Clinical Research

High preterm birth at Cipto Mangunkusumo Hospital as a national referral hospital in Indonesia

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ABSTRAK

Latar belakang: *Kelahiran prematur merupakan penyebab langsung kematian neonatus. Indonesia merupakan salah satu penyumbang kelahiran prematur terbanyak pada tahun 2010. Studi ini bertujuan untuk mengidentifikasi prevalensi dan faktor risiko kelahiran prematur di RSUPN Cipto Mangunkusumo sebagai rumah sakit rujukan nasional.*

Metode: *Studi kohort retrospektif dengan melibatkan 2.612 wanita yang melahirkan dari Januari hingga Desember 2013. Semua data yang berkaitan dengan faktor risiko potensial dan luaran kelahiran prematur dicatat. Selanjutnya dilakukan analisis bivariat dengan chi-square dan t-test atau Mann-Whitney, serta analisis regresi logistik menggunakan SPSS versi 20.*

Hasil: *Sebanyak 1.020 dari 2.616 (38,5%) persalinan merupakan kelahiran prematur. Pasien yang datang karena rujukan meningkatkan 2 kali lipat kelahiran prematur (OR 1,89; 95% IK 1,37–2,61). Wanita dengan kehamilan tunggal (OR 0,17; 95% IK 0,12–0,25), presentasi kepala (OR 0,75; 95% IK 0,63–0,89), dan kunjungan antenatal yang teratur (OR 0,67; 95% IK 0,54–0,84) memiliki risiko rendah mengalami kelahiran prematur. Skor Apgar, berat lahir, dan cara persalinan sangat berbeda antara kelompok lahir cukup bulan dengan kelompok prematur.*

Kesimpulan: *Prevalensi kelahiran prematur di RSUPN Cipto Mangunkusumo 2,5 kali lipat lebih tinggi daripada angka nasional. Beberapa faktor protektif kelahiran prematur adalah kehamilan tunggal, presentasi kepala, dan kunjungan antenatal yang teratur.*

ABSTRACT

Background: Preterm birth is the leading direct that causes neonatal death. Indonesia was listed as one of the countries with the greatest number of preterm birth in 2010. This study aims to identify the prevalence and the potential risk factors of preterm birth among women underwent delivery in Cipto Mangunkusumo Hospital, an Indonesian national reference hospital.

Methods: This retrospective cohort study involved 2,612 women who delivered between January and December 2013. Any clinical data which related to the potential risk factors and outcomes were recorded. The data were managed using chi-square for bivariate analysis and t-test or Mann-Whitney for numerical data followed by multiple logistic regression for multivariate analysis in SPSS version 20.0.

Results: Preterm birth affected 1,020 of 2,616 pregnancies (38.5%). Non-booked patients increased nearly twice risk for preterm delivery (OR 1.89, 95% CI 1.37–2.61). While women with singleton pregnancy (OR 0.17, 95% CI 0.12–0.25), head presentation (OR 0.75, 95% CI 0.63–0.89), and regular ANC (OR 0.67, 95% CI 0.54–0.84) had lower risk for preterm birth. Apgar score, birthweight, and mode of delivery were significantly different between the pre-term group and the full-term group.

Conclusion: Prevalence of preterm birth in Cipto Mangunkusumo Hospital was approximately 2.5 times higher compared to the national number. Several factors reducing preterm birth rate include singleton pregnancy, head presentation, and regular ANC.

Preterm birth is the leading direct cause of neonatal death.[1] The rate of preterm birth has substantially increased in many locations.[2] In 2010, Indonesia were listed as one of the countries with the greatest number of preterm birth. There were 15.5% preterm birth of all livebirths.[3] Preterm deliveries occurred as a part of multi factorial process. Genetic, maternal, fetal and environmental factors affected the occurrence of preterm birth.[4,5] Maternal age, low body mass index (BMI), multiple pregnancies were maternal factors associated with the incidence of preterm labour.[5,6] Complex inflammation was the most responsible condition while infection probably has become the most clearly-understood factor.[7,8]

