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REVIEW ARTICLE

Prevalence and associated risk factors of preterm birth in India: A review

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ABSTRACT

Preterm birth (PTB) is an important health concern and a leading cause of infant mortality and morbidity worldwide. This review article determined potential risk factor(s) associated with PTB and evaluated the overall trend of PTB prevalence in India. A systematic search was conducted in PubMed, Medline, Google Scholar, and Web of Science databases. Appropriate statistical tools were employed to identify the PTB associated risk factor(s). The prevalence of PTB was found to vary across the country. The overall pooled risk of PTB was found to vary with different risk factors such as gestational hypertension of 19.16% (95% CI 8.54 to 29.78, I2 = 84.09 %); 9.49% for gravida (95% CI 2.99 to 16.00, I2 = 86.07%), 8.34 % for anemia (95% CI 4.45 to 12.24, I2 = 79.88%); 8.34% for prior PTB (95% CI 4.45 to 12.24, I2 = 94.89%) and 4.61% for gestational diabetes (95% CI 1.48 to 7.73, I2 = 53.27%). Moreover, low socioeconomic status, inadequate antenatal care, infections during pregnancy, and advanced maternal age were also potential risk factors of PTB among the Indian population. The rate of PTB showed an increasing trend with the high frequency of occurrence in India. Pregnancy induced hypertension, gestational diabetes, prior history of PTB, maternal anemia, and gravida were found to be potential risk factors causing PTB. Understanding the harmful effects of PTB and providing preconception counseling to those mothers who are at high PTB risk should be emphasized to address the PTB associated health consequences.

Key words: PTB, anemia, gestational hypertension, prior PTB, gravida, India

INTRODUCTION

The term preterm birth (PTB) is defined by the World Health Organization (WHO) as babies born alive before completing 37 weeks of gestational age.[1] It is one of the leading causes of neonatal morbidity and mortality in children below five years of age. [2] Approximately 1 million children die each year due to PTB complications. [3-4] Across 184 countries, the rate of PTB ranges from 5% to 18% of the babies born.[4] In developed and developing countries, medically unnecessary

inductions and cesarean section deliveries before the full term also increase PTB rate. The actual rate of PTB remains unexplained in many countries. [1,5] Malawi reported the highest rates, with 18.1 PTB per 100 births in the world. [2,4] Sub-Saharan Africa and South Asia account for over 60% of the PTB worldwide. In India, 3,341,000 babies are born too prematurely, and 361,600 children under the age of five die because of PTB complications.[6] It is also estimated that 23.4% of global preterm births are reported from India.[7] Occurrence of PTB affects both the mother and the children. It is evident from the available literature that maternal age, previous PTB, multiple gestations, pregnancy-induced hypertension (PIH), prolonged premature rupture of membrane (PROM), and urinary tract infections are significantly associated with PTB ($p=<0.05$). [8-9] Among all the adverse birth outcomes observed, PTB comprises 24.71% associated with medical conditions like hypertension, oligohydramnios, and anemia.[10] Severe anemic condition and the number of antenatal visits during pregnancy are also reported as risk factors of PTB. [11] Additionally, inconsistent findings have been reported in other studies. Further studies are required to understand the etiology of PTB as it is complex and multifactorial. However, limited studies have been conducted in India to explore the possible risk factors contributing to PTB. Moreover, most of the available literature is confined only to some particular geographical regions. Therefore, the present review identifies potential and absolute risk factor(s) associated with PTB, which is the primary requirement to devise effective actions to control and implement preventive measures in time. Moreover, this review attempts to understand the overall trend of the prevalence of PTB in India.

MATERIALS AND METHODS

Search Strategy

Search for original research articles published in electronic databases such as PubMed, Medline, Web of Science, and Google Scholar published from 2012 to 2020. The keywords used for searching literature included "PTB", and "India" in combination with "prevalence," "associated risk factors," and "outcomes." Research papers published in non-English languages, seminars/conferences, proceedings and dissertations, and thesis were excluded in the present study. A total of 30 research articles were identified, of which 18 full-text research articles were freely assessable and were therefore included to estimate the effect of the potential and absolute risk factors on PTB. Only nine research articles were analyzed to understand the overall pooled risk of PTB among the Indian population.

Articles were included if (i) the primary exposure of interest was the presence of risk factors like gestational hypertension, gestational diabetes, anemia, gravida and prior history of PTB, (ii) the outcome of interest was PTB, which was defined as delivery at <37 weeks of gestation, (iii) odds ratios (ORs) with their corresponding 95% confidence intervals (CI) or standard errors were reported. Titles and abstracts were screened to exclude duplicates and ineligible studies. Moreover, we examined the full-text papers of the remaining records to confirm that the retrieved reports met our inclusion criteria and extract data for the review (Fig 1). The data extracted from the articles included in the present study includes the first author's name, year of publication, study design, sample size, follow-up period, associated risk factors, ORs and corresponding 95% CI.

