The Risk Factors and Prediction Models of Preterm Birth: An Update Systematic Literature Review

Fika Minata Wathan[1], Kemal N. Siregar[2]

[1]Researcher, Faculty of Public Health, Universitas Indonesia, [2]Scientist, Departement of Biostatistics and Population Studies, Faculty of Public Health,Universitas Indonesia

Abstract

Background: Every year there is an increase in preterm births in the world, and for this condition, Indonesia occupies the highest position in ASEAN, with 15.5% of live births. The purpose of this study is to find for risk factors and prediction models to detect preterm birth.

Method: This study is conducted in multistage process following PRISMA guidelines with the inclusion criteria as follow, a) search for academic journals in the online database of ProQuest, Ebsco, PubMed, SpringerLink and Science Direct, b) publications in the last 10 years (2009-2019), c) articles in English, and d) the article contains outcome in the form of risk factors and prediction models for preterm birth e) the population is pregnant women suspected of having risk factors for preterm birth.

Results: From the 1767 articles found in 5 online databases, only 16 articles fall into the PICOS categories and are discussed in this paper. This study identified some of the most dominant risk factors for the incidence of preterm birth, including demographic and socioeconomic, behavioral characteristics/life style, maternal health/chronic conditions, current fetal conditions/pregnancy characteristics, pregnancy history/genetic characteristics, biological characteristics and others. This study concludes that maternal age and previous preterm birth are the factors that always used by the researchers. For the prediction of preterm birth, many researchers include cervical length as a predictor.

Conclusions: Previous researches were more still focused on risk factors and not much about prediction models. Therefore, this study suggests that the upcoming research should put more emphasis on risk prediction model for detecting preterm birth.

Keywords: *Preterm Birth, Preterm Delivery, Risk Factors, Determinant, Prediction Model.*

Introduction

Preterm birth is the main cause of morbidity and mortality during the perinatal period and an important problem to be solved[1][2][3]. This indicates that every year preterm birth continues to increase and affect the Infant Mortality Rate. About one-fifth of babies born under 32 weeks cannot survive in the first year compared to 1% of babies born at 33-36 weeks of age [4][5] and only about 0.3% of infant deaths if they are born at term. In order to achieve the new global targets for neonatal mortality of less than 10 deaths per 1000 live births by 2035[6][7].

At the world level the number of preterm births is estimated at 15 million each year, with an average in 65 countries experiencing an increase from 7.5% preterm births to 8.6%[8][9]. The incidence of preterm birth is different in each country. In developed countries, for example, the figure ranges from 5 to 11% in Europe, Australia 7% and the United States around 12%. The situation is worse in developing countries, for example in Sudan 31%, India 30%, and South Africa 15%, Uganda 13, 6%[7][9].

Corresponding Author:
Fika Minata Wathan
Researcher, Faculty of Public Health, Universitas Indonesia
e-mail: fikafkunsri07@gmail.com

In the ASEAN level, Indonesia occupies the highest number of preterm birth, followed by the Philippines 14.9%, Myanmar 12.4% and Malaysia 10%. In 1983 the incidence of preterm in Indonesia was 18.5%, then dropped in 1995 to 14.2%. In 2009, preterm births in Indonesia ranged from 10-20% [9][10]. One year after, the figure was at 15.5% which made Indonesia ranked 9th highest out of 184 countries in the world. Indonesia is also ranked 7th out of 10 countries with a high number of premature infant mortality with 25,800 deaths[11][12].

The main reason of the high incidence of preterm birth could be due to lack of knowledge about antenatal factors that contribute to the incidence of preterm birth; the number of factors causing preterm birth; unclear pathophysiology, inadequate diagnostic facilities, and lack of knowledge about preterm birth prevention [13] [14]. Various studies have been conducted to look for risk factors for preterm birth, but the presence of these risk factors does not always lead to preterm birth, even some preterm births that occur spontaneously do not have clear risk factors.

Indonesia needs to seriously handle the case of preterm birth since this issue will have a large and significant impact on health costs, both directly and indirectly[15][9]. The direct impacts of preterm birth include the depletion of health, financial, emotional and psychological resources for parents[10][16], whereas the indirect impact comprises of the burden on the community for long-term care for the sequelae of prematurity and mothers who experience preterm births and have premature babies must be unemployed due to loss of work due to having to care for their children[16][12][15].

