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Determinants and outcomes of preterm births at a tertiary hospital in Ghana

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ABSTRACT

Introduction: Preterm birth remains an important clinical challenge with significant short and long-term complications although its burden in the developing world is not adequately explored. This study determines the incidence, specific determinants and outcomes of preterm birth at a teaching hospital in Ghana.

Methods: Retrospective review of singleton births at Korle-Bu Teaching Hospital (KBTH) in Ghana between 1st January to 31st December, 2015.

Results: Preterm birth (PTB) occurred in 1478 (18.9%) out of 7801 single deliveries with etiological distribution of 879 (59.5%) spontaneous and 599 (40.5%) provider-initiated phenotypes. Gestational age categorization (WHO classification) of the preterm births included 68 (4.6%), 235 (15.9%) and 1175 (79.5%) below 28, between 28-31 and 32–36 weeks respectively. Adverse perinatal outcomes (low birth weight, perinatal deaths and poor Apgar scores) but not adverse maternal outcomes (cesarean and maternal deaths) were significantly higher in preterm compared to term births. Major factors associated with PTB include advanced maternal age (> 35 years), poor antenatal care, hypertensive disorders and preterm premature rupture of membranes (PPROM) whiles obesity was protective. There were 156 stillbirths (105.6 per1000 births) comprising 93 macerated (62.9 per 1000 births) and 63 fresh stillbirths (42.6 per 1000 births), and perinatal mortality rate of 119.8 per 1000 births.

Discussion: Preterm birth is highly prevalent with significant adverse outcomes among singleton gestations at KBTH in Ghana, with disproportionately higher spontaneous etiology compared to provider-initiated phenotype. A paradigm shift in clinical management of preterm births/prematurity is urgently required with proactively dedicated multidisciplinary team and involvement of the global community.

1. Introduction

Preterm birth remains a single most important clinical challenge to both obstetricians and pediatricians with resultant maternal psychological strain and neonatal prognostic uncertainties in early extra-uterine existence [1–3]. It is also considered a major public health challenge because of the associated high frequency of perinatal morbidity and mortality and lifelong complications such as learning disabilities from visual, hearing and cognitive problems [4–8]. To the economist, preterm birth presents considerable longstanding economic implications to health care systems and for the society [9–11]. However, there is a great clinical dilemma in reducing these serious neonatal adverse outcomes due to diagnostic difficulties in identifying modifiable factors that are amenable to prevention or treatment [1].

Generally, preterm birth rates are rising globally with about 15 million recorded annually and major complications result in mortality of approximately 1.1 million babies [1]. However, more than 75% of deaths of preterm babies in low resource settings can be averted with cost-effective interventions such as provision of adequate warmth, breastfeeding and infection prevention [1]. Unfortunately, preterm birth is progressively becoming an acceptable norm in low resourced settings with very and extremely preterm babies perishing and not even accurately counted [8]. Neonatal adverse outcomes are excessively higher in the developing world compared to resource-rich countries. For instance, more than 90% of extremely preterm babies survive in the high income countries compared to less than 10% in the resource-limited settings [1].

The etiologic phenotypes of preterm birth are broadly categorized into spontaneous preterm birth (natural onset of labor or preterm premature rupture of membranes) and provider-initiated preterm birth (induction of labor or pre-labor elective cesarean for maternal or fetal indications) [1,12,13]. Distinction between the two main etiologic entities is significant in understanding certain clinical and public health indicators of importance [14]. Optimal evidence-based management of spontaneous preterm labor remains largely hypothetical as no single therapeutic approach has been globally acknowledged to be effectively applicable in all cases. The etiology of spontaneous preterm birth remains grossly uncertain in spite of the extensive research carried out in the field [13]. Usually, it is a multifactorial process resulting in distortion of the equilibrium between uterine quiescence and active contractions with resultant parturition prior to 37 completed weeks of gestation from interplay of specific-related factors [13,15]. Current

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clinical management strategies are generally based on the hypothesized pathophysiological mechanisms and these have resulted in diverse potential treatment options with lack of consensus from experts around the world. On the other hand, provider-initiated preterm birth is attributed to maternal or fetal indications although significant evidence of non-justifiable iatrogenic preterm births is well documented [16].