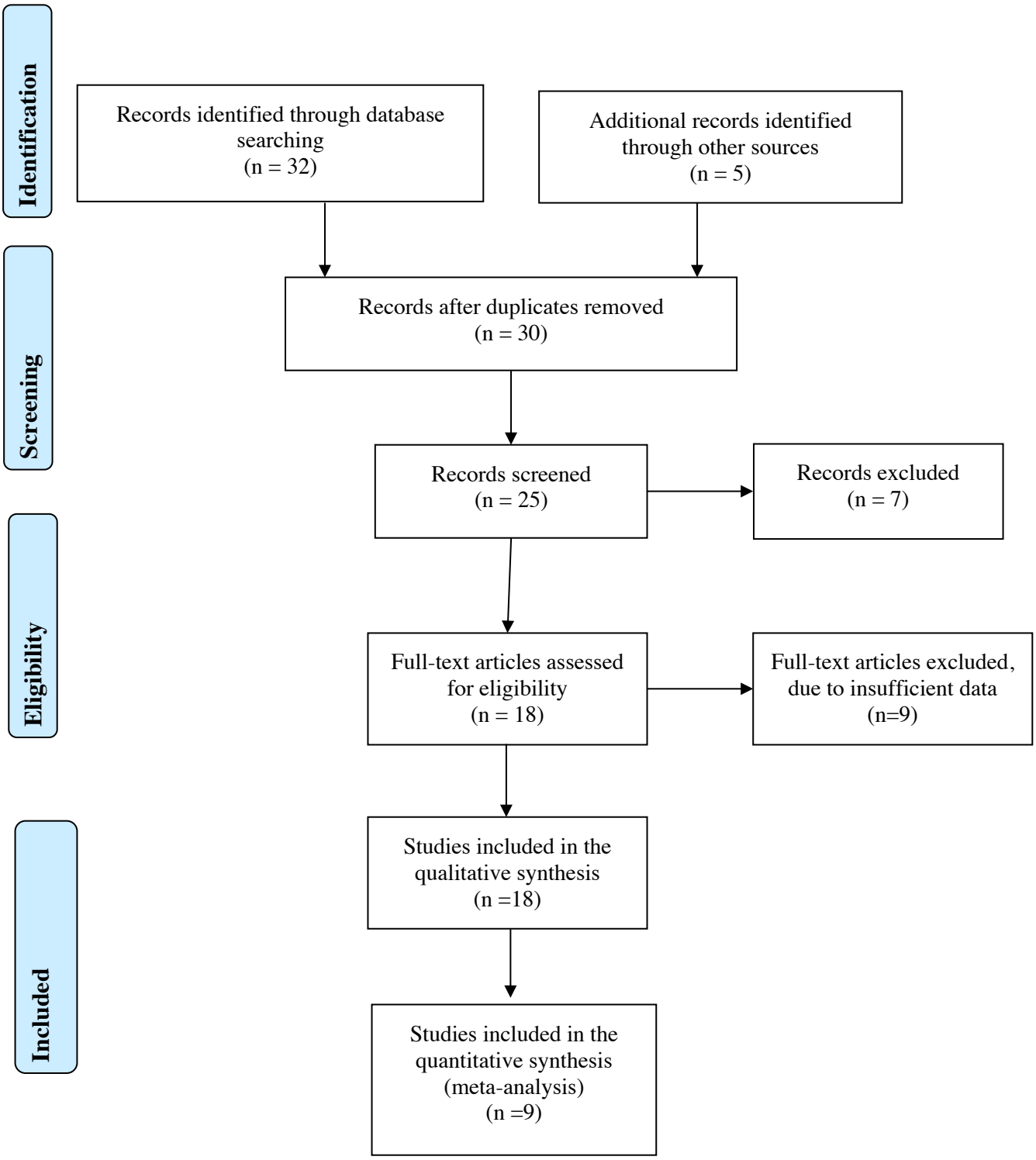


Figure 1. PRISMA flowchart of the literature search and article selection for a review on prevalence and risk factors associated with preterm birth.

Statistical Analysis

A random-effect model was used to estimate the pooled prevalence of the associated risk factors of PTB using MS-Excel.[12] The I^2 statistics were also calculated to describe the variations among various studies caused due to its heterogeneity.[13] A Forest plot was drawn to assess the overall association between various risk factors, and PTB.

RESULTS

It is evident from the available literature that the prevalence of PTB is more frequent in developing countries like India compared to developed countries. [2] In general, the prevalence of PTB is significantly high among the Indian population which is also found to be higher than the prevalence rate estimated by WHO.[14] Most of the existing studies related to PTB in India are concentrated in some specific states, and the studies on PTB has not been explored in most of the Indian population. The available studies were mainly conducted in the states of Gujarat, Karnataka, Maharashtra, Tamil Nadu and Uttar Pradesh; limited studies have been reported from some of the other states like Goa, Haryana, and Punjab. Different study designs have been adopted to understand the risk of PTB including hospital-based studies, case-control studies, community-based studies, and longitudinal cohort study methods; and the majority of the studies were published during the years 2016 and 2017.