Against this backdrop, this study aims to look for what has been studied and what has not been done about this topic by accessing 5 digital libraries in a period of 10 years. The results of this research will be utilized as a foundation to develop a prediction model of preterm birth with the basis of risk factor.

Method

This study used Systematic Literature Review, which was conducted in a multistage process following PRISMA guidelines, to identify all risk factors to predict the occurrence of preterm birth among pregnant women.

The inclusion criteria that used in this study are as follow, a) academic journals that searched on ProQuest, Ebsco, PubMed, SpringerLink and Science Direct online databases, b) publications in the last 10 years (2009-2019), c) English-language articles, d) articles containing outcome risk factors and prediction model of preterm birth, e) the population is pregnant women who are suspected of having risk factors for preterm birth. To search the related articles according to inclusion criteria, this study used some keywords, namely Preterm Birth OR Preterm Delivery AND Risk Factors OR Determinant AND Prediction Model AND Accuracy. From this process, there are 1,767 matched articles, consist of Proquest 474 articles, Ebsco 212 articles, Pubmed 16 articles, Springer 265 articles and Science Direct 800 articles.

References that have been found in line with the keywords are managed using Mendeley software. Since one article can be sourced from different database, a duplicate check needs to be performed afterwards, according to PICOS. After removing 60 duplicates and 1689 article that does not match with PICOS, it has resulted 18 articles. At the last stage, there are 2 additional articles that were excluded, thus the number of articles that match with the requirements are 16.

At the included stage, the selected articles are extracted and analyzed to obtain information: author, year of publication, data collection period, country, sample size, sampling method, data set used and research outcome. Data analysis is carried out thematically and arranged in accordance with the analysis of the theme and written narrative.

Results

Characteristics of Articles: For the past 10 years (2009-2019), there are 16 research articles that have been conducted on risk factors of preterm birth and prediction model. This systematic literature review limits access to academic journal searches to the ProQuest, Ebsco, PubMed, SpringerLink, Science Direct online databases and does not access other databases or gray material articles. Therefore, there are opportunities for risk factor service articles and prediction models for preterm births from other databases or gray materials but cannot be obtained from these online databases.

The latest article was published in 2019 while the oldest one was published in 2009. All of the study was conducted during the period of 2004 until 2017, in which most of them were conducted in the last five years.

In the context of geographical spread, the previous studies have covered all continents, including Sao Luis and Ribeirao Preto (two Brazilian cities)[1]; A French Caribbean (Guadeloupe) [17]; Auckland, New Zealand, and Adelaide, Australia [18]; Messina, Italia[19]; Kampala, Uganda [20]; Nairobi, Kenya [4]; Beijing, China[3]; Finland; Brazilian [5]; Sanandaj, Iran [21]; Lagos, Nigeria[22]; Eastern Slovakia [2]; Hubei Province, China [8]; Cuiaba, MT.[23]

Moreover, in terms of methodology, the selected articles used either cohort, cross-sectional or case-control. The numbers of research samples are varied from 296 up until 3,994,872 with a variation sampling method.

The Most Common Risk Factors: Predominantly, the risk factors of preterm birth are classified into several categories: demographic and socioeconomic, behavioral characteristics/life style, maternal health/ chronic conditions, fetal current conditions/pregnancy characteristics, pregnancy history/genetic characteristics, biological characteristics and others [26][27][28].

Firstly, demographic and socioeconomic category, which consists of maternal age [20][19][4][21], race/ethnicity[1][18][29], educational status [19][2][29], maternal status and socioeconomic status [20][17][22][30]. Specifically, the variables of this category cover the gestational age below 20 years or above 35 years, low maternal education, the status of women (married or divorced), and low socioeconomic status. These factors have been empirically proven to cause preterm birth 3x compared to those aged over 20 years old or under 35 years of education good (above high school or earned a degree), the mother who has support from family and socioeconomic status.

Secondly, behavioral characteristics/ life style category, which consists of alcohol[2][19][3][4], tobacco[2][31][20][5], recreational drugs[1][18][19], psychological and social stress [1][21][5][3]. Apart from it, there is one article that mentions the use of hormonal fertility treatment (excluding Clomiphene) and one article that said fertility-enhancing drug status can lead to preterm birth. However, the article is not explaining enough (name) that drugs can be the risk factors for preterm birth.