Research into preterm births is limited in developing world including sub-Saharan Africa with gross under estimation of the problem although the bulk of the burden is deeply rooted in such settings. Over 15 years ago, Nkyekyer et al. determined that preterm birth occurred in 9.3% of all singleton births in Korle-Bu Teaching Hospital (study site of the current study) in Ghana, with 42%, 18.6% and 39.3% attributed to spontaneous, preterm premature rupture of membranes and medically indicated causes respectively [17]. However, current clinical practice and experience in the same hospital indicates unacceptably high prevalence of preterm births. To compound preterm birth-related issues in the country, the neonatal outcomes are generally suboptimal especially for early preterm phenotypes and this might partly be attributed to lack of adequately equipped neonatal intensive units.

In Ghana, the burden of preterm birth has not been adequately studied. The non-existence of reliable estimate of the true burden of preterm birth and prematurity in most low- and middle-income countries is partly responsible for the associated inertia in clinical management and poor adverse outcomes [1,8]. In this study, our main objective is to determine the current incidence, specific determinants and outcomes of preterm births at a tertiary hospital in Ghana using the WHO classification system, to trigger more attention for and improve clinical management of preterm births in the country.

2. Materials and methods

This was a retrospective descriptive study of all singleton deliveries at the Korle-Bu Teaching Hospital in Accra, Ghana between 1st January to 31st December 2015. Korle-Bu Teaching Hospital is the largest teaching hospital in Ghana with approximately 10,000 births annually. The Department of Obstetrics and Gynecology at the hospital has about 20 Consultants Obstetricians/Gynecologists, evenly distributed into five clinical teams with Residents Doctors and other supporting medical staff. There is a well-established Biostatistics unit that manages clinical data at the Department with experienced research assistants. The data management system involves initial registration of patients with entry of the basic socio-demographic details at the time of their first visit to the hospital. The clients are then issued with folders which would contain all the clinical notes including the medical treatment they receive. The research assistants undertake daily extraction of clinical information from the folders of patients who have just been discharged from the hospital to update and complete the initial data collection. The electronic data management system has been in place for over six years and annual maternal health indicators and reports are produced at the end of each year.

The current study involved data extraction from the pre-existing electronic data as described above. Initially, all the terminations of pregnancies including childbirths that occurred between first day of January to last day of December in the year 2015 were retrieved and screened. The specific inclusion and exclusion criteria were applied to the data and the resultant patients were included in the final analysis for the purpose of this study. The main inclusion criteria were singleton births occurring at the gestational age of 28 weeks or more but less than 37 weeks. However, any termination of pregnancy that resulted in a live birth was included regardless of the gestational age. Specific exclusion criteria were multiple pregnancies, grossly incomplete data especially where the gestational age is not recorded. Also excluded were pregnancies below 28 weeks which ended in stillbirths as well as in situations where the gestational is unknown. Maternal parameters extracted included age (years), weight (kg) at booking (first visit), height (m), gravidity, parity, marital status, educational level, number antenatal visits, gestational age at delivery, mode of delivery and occurrence of hypertension in pregnancy. Antenatal visits of less than 4 and 4 or more were considered poor and good respectively. Neonatal parameters obtained included birth weight, sex of baby, APGAR score, fetal outcome (live birth of stillbirth), neonatal death, admission to neonatal intensive unit (NICU). In this study, preterm birth was defined as all births that occurred prior 37 completed weeks of gestation or less than 259 days since the first day from the last menstrual period [1,18]. This definition includes of all live births irrespective of the gestational age at delivery. Spontaneous preterm birth was defined as spontaneous or natural initiation of labor or following pre-labor premature rupture of membranes prior to 37 completed weeks and provider-initiated preterm birth defined as induction of labor or elective caesarean birth before 37 completed weeks of gestation based on indications attributed to either maternal or fetal conditions [12]. Based on the recommended classification by WHO, preterm births were further classified according to gestational age as moderate preterm (between 32 and 36 weeks, very preterm (between 28 and 31 weeks), or extremely preterm (below 28 weeks) [1]. Perinatal mortality was defined as sum of neonatal deaths that occurred within the first week of life (early neonatal deaths-ENND) and stillbirths (macerated- and fresh stillbirths). The study protocol was approved by the ethical and protocol review committee of the School of Medicine and Dentistry of the College of Health Sciences, University of Ghana. There was no need for informed consent from the patients whose medical records were used in the study as there was no direct contact with the patients.

