OR stillbirth". Second, we added studies outside the database that matched to the research objectives. Third, the research team selected the studies and 22 studies were eligible. The selection process for this scoping review can be seen in the Fig. 1.

3 Results and Discussion

We summarized the result of 22 studies. The key ideas are summarized into subthemes which are grouped into 3 main subthemes: Measurement of adverse pregnancy outcomes, prevalence and risk factors that are predictors of adverse pregnancy outcomes (Table 1). The writing team cross-checked the themes with the tables to ensure accuracy and reliability.

A. *Study Characteristics*

Most studies on adverse pregnancy outcomes were published in the last five years. The selected articles were pread geographically in Asia, Europe, Africa and America. The

Table 1. Themes in selected text

Main theme	Subtheme	Relevant study quotation
Measurement	Low Birth Weight	Digital scale [13, 16, 28], medical record [5], mother's memory [17, 35],
	SGA	Head circumference and length [13], birth weight for gestational age < 10 persentil [18]
	Makrosomia	Immediate birth weight measurement using calibrated digital scale [17], Hospital medical record and electronic medical record [35]
	Preterm Birth	Symphysis-fundal height after birth using Ballard Score [21], Last menstruation period, gestational age < 37 weeks [11], Measuring the crown length using trans-abdominal ultrasonography in first trimester [13, 17]
	Stillbirth	Weeks of pregnancy at delivery > 24 weeks with birth weight ≥ 500 gr and no sign of live at birth [5, 19]
Prevalence	Low Birth Weight	17.5% in India, mainly among mothers with stillbirth history and pregnancy complication [34] 12.5% in Jordan [5], 5.64% China [17] 1,41% in United Kingdom especially because unwanted pregnancy [19]
	Preterm Birth	9.8% in Jordan [5], Pregnant women infected by P.Vivax in first trimester had 8.12% premature birth in Brazil [13], 7.0% in Netherland [18], 5.55% in China [17] 4% in Mozambique and Tanzania [21]

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Table 1. (*continued*)

Main theme	Subtheme	Relevant study quotation
	Stillbirth	Stillbirth among Advanced Maternal Age (AMA) with age > 35 years old (4.7%) and maternal age > 40 years old (2.7%) in United Kingdom [9] 2.36% in China [23] 1.04% in Jordan [5], 0.22% in Netherland [18]
Risk factor Significan correlated	Low Birth Weight (LBW)P	Very young mother (≤16 years old), country, the first antenatal care visit, parity, BMI < 18.5 and MUAC < 240 mm [21], household combustion of solid fuels [11] Maternal factors: stillbirth history and pregnancy complication, low weight and anemia [10, 28]. Health service factors: ANC 4 times, iron tablet consumption and delivery in health facility decrease LBW. Covariate: maternal age < 25–34 years old, live in urban area, non Muslim, primigravida, low education level and low quartile of wealth [34] low occupational level or low social class [36] BMI pre-pregnancy < 18,5 kg/m2 and female fetus [17], unwanted pregnancy [19], smoking mother or exposed to tobacco [18]
	Preterm Birth	Very young mother (≤16 years old), country, BMI < 18,5 low education level [13, 21] prematur birth history, multiple pregnancy, Chronic disease such as diabetes, hypertension, mother with anemia condition [10], asthma, thyroid disease. Infection, Genetic influences. Nutritional factors: poor nutrition, obesity, nutrition deficiency and Women life style: smoking, alcohol consumption, drugs, Stress, over physical work [15, 22], live in rural area and no permanent job. Mother infected with sexual transmitted disease [18], pregnant woman with anemia in first trimester [25]

(*continued*)

Table 1. (*continued*)

Main theme	Subtheme	Relevant study quotation
	Stillbirth	Household combustion of solid fuels [11] pregnant women infected by influenza A virus [23] maternal age more than 36 years old [9] pregnant woman infected by syphilis [24] lower levels of occupation [15]

sample size of the studies were varied. The largest sample size was 44,723,207 births in Lean et.al's study (2017) [10], while the smallest sample size was 344 pregnant women in Yeshialem et.al's study (2017) [11]. The research design of the articles in this study was observational (cohort, case-control and cross-sectional) and reviewed (systematic literature review and meta-analysis).

B. *Measurements of Adverse Pregnancy Outcome (APO)*

Seventeen studies measured APO as low birthweight [6, 7, 12–20]. Other studies used Small for gestational age (SGA) or intrauterine growth retardation (IUGR) and macrosomia [19–21] to measure APO. Twelve studies measured APO as preterm birth or weight for gestational age [6, 7, 12, 14, 16, 18–20, 22, 23] We found that seven studies measured APO as stillbirth [6, 10, 15, 16, 24–26] and only one study that measured APO as congenital anomalies [27]. The APO was also measured on mother's side, such as Gestational Diabetes Mellitus, pre-eclampsia and gestational hypertension [20, 26].