Preterm birth is associated with significant maternal, fetal, and neonatal risks. It accounts for 28% of causes in neonatal death and up to 75% of neonatal morbidity.[9] In Indonesia, preterm birth contributed as many as 36% of all neonatal death causes.[10] It possibly leads the newborn to neurocognitive deficits, pulmonary dysfunction and ophthalmologic disorders.[9] Intrauterine fetal death (IUFD), intrauterine growth restriction (IUGR), heart rate abnormalities, early onset neonatal sepsis, intraventricular hemorrhage, cerebral palsy, anemia, constipation, and twin-twin transfusion syndrome were also associated with the preterm deliveries.[7,11] These situations raise the needs for local epidemiological study of preterm birth in every level hospital in Indonesia. One of the tertiary national referral center hospital in Indonesia is Dr. Cipto Mangunkusumo Hospital. We assume that the prevalence of preterm birth in tertiary referral hospital will be higher than other hospitals because preterm delivery, especially the babies, needs advanced technology to increase the neonatal survival rate. Therefore, this study aims to determine the prevalence and potential risk factors for preterm birth among women underwent delivery in Dr. Cipto Mangunkusumo Hospital. The authors hope that by determining this prevalence and risk factors, the clinician, especially obstetrician, can perform strategic step to protect and early diagnose of preterm birth.

METHODS

The database used in this study was collected from the medical record of patients during the year of 2013. For each patient, we entered demographics, obstetric history, diagnosis, management, laboratory data, as well as maternal and neonatal outcomes. Maternal age was classified into less than 20, 20 to 35 and more than 35 years old because the optimal and recommended reproductive age is 20 to 35 years old. Validated clinical information was recorded into the database in a consistent manner. Non-complete medical records were included in this study. However, for each analysis, medical records without required data have been excluded. The data for all patients were entered by a single data manager at the end of study period. The study has been approved by the Institutional Review Board at University of Indonesia number 503/H2.F1/ETIK/2014.

Retrospective analysis was conducted on the entire cohort of singleton and twin pregnancies. The patient could be both of booked and non-booked cases. The primary independent variable for this study was maternal age, number of fetus (single or multiple), parity, previous cesarean section (CS), referral type (booked-case or not), regularity of antenatal care (ANC), and leukocytes count at presentation. Gestational age was analyzed categorically as full-term (≥37 weeks), extremely preterm (<28 weeks), very preterm (28–<32 weeks), and moderate or late preterm (32–<37 weeks) newborns. Several preterm birth outcomes such as methods of delivery, Apgar score, birth weight, and amniotic fluid color (color of amniotic fluid observed during labor) were studied secondarily.

IBM SPSS Statistics version 20.0 was used for statistical analyses. Bivariate analyses for categorical data using chi-square was performed to find the association between preterm birth and independent t-test or Mann-Whitney test used for numerical data. We considered p value <0.05 as statistically significant. Multiple logistic regression analysis with a backward elimination stepwise regression approach was used to evaluate the association between preterm delivery and potential risk factors. Adjusted odds ratios with their confidence intervals were used to describe the relative risk of the potential risk factors.

RESULTS

Preterm birth affected 1,020 of 2,616 (38.5%) all pregnancies was analyzed. Moderate to late

Table1. Distribution of gestational age at birth according to gestational age group and subgroup

	Gestational Age	Proportion of all birth (n,%)
Preterm	<37 weeks	1,020(38.5%)
Extremely preterm*	<28 weeks	99(9.7%)
Very preterm*	28–<32 weeks	234(22.9%)
Moderate to late preterm*	32–<37 weeks	687(67.4%)
Full-term	≥37 weeks	1,574(59.9%)
Post-term	≥42 weeks	35(1.3%)

* Proportion of all preterm birth

preterm births were accounted for 67.4% of all preterm births while very preterm and extremely preterm were 22.9% and 9.7%, respectively. The preterm birth cohort was characterized by a significantly higher prevalence of women aged 20–33, multiparous, non-booked cases patients, and singleton head presentation. Incomplete fields were not eligible for analysis. Therefore, the number of subjects for each bivariate analysis resulted in various number (Table 1). Maternal age, referral type, presentation, number of babies, and regularity of ANC were associated with preterm birth (Table 2). In multivariate analysis,

Table 2. Clinical characteristics of pregnancies according to gestational age at deliveries