The rate of prevalence of PTB reported in India varies greatly. The highest PTB frequency was reported from Tamil Nadu (28.25%)[15] and the lowest from Maharashtra (6.1%)[16]. According to the available data, it is evident that the degree of prevalence of PTB varies within the state of Uttar Pradesh, ranging from 18.4% to 25.6%. [17-19]

Regarding the types and prevalence of PTB, a study conducted among women in rural communities near Nagpur, Central India, reported high rates of moderate to late PTB (67%), very preterm (22%) and extreme preterm (11%).[20] Other similar studies also revealed a high prevalence of extreme PTB in Punjab (60%), Gujarat (15.6%), and Haryana (7%).[20-22] The highest frequency of very PTB is reported from Gujarat (52.6%). It is followed by Haryana (38%) and Punjab (22%), whereas frequencies of moderate to late PTBs the highest in Haryana (55%), followed by Gujarat (31.6%) and Punjab (18%) (Figure 2).

[a]Mahajan et al.,2017[21]; [b]Garg et al.,2017[22]; [c]Dayanithi, 2018[17]; [d]Singh et al.,2018[19]; [e]Jamal et al.,2017[18]; [f]Trivedi et al.,2019[34]; [g]Radhanpuri et al.,2014[30]; [h]Patel et al.,2015[26]; [i]Ahankari et al.,2017[16]; [j]Bangal et al.,2012[28]; [k]Avachet et al.,2013[31]; [l]Shetty et al.,2017[27]; [m]Tellapagadra et al.,2016[29]; [n]Rashmi et al.,2016[33]; [o]Fernnades et al.,2015[25]; [p]Rao et al, 2014[23]; [q]Soundarajan et al, 2016[24]; [r]Kuppusamy et al, 2016[15]

Figure 2 Map of India indicating prevalence (%) of preterm birth in various states

The incidence of PTB in India was examined using the available published data during the period 2012 to 2020. The data on the prevalence of PTBindicates an increasing trend during the last nine years (Figure 3).

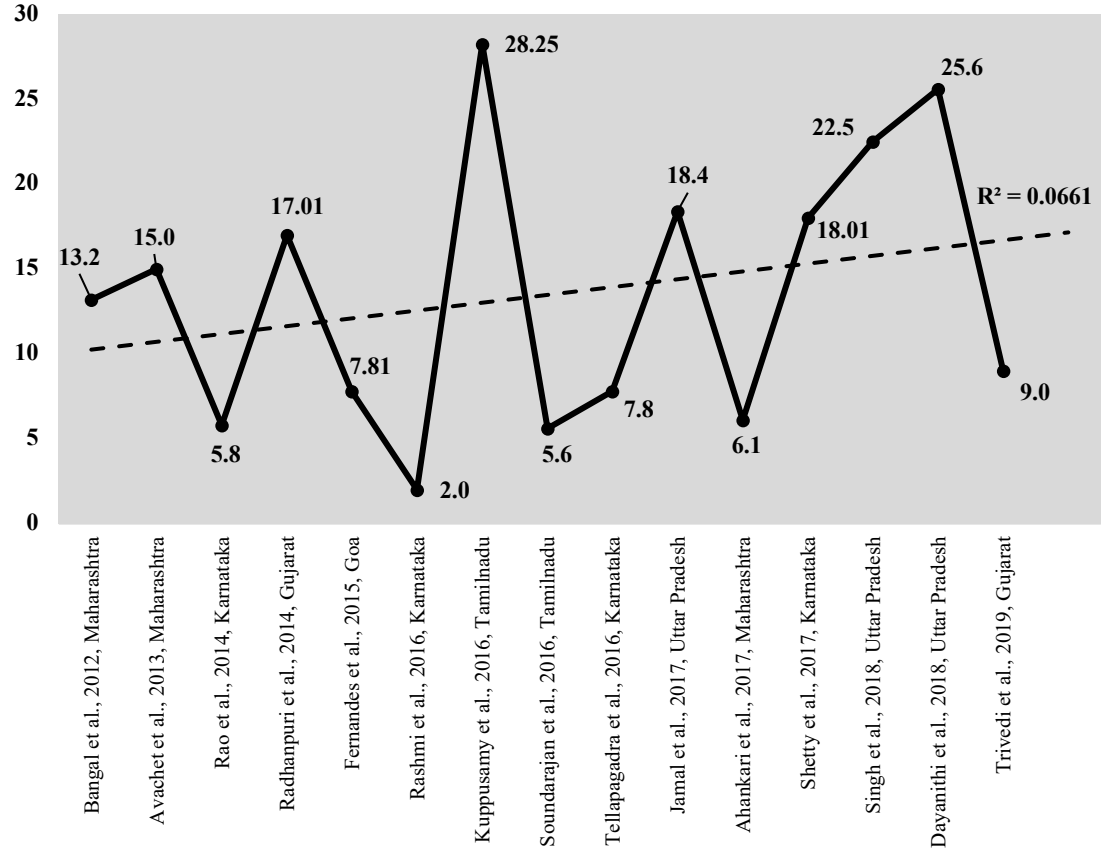


Figure 3 Incidence of preterm birth over the study period with trend line

The available data from PTB studies have identified various potential risk factors causing PTB. These risk factors could be broadly categorized into two major groups based on their nature of risk: modifiable and non-modifiable risk factors. Each group consists of various sub-groups with different type of risk factors. The modifiable risk factors include mother's behavior at the time of pregnancy, level of awareness, socio-demographic factors, socioeconomic status, nutritional status, and medical history of illness. Non-modifiable risk factors include genetics, pregnancy-induced medical conditions, infection during pregnancy, and the mother's pregnancy history.