The measurement of low birth weight (LBW) (<2500 g) in those studies were carried out within 24 h immediately after baby birth using a calibrated digital scale [14, 19, 23] using medical records and maternal memories [16, 21, 27]. Small for gestational age (SGA) was decided with the measurement of birth weight, head circumference and length below the 10th percentile sex-specific for gestational age according to the standard (Dombrowski et al., 2021; Op de Coul et al., 2021). The macrosomia (>4000 g) was measured by measuring birth weight immediately after delivery using a calibrated electronic scale or hospital records and medical records [19, 28].

Furthermore, the measurement of preterm birth was carried out by measuring the crown length using trans-abdominal ultrasonography in the first trimester, symphysis-fundal height by bimanual palpation at the first antenatal visit, woman's last menstrual period and the earliest ultrasound examination. It was decided as preterm birth if the gestational age is less than 37 weeks according to Ballard Score [14, 16, 19, 23]. Stillbirth was measured by knowing the gestational age at the time of delivery is more than 24 weeks. With a birth weight equal $\leq$ 500 g and there is no signs of life of the newborn at birth [6].

The measurement of adverse pregnancy outcomes (APO) was mostly performed in terms of LBW, preterm birth or weight for gestational age, and stillbirth. The results of this scoping review are in line with other studies that concluded these three APO as the

major causes of long-term morbidity, mortality, physical and psychological problems that have serious consequences for health in both developing and developed countries [6, 7]. Birth weight in was measured immediately within 24 h after delivery. It should be done not more than 72 h after birth. Measuring birth weight is limited in time because there is a decrease in newborn weight physiologically as a process of adaptation of baby from intrauterine life to life outside the womb. A baby is indicated as low birth weight (LBW) if the birth is more than 37 weeks of gestation with a birth weight < 2500 g [14].

Other measurement of APO is preterm birth. However, measuring preterm birth is more challenging than LBW. One of the reasons LBW continues to be reported and studied by epidemiologists and public health practitioners because it can be measured with excellent validity and precision while measuring preterm birth or IUGR requires valid estimates of gestational age, which is often difficult to do in developing countries due to late access to first examination to determine the gestational age based on documentation of the first day of the last menstrual period, and less supported in ultrasound examination in early gestational age [29, 30].

The method of measuring stillbirth are varied. Some studies determined gestational age from 22 weeks to 27 weeks of gestation at the time of delivery, with birth weight equal to or more than 500 g [6]. Determining gestational age is still controversial. Many epidemiologists and public health practitioners categorize the stillbirth by measuring gestational age or birth weight. The UN Inter-agency Group for Child Mortality Estimation (UN IGME) and the Core Stillbirth Estimation recommend using gestational age as a predictor of survival and this data is available globally. The International Classification of Diseases (ICD) defines stillbirth as no signs of life at birth and the birth weight is 1000 g or more or the gestational age of 28 weeks or more. The high number of stillbirths globally reflects the importance of quality antenatal and intranatal care [32].

C. *Prevalence of Adverse Pregnancy Outcome (APO)*

The prevalence of LBW incidence is 17.5% in low-income countries [28] and only 1.41% in high-income countries [15]. The prevalence of preterm birth is 9.8% in low-income countries [6, 22], and 1.31% in high-income countries [15]. Furthermore, stillbirth prevalence was 4.7% in the Netherlands which associated with Advanced maternal age (AMA) aged >35 years [10], 2.36% in China among pregnant women infected with the influenza A virus [24] and 1.06% in Jordan during COVID-19 pandemic [6].

The high prevalence of APO is caused by LBW, followed by preterm birth and stillbirth. Previous study mentioned that the most common APO was LBW and preterm birth [23]. In developing countries such as Indonesia, they found that there were 72.0% of neonatal deaths with the most common causes are LBW (35.2%), asphyxia (27.4%) and other causes of death (22.5%), congenital abnormalities (11.4%) and infections (3.4%) during 2020 [2]. Most children with LBW have stunted growth compared to children with premature birth. In addition, the prevalence of stillbirth is existed in developed and developing countries influenced by demographic factors. Women in high-income

countries tend to delay pregnancy [10], while those in low-income countries tend to experience pregnancy at a young age [23].