Thirdly, maternal health/chronic conditions category, which also become one of the most dominant factors that can cause of preterm birth. This category consists of Body Mass Index (BMI) [17][3][18], diabetes[17][3], hypertension [17][18][21], anemia [5], asthma [17] and thyroid disease. According to Body Mass Index (BMI), overweight or obese is one of the most frequent cause of preterm birth compared to those who have a normoweight BMI, while those who have underweight can cause low birth for their babies (LBW).

Fourth, current fetal condition/pregnancy characteristics category, which consists of multiple fetuses, infertility treatments, infant weight, and drugs used during pregnancy[18]. The discusses the use of marijuana pre-pregnancy which can lead to preterm births 16% compared with those who did not consume[31].

Fifth, pregnancy history/genetic characteristics category, which comprises of previous preterm birth[17][19][3][18][31], diabetes[17][19][3][18], hypertension [17][19][21][22], and obesity[17][3]. According to the articles, this category is also one of the most influential factors that causes of preterm birth.

Sixth, biological characteristics category, that consists of infection. The discussed variables in this category include bacterial vaginosis[1][19][4], urinary tract infection[1][17][19][4], and periodontis[1]. From all infections, urinary tract is an the most significant infection that highly associated with the risk of spontaneous preterm birth.

Lastly, other factors, that includes ultrasonography[20][22][2], insurance details, and cervical measurement[4][18][31][21]. The most discussed factor is obstetric maternal and prenatal care (ANC), where it is mentioned in four articles as factors associated with preterm birth.

Prediction Models: From the 16 selected articles, only 6 of them discusses the prediction models of preterm birth. The model explains that clinical prediction is looking directly at risk factors for preterm births, including psychosocial, genetic, infectious mechanism, history of preterm birth, short stature, living in rural areas, those who do not attend antenatal care, marital status, occupation, residential accommodation with shared sanitation facilities, absence of previous cesarian section, hypertensive disorders and antepartum hemorrhage as the predictor. Another predictor mentioned about cervical length and uterine artery examination of Doppler ultrasound measurement at 20 weeks. The prediction model works by looking at the value of the odd ratio, as well as the sensitivity and

specificity values seen from the value of the Receiver Operating Characteristic (ROC) curve and the Area Under Curve (AUC). The value used as a benchmark for measuring effective AUC and ROC is above 0.7[18][31].

Discussions

Characteristics of Articles: Publications about preterm birth are still very focused on risk factors. There are not many articles that discuss prediction models and the importance of research like this to develop efforts to prevent premature birth. Geographically, the results of research on preterm birth have been discussed on all continents, including America (A Fench Caribbean (Guadeloupe); Sao Luis and Ribeirao Preto; Cuiaba MT; and the United States), Europe (Messina, Italy; Finland; Eastern Slovakia), Australia (Auckland, New Zealand, Adelaide, Australia), Africa (Kampala, Uganda; Nairobi, Kenya; Langos, Nigeria) and Asia (Beijing, China; Sanandaj, Iran; Hubei Province, China; Jordan). However, there are no articles originating from Indonesia, even though Indonesia is the number one country in ASEAN and the ninth in the world with the highest premature birth rate.

The Most Common Risk Factors: From the 16 articles discussing risk factors, only 6 discussed the model predictions. Most articles only discuss risk factorsand have not discussed much about the use of these risk factors to build a model that can predict well premature births. Modeling that is able to predict well is very important as an effort to prevent neonatal deaths caused by preterm birth. As one of the countries with a high number of preterm births, Indonesia must have a number of studies relating to risk factors and even more so regarding the development of predictive models for preterm birth.

Factors related to preterm birth include mother's own prematurity, history of previous labor, prematurity in the first degree family members, history of dead children, premature rupture of membrane, multiple pregnancies, diabetes, hypertension, preeclampsia/ eclampsia, infertility and cervical incompetence had significant relationship with preterm birth. However, in the result, he emphasised that only abnormal amniotic fluid, premature rupture of membrane (PROM), multiple pregnancies, hypertension, family history of premature birth, mothers age over 35 years and cervical incompetence have significant relationship with the preterm birth, thus some of these factors are not related to the cause of preterm birth.

Prediction Models: The results of Systematic Literature Review mention that of 16 articles, six of them discuss predictor of preterm birth. Prediction herein is not necessarily a screening test because there is no routine screening test yet for preterm birth, which separate from the history to look for risk factors such as history of a previous preterm birth. Correct prediction will provide an opportunity to intervene effectively.