Table 1 Studies on preterm birth and its risk factors among the Indian population

Author and year of publication (state)	Study design	No of cases	No of Control	Prevalence (%)	Associated Risk factors	*OR/*ARR with 95% CI	Outcomes
Bangal et al., 2012 (Maharashtra)[28]	Prospective observational study	21	125	13.2	Antepartum haemorrhage, maternal anemia, hypertension	-	Preterm labor, perinatal mortality
Avachet et al., 2013 (Maharashtra)[31]	Cross-sectional study	315	2105	15	Low socioeconomic status, urinary tract infections, prior history of preterm birth	-	Preterm labor
Rao et al., 2014 (Karnataka) [23]	Case-control study	154	334	5.8	Gestational hypertension	*3.23 (1.85-5.63)	Preterm birth, Low birth weight
					Height <1.50m	*1.96 (1.12-3.42)	
					Polyhydramnios	*1.90 (1.00-3.61)	
					Twin gestation	*7.60 (2.44-23.73)	
					Threatened abortion	*2.94 (1.30-6.63)	
Radhanpuri et al., 2014 (Gujarat)[30]	Retrospective hospital-based study	272	1599	17.01	Poor socioeconomic status, previous preterm birth, anemia and Malnutrition, advanced maternal age	-	Preterm birth
Fernandes et al., 2015 (Goa)[25]	Case-control study	410	250	7.81	Hypertensive disorders, antepartum haemorrhage, malpresentation, multiple gestations, UTI, and presence of vaginal infections	-	Preterm birth
Patel et al., (2015) (Baroda, Gujarat)[26]	Prospective comparative study	120	120	EP- 15.6 VP- 52.6 MLP-31.6	Low socioeconomic status	*2.02 (1.18-3.45)	Preterm labor
					Prior preterm birth	*5.11 (1.67-15.61)	
					Prior second trimester abortion	*3.53 (1.25-9.99)	
					Inadequate antenatal care	*1.90 (1.13-3.18)	

Author and year of publication (state)	Study design	No of cases	No of Control	Prevalence (%)	Associated Risk factors	*OR/*ARR with 95% CI	Outcomes
					Maternal medical disorders (anemia, Pregnancy induced hypertension, jaundice, cardiac disease, diabetes mellitus, tuberculosis etc)	*7.97 (4.32-14.69)	
					Uterine over distension	*31.31 (4.16-235.34)	
					Urinary tract infection	*3.28 (1.15-9.35)	
					Bacterial vaginosis	*5.29 (2.49-11.23)	
					CRP reactive (chorioamnionitis)	*6.36 (2.35-17.20)	
					Other infections (associated with fever)	*8.6 (1.04-69.05)	
Rashmi et al., 2016 (Karnataka)[33]	Community-based longitudinal study	5	246	2.0	Gestational diabetes mellitus	*11.8 (1.11-125.41)	Preterm birth
					Age of the father	*7.57 (1.47-38.99)	
					Previous stillbirths, Intrauterine death, Previous caesarean section	*5.76 (0.91-36.14)	
Kuppusamy et al., 2016 (Tamilnadu)[15]	Retrospective hospital-based study	609	1547	28.25	Anemia, PROM, Pregnancy-induced hypertension, oligohydramnios, multiple pregnancies, gestational diabetes mellitus	-	Preterm birth
Soundarajan et al., 2016 (Tamilnadu)[24]	Case-control studies	356	579	5.6	Prior preterm birth	*12.7 (3.9-40.4)	Preterm birth
					Hypertension	*7.3 (2.1-25.4)	
					Oligohydramnios	*3.9 (1.6-9.5)	
					Diabetics	*3.7 (1.1-11.8)	

Author and year of publication (state)	Study design	No of cases	No of Control	Prevalence (%)	Associated Risk factors	*OR/*ARR with 95% CI	Outcomes
					Prepregnancy low BMI	*2.0 (1.1-3.8)	
					Urinary tract infection	*1.8 (1.0-3.2)	
					Hypothyroid	*2.0 (1.0-3.8)	
Tellapagadra et al., 2016 (Karnataka)[29]	Prospective hospital-based study	61	790	7.8	Previous preterm delivery	**5.37 (1.5-19.1)	Preterm birth
					Periodontitis	**2.75 (1.1-4.9)	
					Oligohydramnios	**5.23 (2.4-11.5)	
					Presence of Nugent's intermediate vaginal flora	**2.75 (1.4- 5.1	
					Gestational diabetes mellitus	**2.91 (1.0-8.3)	
					Maternal height <1.50 m	**2.21 (1.1-4.1)	
Jamal et al., 2017 (Uttar Pradesh)[18]	Retrospective analytical study	436	2128	18.4	Teenage mother, elderly gravidas, multiparity, inadequate antenatal care, PROM, Pregnancy-induced hypertension	-	Preterm birth, high labor induction, and caesarean section rates
Ahankari et al., 2017 (Maharashtra)[16]	Retrospective hospital-based study	40	615	6.1	Maternal age	*3.21 (1.54-6.69)	Preterm birth
					Primigravida	*3.75 (2.21-6.37)	Low birth weight
Mahajan et al., 2017 (Jalandhar)[21]	Prospective study	100	100	EP- 60.0 VP- 22.0 MLP- 18.0	Preeclampsia, PROM, history of previous preterm births, genitourinary infections, polyhydramnios	-	Preterm birth
Garg et al., 2017 (Haryana)[22]	Hospital-based study	100		EP-7.0 VP-38.0 MLP-55.0	Genitourinary tract infections, PROM, history of Preterm birth and abortions	-	Preterm birth
Shetty et al., 2017 (Karnataka)[27]	Retrospective cohort study	343	1904	18.01	Hypertensive disorder during pregnancy, PROM,	-	Neonatal mortality Stillborn