D. *Risk factors to predict Adverse Pregnancy Outcome (APO)*

Risk factors that predict APO in case of LBW are very young maternal age (<16 years old), not having a first trimester antenatal care (ANC) visit, primigravida, body mass index (BMI) <18.5 kg/m^2, and mid-upper arm circumference (MUAC) <24 cm, female baby [10, 19, 23], having stillbirth history and pregnancy complications, underweight, anemia, ANC visits <4 times, not taking iron tablets and not giving birth in health facilities [28], mother with infection influenza A virus [24], low level of occupation/social class [16], mothers with pregnancy complications including the estimated glomerular filtration rate (eGFR), current delivery complications [11, 18], mother has syphilis [25], unwanted pregnancy [15] and household combustion of solid fuels [16].

The predictors of preterm birth: very young maternal age (≤16 years), BMI <18.5, low maternal education [14, 23], maternal age ≥36 years old [19], having premature birth history, multiple pregnancies, having chronic diseases (diabetes, hypertension, anemia, asthma, thyroid disease). The other predictors are nutritional factors (undernutrition, obesity, nutritional deficiency), lifestyle (smoking, alcohol consumption, drugs, stress, excessive physical work) [16, 22], low education level and live in rural area, malaria infection in the first trimester of pregnancy [14], experiencing one or more current pregnancy complications [11, 18, 29].

The scoping review also revealed that the predictor of stillbirth are household solid fuel combustion [16], mother with influenza A virus infection [24], maternal age ≥35 years old [10], mothers detected syphilis [25], and maternal anemia [26].

Several risk factors that become predictors in this study are low birth weight, preterm birth and stillbirth which are preventable if it is early detected. But in reality, it is not easy to detect these risk factors. Identifying risk factors during pregnancy does not require high costs. It is a priority to develop cost-effective interventions to reduce maternal and infant mortality. Risk factors for APO are related to socio-demographic factors, general morbidity episodic illness, infections & environment, behaviour, infant characteristics and obstetrics. This scoping review found that socio-demographic factors were the predictors of APO (Mombo-Ngoma et al., 2016). Young maternal age was the strongest predictor of adverse pregnancy outcome. Very young mothers are more likely to have premature birth, low birth weight of baby and stillbirth [23, 33]. On the other hand, maternal age 36 years or more also increases the risk of stillbirth and the frequency of APO including Fetal Groud Retardation, pre-eclampsia and placental abruption. These conditions are associated with placental dysfunction although it has not been proven to be associated with an increased prevalence of maternal comorbidities [10]. Lower levels of occupation or social class have been shown to increase the risk of stillbirth, neonatal death, perinatal death, premature birth and low birth weight by about 40%, including in unemployed parents. Socio-economic conditions affect health behavior and other factors, where mothers who face economic difficulties tend to smoke during pregnancy [16]. Unwanted pregnancies were 1.4 times more likely to have a low birth weight baby and 1.3 times more likely to have a preterm birth. A better understanding of the impact

of unwanted pregnancy on pregnancy outcomes allows tailoring of service delivery to preconception, antenatal, intranatal and postnatal care [15].

Pregnant women who have a BMI before pregnancy less than 18.5 or MUAC less than 24 cm which indicates that they are underweight have a higher risk of giving birth to LBW babies, SGA and premature [34]. On the other hand, genetic factors such as obesity that occurs before pregnancy and excessive weight gain in pregnant women will correlate with MUAC of more than 25 cm and has been shown to be associated with high birth weight babies of gestational age or macrosomia [19, 34]. This double nutrition problem has become a concern in low-middle income countries like Indonesia and requires attention during pregnancy by health workers and pregnant women themselves.

Chronic diseases in pregnant women such as diabetes, hypertension, anemia, asthma, anemic mothers, first trimester antenatal visits, primigravida, previous stillbirth history, signs of pregnancy complications, antenatal care visits less than 4 times can increase the risk of LBW, premature and stillbirth babies due to lack of monitoring of maternal health and undetected danger signs of pregnancy [14, 28]. Other factor such as did not take iron tablets and gave birth not in health facilities, pregnancy and childbirth complications history including the estimated glomerular filtration rate (eGFR) or current delivery complications [7, 18], preterm birth history, experienced one or more current pregnancy complications are considered to be predictors for APO [11, 18, 29].

4 Conclusion

This scoping review concludes that APO can be predicted by LBW, preterm birth, and stillbirth. The prevalence of APO is varied between low-middle income countries and high-income countries. The main risk factor for APO are young maternal age, pregnancy and childbirth complication history, current pregnancy complication, nutritional status, low social economic status. As for the limitation of study, this scoping review only selected articles from four databases and did not compare the quality of the articles. However, we used the article from peer-review journal to ensure the quality of the articles. Further research is needed to find the best model for early detection of APO by using current digital technology.

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