The data were analyzed using SPSS version 22.0 (IBM, New York). Basic descriptive analyses were performed and compared between preterm and term births. Univariate and multivariate analyses were done to determine significant associations between the characteristics of the women and the occurrence of preterm births. Maternal and neonatal outcomes between term and preterm birth were compared using chi square test. In this study, p-value of less than 0.05 was considered significant.

3. Results

Over the study period, there were 8930 singleton births in the hospital and 1129 (12.6%) were excluded from the analysis on account of incomplete data and multiple pregnancies. The remaining 7801 (87.4%) single births were included in the study comprising 1478 (18.9%) and 6323 (81.1%) preterm and term births respectively. The etiological distribution of the preterm births included 879 (59.5%) spontaneous and 599 (40.5%) provider-initiated preterm deliveries. The spontaneous preterm births comprise 139 (9.4%) women with preterm premature rupture of membranes (PPROM) and 740 (50.1%) with spontaneous onset of labor without rupture of membranes. Among the 1478 preterm babies 737 (49.9%) and 741 (50.1) were males and females respectively and there was no statistical difference between the frequencies of the sex distribution. The characteristics of women with both term and preterm births are shown in Table 1.

In terms of gestational age categorization of the 1478 preterm births 68 (4.6%), 235 (15.9%) and 1175 (79.5%) were below 28 weeks, between 28-31 weeks and 32–36 weeks respectively (Table 2). Advanced maternal age, poor antenatal care and maternal hypertension and premature rupture of membranes were significantly associated with preterm birth at KBTH (Table 3). Maternal obesity (at booking) was associated with reduced frequency of preterm births. Maternal characteristics such as maternal age < 20 years, Grandmultiparity, unmarried status, maternal BMI (at booking) < 18.5 kg/m^2 showed significant tendencies of being associated with the occurrence of preterm birth, however, there was no statistical significance after adjusting for confounders.

There was no significant difference between preterm and term births with respect to cesarean section as a mode of delivery. There was statistically significant difference between preterm and term births

Table 1
General characteristics of women with term and preterm births at KBTH.

Indicator	< 37 weeks (1478) n (%)	= > 37 weeks (6323) n (%)	Total n (%)
AGE (YEARS)			
< 20	86 (24.2)	269 (75.8)	355 (4.6)
20–34	1031 (17.9)	4733 (82.1)	5764 (73.9)
= > 35	361 (21.5)	1321 (78.5)	1682 (21.6)
PARITY[a]			
Nullip	470 (18.8)	2036 (81.2)	2506 (32.5)
Para 1-4	943 (19.0)	4010 (81.0)	4953 (64.2)
Grand multiparity	42 (16.8)	208 (83.2)	250 (3.2)
MARITAL STATUS			
Single	291 (21.8)	1043 (78.2)	1334 (17.1)
married	1187 (18.4)	5280 (81.6)	6467 (82.9)
EDUCATION[b]			
Primary/None	303 (21.9)	1082 (78.1)	1385 (18.0)
Secondary	924 (19.2)	3884 (80.8)	4808 (62.4)
Tertiary	230 (15.2)	1287 (84.8)	1517 (19.7)
BMI[c]			
< 18.5	19 (26.0)	54 (74.0)	73 (2.0)
18.5–24.9	158 (16.6)	1085 (83.4)	1301 (35.7)
25.0–29.9	161 (13.8)	985 (86.2)	1127 (31.4)
= > 30.0	140 (12.4)	987 (87.6)	1138 (30.9)
ANC visits[d]			
Good	764 (14.3)	4592 (85.7)	5356 (71.3)
Poor	648 (30.0)	1513 (70.0)	2161 (28.7)
HDP	384 (33.7)	754 (66.3)	1138 (14.6)
No HDP	1094 (16.4)	5569 (83.6)	6663 (85.4)
PROM	139 (37.7)	230 (62.3)	369 (4.7)
No PROM	1339 (18.0)	6093 (82.0)	7432 (95.3)