One article mentioned that the reason behind the selection of psychosocial, genetic and infectious mechanisms are because of the indications that they play an expressive role in determining of preterm birth. Risk factors have been tested individually, with few protocols have been proposed like the present one, in which the factors are investigated using an integrated multidisciplinary approach and a hierarchical modeling based on data samples with contrasting socioeconomic profiles. Data will be analyzed by multiple binary logistic regression with the estimation of the odds ratio [28].

Nevertheless, all the results of research on preterm birth, either clinically or using physical and biological parameters, can only predict the occurrence of preterm birth until seven days after the examination before 37 weeks' gestation. However, to have predictability in preterm birth, doctors could intervene at the early stage thus the premature infants will be born better.

Conclusions

There are number of risk factors for preterm birth, where each researcher has a different set of risk factors. However, researchers basically have a group of risk factors, which include the following factors: demographic and socioeconomic, behavioral/lifestyle characteristics, maternal health/chronic conditions, current fetal condition/pregnancy characteristics, pregnancy history/genetic characteristics, and biological characteristics. Among all these risk factors, maternal age and previous history of preterm birth are factors that are always used by researchers.

To make predictions about preterm birth, many researchers include the length of the cervix as a predictor, where the level of accuracy obtained has reached 0.7. In the last 10 (ten) years, the number of research publications on prediction models based on risk factors for preterm birth is still limited. Rarely, research articles discuss at the same time about risk factors and models

that can predict premature birth. This study recommends that future research put more emphasis on risk prediction models for detecting preterm birth.

Conflict of Interest: The authors states that there is no conflict of interest in conducting this study.

Acknowledgment: We would like to thank to the Department of Biostatistics and Population Studies, Faculty of Public Health, Universitas Indonesia for providing the authors the opportunity and facilities to conduct this study.

Ethical Clearance: This is a systematic literature review journal, so this article no need ethical clearance.

Source of Funding: Self

References

1. da Silva AAM, Simões VMF, Barbieri MA, Cardoso VC, Alves CMC, Thomaz EBAF, et al. A protocol to identify non-classical risk factors for preterm births: the Brazilian Ribeirão Preto and São Luís prenatal cohort (BRISA). Reprod Health 2014;11:79.
2. Diabelková J, Rimárová K, Urdzík P, Dorko E, Bušová A. Risk factors of preterm birth and low birth weight neonates among Roma and non-roma mothers. Cent Eur J Public Health 2018;26:S25–31.
3. Zhang Y-PP, Liu X-HH, Gao S-HH, Wang J-MM, Gu Y-SS, Zhang J-YY, et al. Risk Factors for Preterm Birth in Five Maternal and Child Health Hospitals in Beijing. PLoS One 2012;7(12):e52780.
4. Wagura P, Wasunna A, Laving A, Wamalwa D, Ng'ang'a P. Prevalence and factors associated with preterm birth at Kenyatta National Hospital. BMC Pregnancy Childbirth 2018;18.
5. Räisänen S, Gissler M, Saari J, Kramer M, Heinonen S. Contribution of Risk Factors to Extremely, Very and Moderately Preterm Births – Register-Based Analysis of 1,390,742 Singleton Births. PLoS One 2013;8(4):e60660.
6. Gu Y, Li L, Zhou C, Yang T, Dong H. Factors influencing voluntary premarital medical examination in Zhejiang province, China: A culturally-tailored health behavioral model analysis. BMC Public Health 2014;14(1):1–11.
7. Sehhati-Shafaii F, Asadollahy M, Piri R, Naghavi-Behzad M, Farzollahpour F. Prevalence and risk factors of preterm labor in health educational centers of northwest Iran (2009-2010). Life Sci J 2013;10(3):231–6.
8. Xu H, Dai Q, Xu Y, Gong Z, Dai G, Ding M, et al. Time trends and risk factor associated with premature birth and infants deaths due to prematurity in Hubei Province, China from 2001 to 2012. BMC Pregnancy Childbirth 2015;15.
9. Gravett MG, Rubens CE, Nunes TM. Global report on preterm birth and stillbirth (2 of 7): Discovery science. BMC Pregnancy Childbirth 2010;10(SUPPL. 1):1–16.
10. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller A-B, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet 2012;379(9832):2162–72.
11. Lawn JE, Davidge R, Paul VK, Xylander S von, de Graft Johnson J, Costello A, et al. Born Too Soon: Care for the preterm baby. Reprod Health 2013;10:S5.
12. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Neonatal morbidity associated with late preterm and early term birth : the roles of gestational age and biological determinants of preterm birth. 2014;(December 2013):802–14.
13. Schleußner E. The Prevention, Diagnosis and Treatment of Premature Labor. Dtsch Aerzteblatt Online 2013;110(13):227–36.
14. Ratzon R, Sheiner E, Shoham-Vardi I. The role of prenatal care in recurrent preterm birth. Eur J Obstet Gynecol Reprod Biol 2011;154(1):40–4.
15. UNICEF, WHO, Bank W, Division U-DP. Child Mortality Report 2015 Organizations and individuals involved in generating country-specific estimates of child mortality Special thanks to the Technical Advisory Group of the UN IGME for providing technical guidance on method for child mortality es. Who 2015;
16. Gladstone M, Oliver C, Broek N Van den. Survival, Morbidity, Growth and Developmental Delay for Babies Born Preterm in Low and Middle Income Countries – A Systematic Review of Outcomes Measured. PLoS One 2015;10(3).
17. Rouget F, Lebreton J, Kadhel P, Monfort C, Bodeau-livinec F, Janky E, et al. Medical and Sociodemographic Risk Factors for Preterm Birth in