	Preterm	Full-term	P value	OR (95%CI)
Maternal age (n=2608)			<0.001*	-
<20	151 (15.6%)	157 (9.6%)		
20–35	654 (67.4%)	1,177 (71.9%)		
>35	165 (17.0%)	304 (18.6%)		
Parity (n=2609)			0.097*	-
Nulliparous	456 (47.0%)	711 (43.4%)		
Primiparous	264 (27.2%)	446 (27.2%)		
Multiparous	250 (25.8%)	482 (29.4%)		
Referral type (n=2598)			<0.001*	1.80 (1.32–2.45)
NBC	908 (94.0%)	1,464 (89.7%)		
BC	58 (6.0%)	168 (10.3%)		
Previous cesarean section (n=2591)			0.870*	-
Yes	98 (9.6%)	154 (9.8%)		
No	922 (90.4%)	1,417 (90.2%)		
Maternal morbidity				
PROM (n=2588)	420 (43.7%)	689 (42.3%)	0.500*	1.06 (0.90–1.24)
Preeclampsia with severe features (n=2601)	238 (24.6%)	344 (21.0%)	0.033*	1.23 (1.02–1.48)
Eclampsia (n=2600)	43 (4.5%)	31 (1.9%)	<0.001*	2.41 (1.51–3.85)
Anemia (n=2594)	207 (21.4%)	273 (16.8%)	0.003*	1.35 (1.11–1.66)
Presentation (n=2609)			<0.001*	-
Head	809 (83.4%)	1,485 (90.6%)		
Breech	98 (10.1%)	92 (5.6%)		
Transverse	63 (6.5%)	62 (3.8%)		
Number of babies (n=2608)			<0.001*	0.17 (0.12–0.25)
Singleton	841 (86.7%)	1,596 (97.4%)		
Multiple	129 (13.3%)	42 (2.6%)		
ANC>3 times (n=2574)			0.001*	0.69 (0.56–0.86)
Yes	784 (81.9%)	1,403 (86.8%)		
No	173 (18.1%)	214 (13.2%)		
Leukocyte counts at presentation (x 10^3 µl) (n=2560) (median(min-max))	13,550 (2,100–42,500)	12,600 (1,860–39,300)	<0.015[†]	-

* Chi-Square Test; [†] Mann-Whitney U Test; NBC= non-booked case; BC= booked case; PROM= premature rupture of membrane; ANC= antenatal care

age less than 20 years old, referral type, eclampsia, and anemia increased the risk of preterm birth while singleton baby, head presentation, and regular ANC reduced the risk (Table 3).

Apgar score, birthweight, need for induction, and mode of delivery were significantly different between the pre-term group and the full-term group (Table 4). Apgar score and birthweight were significantly lower in the preterm group. Preterm pregnancy significantly led to higher cesarean section rate compared to the full-term group.

DISCUSSION

To best knowledge, this is the largest hospital-based study finding at preterm birth prevalence in Indonesia. The prevalence of preterm birth in this study was 2.5 times higher compared to the national prevalence (15.5%). It is predominantly affected by the high number of referral cases to this hospital. In accordance with a systematic review on prevalence of preterm birth, moderate to late preterm birth rate was the highest proportion of all preterm deliveries.[3] The result was similar with our study (67.4% cases of moderate to late preterm birth). Application of standard preterm definitions is important to study the survival probability of the neonates.[3]

Primiparity did not increase the risk for preterm birth in our study. However, Erez et al[12] concluded that primiparity was the independent risk factors for preterm delivery (OR 1.45, 95% CI 1.18-1.78). The age distribution of our population was

Table 3. Results of multiple logistic regression analysis on risk and protective factors for preterm delivery*

Variable	Coefficient	p	Adjusted OR	95%CI
Age <20 years old	0.47	0.03	1.60	1.17–2.18
Referral type (NBC)	0.63	<0.001	1.88	1.34–2.63
Singleton baby	-1.76	<0.001	0.17	0.12–0.25
Head presentation	-0.56	0.006	0.57	0.39–0.85
Eclampsia	0.87	0.001	2.39	1.44–3.96
Anemia	0.29	0.009	1.33	1.07–1.65
ANC>3 times	-0.27	0.022	0.76	0.60–0.96
Constant	1.11	0.001	3.05	