Author and year of publication (state)	Study design	No of cases	No of Control	Prevalence (%)	Associated Risk factors	*OR/*ARR with 95% CI	Outcomes
					idiopathic, and previous LSCS		
Singh et al., 2018 (Uttar Pradesh)[19]	Cross-sectional study	45	155	22.5	Advanced maternal age, lower socioeconomic status, women residing in a rural area with primary or illiterate education status	-	Preterm birth
Dayanithi., 2018 (Uttar Pradesh)[17]	Cross-sectional study	103	406	25.6	Joint families, ≤Rs 2999/- monthly income, maternal illiteracy, and housewives	-	Preterm birth
Trivedi et al., 2019 (Gandhinagar, Gujarat)[34]	Cohort study	180	1797	9.0	Periodontal disease, long sleep duration during pregnancy, sex during any trimester	-	Preterm birth

*N.B: EP- Extreme preterm; VP- very preterm; MLP- moderate to late preterm; UTI- urinary tract infection; LSCS- Lower segment caesarean section; PROM- Premature rupture of membrane; *OR- Odd ratio; *ARR- Assisted relative risk*

The risk of PTB is associated with various maternal health conditions induce during pregnancy. Pregnancy-induced hypertension (PIH) is one of the most common medical conditions causing PTB in India.[18,20,23] It is evidently the most common (21.45%) obstetrical PTB risk factor among the Southern Indian population.[23] Moreover, the risk of occurrence of PTB more than triples among mothers experiencing PIH (OR=3.23, CI 1.85-5.63). Such positive association have also been reported from different population groups by different studies.[15,18,20,21,24] It is followed by gestational diabetes, which significantly contributes to the increased risk of PTB occurrence.

Community-based longitudinal studies conducted among the rural population of Mysuru have revealed a strong positive association between mothers with gestational diabetes and preterm delivery (OR=11.8, CI 1.11-125.41).[14,22,23,25,26] The premature rupture of membrane (PROM) before the onset of labor, one of the common complications of pregnancy, is also reported to be significantly associated with preterm birth by various studies.[15,18,21,22,27] Abnormal volume of amniotic fluid during gestational age (oligohydramnios and polyhydramnios) is also reported to be significantly associated with PTB.[15,18,21,22,27]

In addition to the above risk factors of PTB, other pregnancy-related medical conditions have been reported to be a risk for PTB by different studies such as threatened abortion, idiopathic, hypothyroid, antepartum haemorrhage,