a French Caribbean Population of African Descent. Matern Child Health J 2013;17(6):1103–11.

18. Dekker GA, Lee SY, North RA, McCowan LM, Simpson NABB, Roberts CT. Risk Factors for Preterm Birth in an International Prospective Cohort of Nulliparous Women. PLoS One 2012;7(7):e39154.
19. Granese R, Gitto E, D'Angelo G, Falsaperla R, Corsello G, Amadore D, et al. Preterm birth: seven-year retrospective study in a single centre population. Ital J Pediatr 2019;45.
20. Ayebare E, Ntuyo P, Ombeva MO, Gorrette N. Maternal, reproductive and obstetric factors associated with preterm births in Mulago Hospital, Kampala, Uganda: a case control study. Pan Afr Med J 2018;30.
21. Derakhshi B, Esmailnasab N, Ghaderi E, Hemmatpour S. Risk Factor of Preterm Labor in the West of Iran: A Case-Control Study. Iran J Public Health 2014;43(4):499–506.
22. Olusanya BO, Ofovwe GE. Predictors of Preterm Births and Low Birthweight in an Inner-City Hospital in Sub-Saharan Africa. Matern Child Health J 2010;14(6):978–86.
23. Broek NR van den, Jean-Baptiste R, Neilson JP. Factors Associated with Preterm, Early Preterm and Late Preterm Birth in Malawi. PLoS One 2014;9(3).
24. Acharya S, Pentapati KC, Bhat P V. No Title. Int J Dent Hyg 2013;11(2):91–8.
25. Ghoneim N, Bauchart-Thevret C, Oosterloo B, Stoll B, Kulkarni M, De Pipaon MS, et al. No Title. PLoS One 2014;9(9):e106888.
26. Offiah I, ODonoghue K, Kenny L. Clinical Risk Factors for Preterm Birth. Preterm Birth - Mother Child 2012;
27. Brkièeviæ E, Grgiæ G, Ljuca D, Ostrvica E, Tulumoviæ A. Etiological factors of preterm delivery. 2013;3(2):159–63.
28. Safari S, Hamrah MP. Epidemiology and Related Risk Factors of Preterm Labor as an Obstetrics Emergency. 2017;5(1):1–8.
29. Zhang C, Garrard L, Keighley J, Carlson S, Gajewski B. Subgroup identification of early preterm birth (ePTB): informing a future prospective enrichment clinical trial design. BMC Pregnancy Childbirth 2017;17.
30. Factors associated with prematurity: an analysis of information system data about born alive. Rev Enferm UFPE Line 2015;9(12):1110–7.
31. Passini R, Cecatti JG, Lajos GJ, Tedesco RP, Nomura ML, Dias TZ, et al. Brazilian Multicentre Study on Preterm Birth (EMIP): Prevalence and Factors Associated with Spontaneous Preterm Birth. PLoS One 2014;9(10):e109069.