*Adjusted for maternal age, parity, referral type, premature rupture of membrane, preeclampsia with severe features, eclampsia, anemia, presentation, number of babies, antenatal care more than 3 times, and leucocyte more than 15,000/μL

Table 4. Perinatal outcomes associated with preterm birth according to gestational age at deliveries

	Preterm	Full-term	p
APGAR score (mean (SD)) (n=2197)			<0.001*
First minute	6.97 (2.54)	8.35 (1.28)	
Fifth minutes	8.35 (2.44)	9.50 (1.11)	
Birth weight (grams) (mean (SD)) (n=2197)	1,925 (608)	3,045 (471)	<0.001*
Mode of delivery (n=2590)			0.003†
Vaginal delivery	490 (48.1%)	848 (54.0%)	
C-section	529 (51.9%)	723 (46.0%)	
Amniotic fluid color (n=2289)			<0.001†
Clear	772 (87.3%)	1142 (81.3%)	
Scanty-green	98 (11.1%)	196 (14.0%)	
Thick-green	14 (1.6%)	67 (4.8%)	

* Chi-square test; † Mann-Whitney U test

similar to a study conducted by Chen et al. among upper middle class in Chinese population.[13] The percentage of women aged below 20 years old were higher in the preterm group compared to the non-preterm group in our study. Moreover, the association between maternal age and preterm birth was statistically significant. Nguyen et al[14] found that women aged 24 or below were tend to deliver preterm babies 1.9 times compared to 24–35 years old women. Meanwhile, a systematic review found that older maternal age was associated with preterm birth.[15] Therefore, there is insufficient evidence to conclude that older or younger maternal age is an independent risk factor for preterm birth.

This study did not find correlation between previous CS with preterm birth. Conversely, Di Renzo et al. found approximately three times increased risk for spontaneous preterm birth in women underwent previous CS.[16] Regular ANC was one of the independent protective factors for having preterm birth. It had been described previously by Bastek,[17] which stated that no prenatal care was one of the components in prediction models of women for having delivery before 37 weeks.

Singleton pregnancy revealed a reduced risk to preterm labor (p<0.001; OR 0.17; 95% CI 0.12-0.25). Nice Clinical Guidelines stated that more than 50% of twins and almost all triplets were born before 37 weeks of gestation, and 15–20% would be admitted in neonatal unit related to preterm.[18] In this study, there was a significant association between white blood cell count and prevalence of preterm birth. However, it did not affect in multivariate analysis. Surabhi et al[19] stated that stress of delivery may lead to brisk leukocytosis. Apart from that, the increase of white blood cell was usually identified in patients with intrauterine infection and adverse perinatal outcome. Nevertheless, amniotic fluid white blood cell was a better independent predictor than white blood cell.

Significant lower birthweight was found in most of preterm studies.[20,21] The birthweight of preterm babies in this study was 1,925 grams. It is comparable with 33–35 weeks gestation babies delivered in ten California and Massachusetts hospitals, ranging from 1,759 to 2,215 grams.[22] In another large study, the birthweight of 34–36 weeks babies ranged from 2,195 to 2,687 grams.[21] Very preterm babies included in the analysis could lower the mean of birthweight. Apgar scores in both 1st and 5th minutes were significantly associated with preterm birth. It had been previously described in China, with Apgar score on 1st min and 5th min was 7.7 (SD 2.43) and 8.9 (SD 1.81).[13] Consequently, this situation will possibly lead to the substantial risk for neonatal deaths.[20]

The limitation of this study is that we collected the data from a tertiary, national referral hospital. Thus, the result might be hardly applied in general setting. The Apgar score was prepared by the attending neonatologist or neonatology residents. This could possibly lead to bias secondary to inter-practitioner variability in diagnostic criteria. However, it is difficult to eliminate this potential bias due to the academic hospital system.

In conclusion, prevalence of preterm birth in Dr. Cipto Mangunkusumo Hospital was approximately 2.5 times higher compared to national number. Several factors reducing the preterm birth rate include singleton pregnancy, head presentation, and regular ANC.

Conflict of interest
The authors affirm no conflict of interest in this study.

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