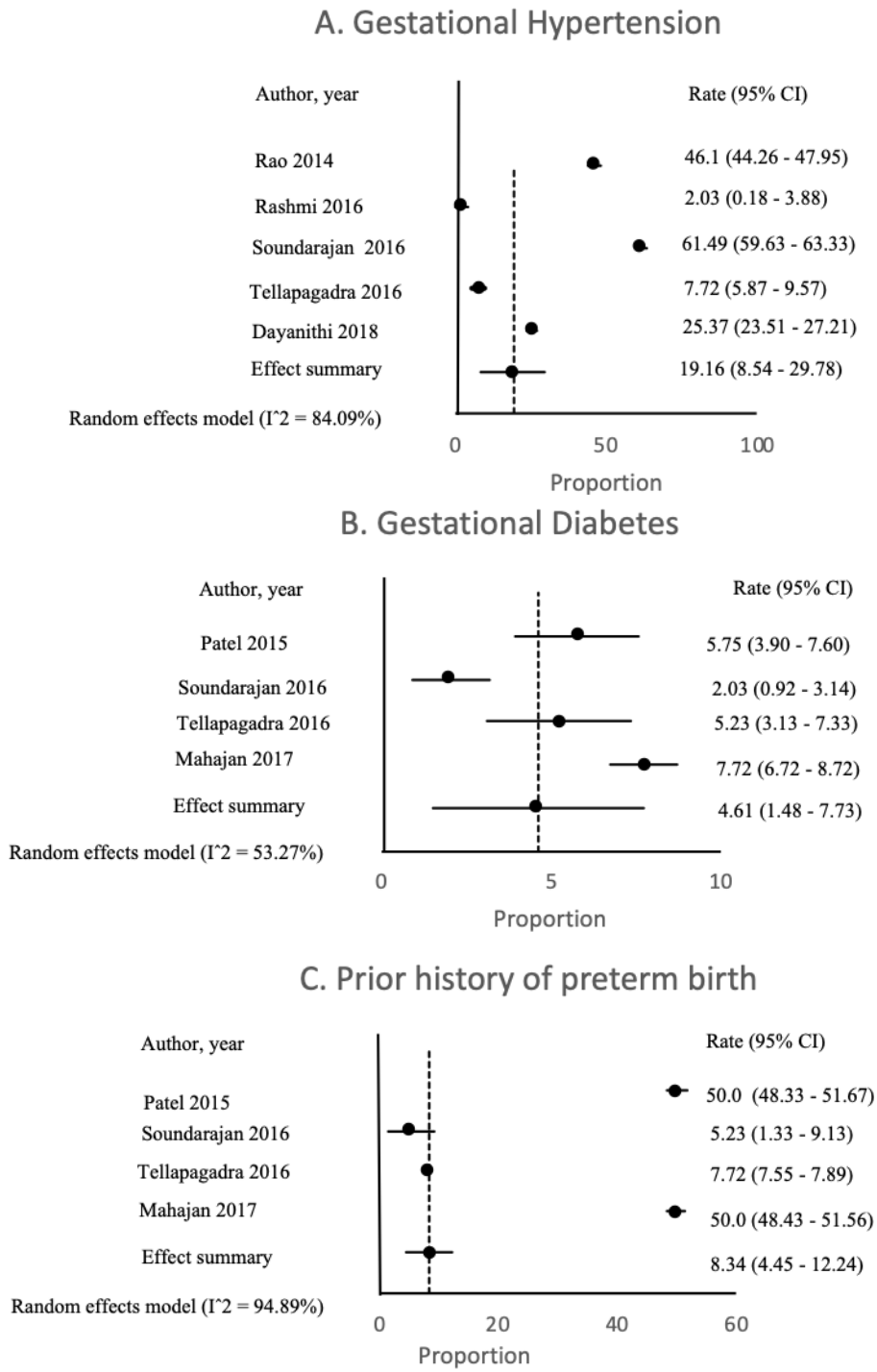
malpresentation, and uterine over distension.[23-25,27-28] Moreover, multiple pregnancy, i.e. pregnancy with more than one baby at a time, such as multiparity[18] and multiple gestation[15,23,35] have been reported to have a significant relationship with PTB.

Mothers having a prior history of preterm delivery are more likely to have PTBs as compared to mothers with a history of term birth delivery.[20-22,24,29-31] Pregnancies for the first time (both primigravida and elderly gravida) are also more likely to deliver preterm babies.[19,32] Besides, the history of abortion[18,20], intrauterine death, previous stillbirth, and delivery via cesarean section are also reported to be at higher risk of causing preterm delivery[18,27,33]. Mothers with urinary tract infection, bacterial vaginosis, and other infections such as fever and periodontitis are also at risk for PTB.[16,21-22,29,34] Low body mass index (BMI) before pregnancy is at higher risk of PTB.[24] Mothers with height <1.50 m showed more than one fold increased risk for PTB delivery.[22,29] However, inconsistent results have also been reported[20]. The incidence of PTB was significantly much higher among the malnourished mother and the mother having different degrees of anemia.[23] Low intake of folate supplements during pregnancy also shows an increased risk of PTB.[35]

Mothers with low educational status are more likely to deliver preterm babies than mothers with higher educational status.[17,19-20] The majority of the rural women who delivered prematurely belong to the low socioeconomic class.[28,31] It is also evident that women living in joint families, having a low monthly income, and those who are housewives are at higher risk for PTB.[19,32]

The risk of delivering a low birth weight baby was twice as high as in teenage mothers (maternal age ≤19 years).[16,36-37] Moreover, the advanced maternal age (40 and above) was shown to be associated with PTB.[19,30] An increase in paternal age has also been reported to be associated with PTB.[33] It is evident that most of the mothers who had preterm deliveries had never sought antenatal care (ANC).[18,20-21] Moreover, behaviors of the mother during pregnancy, such as long term sleep and sexual intercourse during any trimester, are also more likely to deliver preterm babies.[34]

Nine research articles met all of the inclusion criteria for full-text review in the quantitative analysis involving 18,470 women regarding the pooled prevalence rate. The included studies were all almost entirely case-control and cross-sectional studies[19,22-25,31-32], with only one cohort study[34]. Five studies published during the period 2014-2018 were included for estimation of pooled prevalence of associated gestational hypertension with PTB.[15,23-24,29,33] The sample size of the studies ranges from 246 to 4137, giving 6158 samples. The pooled risk is 19.16% for gestational hypertension with I^2 = 84.09% (95% CI 8.54 to 29.78) (Figure 4A). Four studies published from 2015 to 2017 were included to estimate pooled risk of PTB due to gestational diabetes. [20,24,29,32] The pooled risk of PTB among women with gestational diabetes was 4.61% (95% CI 1.48 to 7.73) with I^2 = 53.27% (Figure 4B).


A. Gestational Hypertension
Author, year
Rate (95% CI)
Rao 2014
46.1 (44.26 - 47.95)
Rashmi 2016
2.03 (0.18 - 3.88)
Soundarajan 2016
61.49 (59.63 - 63.33)
Tellapagadra 2016
7.72 (5.87 - 9.57)
Dayanithi 2018
25.37 (23.51 - 27.21)
Effect summary
19.16 (8.54 - 29.78)
Random effects model (I^2 = 84.09%)
0
50
100
Proportion
B. Gestational Diabetes
Author, year
Rate (95% CI)
Patel 2015
5.75 (3.90 - 7.60)
Soundarajan 2016
2.03 (0.92 - 3.14)
Tellapagadra 2016
5.23 (3.13 - 7.33)
Mahajan 2017
7.72 (6.72 - 8.72)
Effect summary
4.61 (1.48 - 7.73)
Random effects model (I^2 = 53.27%)
0
5
10
Proportion
C. Prior history of preterm birth
Author, year
Rate (95% CI)
Patel 2015
50.0 (48.33 - 51.67)
Soundarajan 2016
5.23 (1.33 - 9.13)
Tellapagadra 2016
7.72 (7.55 - 7.89)
Mahajan 2017
50.0 (48.43 - 51.56)
Effect summary
8.34 (4.45 - 12.24)
Random effects model (I^2 = 94.89%)
0
20
40
60
Proportion

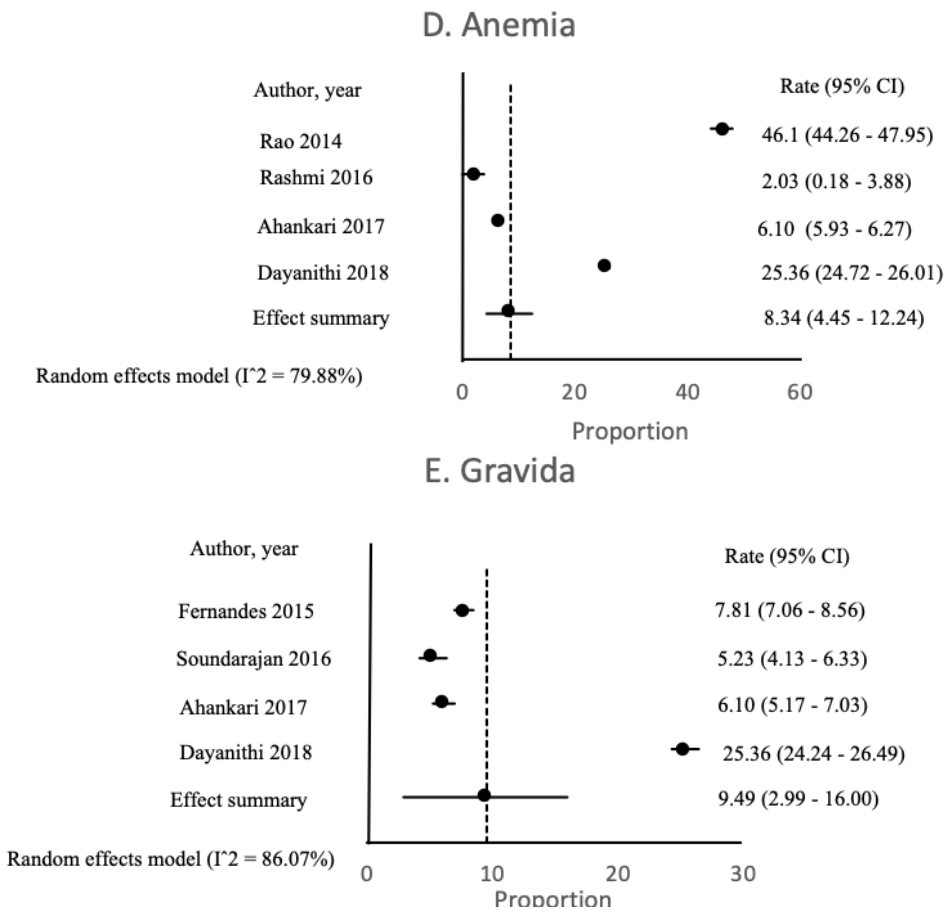


Figure 4 Forests plots of Preterm birth with (A) Gestational Hypertension, (B) Gestational Diabetes, (C) Prior history of preterm birth, (D) Maternal Anemia, and (E) Gravida

Out of nine studies, four studies reporting the prior history of PTB as a risk factor of preterm delivery were included for assessing the pooled risk of PTB with a total sample size of 8035 and published from 2015 to 2017. [20,21,24,29] The pooled risk of PTB was 8.34% (95% CI 4.45 to 12.24, I^2 = 94.89%) for mothers having a prior history of preterm delivery (Figure 4C). Four studies reported the overall risk of anemia at <37 weeks of gestation with a total sample size of 5746 and published from 2014 to 2018.[16,17,23,33] The risk of PTB (ranging from 2.03% to 46.1%) among anemic mothers was 8.34 % (95% CI 4.45 to 12.24, I^2 = 79.88%)(Figure 4D).[14,19,21,22] Regarding gravida, four studies published during the period 2015 to 2018 are included, reporting the association of PTB with gravida with a total of 14,021 samples.[16,24,25,33] The pooled risk of PTB among the Indian population was 9.49% for gravida with I^2 = 86.07% (95% CI 2.99 to 16.00) (Figure 4E).

DISCUSSION

The present review, including 18 studies and representing 18,470 women provides an overview of PTB's potential risk factor(s) among the Indian population. The selection of studies was based on a clearly defined search strategy. The WHO estimates PTB prevalence from 5% to 18%

across 184 countries of which the highest rates are reported in Sub-Saharan Africa and South Asia[1]. The present review provides the current trends in the prevalence of PTB in India. The overall prevalence of PTB rates in India is above 15% level as estimated by WHO[4]. The prevalence of PTB among the Indian population is higher than that reported by studies from other parts of the world. The highest PTB rate was reported as 18.5% among Tanzania's population, and the lowest rate was reported from Ethiopia (4.4%). [38-39]

The findings of the present review on risk factors associated with PTB show similar results compared with studies reporting risk factors associated with PTB outside of India. A study conducted in China reported that advanced or young maternal age, hypertensive disorders in pregnancy, and miscarriage or stillbirth history were significantly associated with PTB (p=<0.05).[40] A hospital-based study in Brazil indicates that multiple pregnancies and inadequate prenatal care have been indicated as PTB risk factors.[41] Furthermore, the prior history of PTB increased the chance of PTB delivery by 23% among Brazilian women. Maternal medical complications, maternal age <20 or ≥40 years were positively associated with an increased risk of preterm delivery.[42] Moreover, PTBs have increased odds of occurring among the African-American and Asian-American/Pacific Islander women having chronic hypertension.[43] Urinary tract infections increase a woman's risk of preterm delivery.[44] It is also evident that low socioeconomic status, and stress, prolonged working hours, and advanced maternal age at childbirth are associated with increased odds of preterm delivery.[45]

The overall pooled risk of PTB with gestational diabetes in the present study is inconsistent with a previous review conducted among the Ethiopian population reporting a 4.69% risk with I^2=67.6% among mothers with gestational hypertension (95% CI 2.32 to 9.49).[46] Similarly, the risk of PTB with the previous history of PTB was 30.0% (95% CI 27 to 34, I^2 = 98.6%) indicating between-study heterogeneity.[47] It supports the findings of the present review in which the pooled risk of PTB was 8.34% with I^2 94.89% among mothers having a history of preterm delivery (95% CI 4.45 to 12.24), which is also observed to be high in heterogeneity. Regarding maternal anemia and its association with PTB, one of the studies revealed that maternal anemia during pregnancy increases the risk for premature birth with a relative risk of 1.56 [95%CI, 1.25 to 1.95]).[48] Similarly, a study conducted among the low and middle-income countries including 13 studies showed a significantly greater risk of PTB among anemic pregnant women (RR=1.63, 95% CI 1.33-2.01, I^2=88%).[49] Our findings are consistent with previous studies[44-47] showing that PIH, prior history of PTB, and maternal anemia are associated with PTB. Besides, the present review also found that gestational diabetes (4.61%, 95% CI 1.48-7.73, I^2 =53.47%) and gravida (9.49%, 95% CI 2.99-16.00, I^2 = 86.07%) are risk factors of PTB which have not been reported previously. Considering, the overall pooled risk and its heterogeneity I^2 values, PIH, gestational diabetes, prior history of PTB, maternal anemia, and gravida could pose a higher risk of PTB among the Indian population.

STRENGTHS AND LIMITATIONS

Strengths of the present review include a thorough and systematic search of multiple databases, so all the relevant publications were likely identified. It provides a reference target of the already-

existing evidence for each associated risk factors as well as charts out the direction in which further research is needed from an Indian perspective. Since there has been no similar previous study, this review showed the national pooled prevalence of the effect of absolute risk factors like PIH gestational diabetes, prior history of PTB, maternal anemia, and gravida on PTB in India.

The search strategy was limited to articles published in English and freely accessible. This could have led to the risk of publication bias. A limited number of studies performed on PTB among the Indian population, thus not being a true representation of the entire country. Moreover, hand searching for gray literature has not been detailed in the search strategy. Considering the limited number of studies included for statistical analysis, the quality of the analysis may have been hampered since many other potential risk factors could not be pooled and all of the existing evidence could not be summarised. Relevant predictors are likely to have been missed, and hence future research should include other risk factors of PTB for further in-depth research.

IMPLICATIONS AND FUTURE DIRECTIONS

The present study, being the first of its kind, might raise several important implications for future research and clinical practice. More research will be necessary to refine and further elaborate the outcomes of the present review. Findings of the present review can be used to identify the most significant risk factors of PTB to target the gaps in care to detect and implement solutions for better-quality outcomes. Further, updating systematic literature reviews might define the research gaps and propose new interventions to reduce various risk factors during pregnancy.

CONCLUSION

The prevalence of PTB is high and varies between different populations in India. Preterm delivery is significantly associated with various risk factors. It could be reduced significantly if pregnant women receive at least eight antenatal visits and if further culturally-appropriate maternity care is provided. The dynamic approach, combined with the improvement of the health care system and women's knowledge of ANC might also reduce PTB. There is an urgent need to focus on intervention programs at the community level to reduce neonatal morbidity and mortality in children and reduce mothers' future health risks. Further research will be necessary to refine and elaborate on the present review outcomes; future research may also build on the potential risk factors observed in the present review. Population-specific research studies should also be encouraged to address the unanswered issues that matter most to women at high risk of PTB.

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