[a] 92 (1.2%) missing.
[b] 91 (1.2%) missing.
[c] 4162 (53.4%) missing.
[d] 284 (3.6%) missing; BMI: body mass index; ANC: antenatal care; HDP: hypertensive disorders in pregnancy.

regarding the occurrence of adverse perinatal outcomes (Table 4). Among the women with preterm births (1478) induction of labor occured in 44 (3.0%) comprising 3 (4.4%), 7 (3.0%) and 34 (2.9%) in gestational ages of < 28, 28–31 and 32–36 weeks respectively. There were 624 (42.2%) cesarean sections (CS) comprising 590 (94.6%) and 34 (5.5%) pre-labor and emergency (cesarean following onset of labor) types among the preterm births. There was no statistical difference between CS rate in term and preterm deliveries (Table 4). There were no maternal deaths directly attributed to preterm births.

Among the 1438 preterm births, there were 156 stillbirths (105.6 per1000 births) stillbirths comprising 93 macerated stillbirths (62.9 per1000 births) and 63 fresh stillbirths (42.6 per 1000 births) with live births constituting 1322 (98.4%). In all there were 177 perinatal deaths resulting in a perinatal mortality of 119.8 per 1000 births (Table 5). Early neonatal death occurred in 21 (1.6%) of all the livebirths comprising 3 (4.6%), 4 (2.2%) and 14 (1.3) in preterm births < 28 (n = 65), between 28 and 31 (n = 179) and 32–36 (n = 1078) weeks respectively with a total of 1322 Livebirths. Among the preterm babies, 116 (7.8%), 163 (11.0), 529 (35.8%) and 630 (42.6%) were < 1.0 kg, between 1.0 and 1.49 kg, 1.5–2.49 kg and ≥ 2.5 kg respectively with 40 (2.7%) having incomplete data (Table 6).

4. Discussion

In this study, we set out to determine the incidence, outcomes and specific determinants of preterm births at a tertiary hospital in Ghana. Preterm birth occurred in 18.9% of all singleton childbirths comprising 59.5% and 40.5% spontaneous and provider-initiated etiologies respectively. The major factors associated with the occurrence of preterm delivery include advanced maternal age of over 35 years, poor antenatal care, hypertensive disorders and preterm rupture of membranes whiles maternal obesity was protective.

The high incidence of preterm birth determined in this study is comparable with the 16.8% reported by Butali et al. in Nigeria [19] but smaller than 9.3% rate determined by Nkyekyer et al. [17] in the same institution over a decade ago. Globally, preterm birth constitutes between 5 and 18% of all births with most of these occurring in the developing world [15]. Beck et al. determined a global preterm birth rate of 9.6% among all births worldwide in the year 2005 with the highest and lowest rates occurring in Africa (11.9–18%) and Europe (5–6.2%) respectively [6]. More recently, Vogel et al. reported a preterm birth rate of 8.2% in 22 low and middle income countries and determined that a significant proportion of provider-initiated preterm births was not medically indicated and could have been avoided [20]. The wide variation in preterm birth rates globally might be attributed to different definitions and clinical guidelines applicable to various regions worldwide [20–22]. Lack of comprehensive consensus regarding preterm birth definitions and phenotypes presents a major hindrance in accurate estimation of the true burden of prematurity [23].

In the study by Nkyekyer et al. [17] in the same teaching hospital over a decade ago, 42%, 18.6% and 39.3% of preterm deliveries were due to spontaneous onset of preterm labour, preterm premature rupture of membranes and provider-initiated respectively compared to 50.1%, 9.4% and 40.5% determined in the current study respectively. The major significant changes recorded over the past decade include doubling of the overall preterm birth rate (9.3% to 18.9%), halving of the proportion of PPROM from 18.6 to 9.4% and marked increase in the burden of spontaneous onset of labour without PPROM from 42 to 50.1% in the causation of preterm births in the same tertiary facility. The finding of significant increase in spontaneous PTB without PPROM in the etiopathogenesis of preterm births is definitely worrying and requires a more detailed pragmatic research into spontaneous preterm birth phenotypes in the country.

Generally, very preterm birth accounts for approximately 10% of preterm births with most of the neonates achieving optimal survival although significant long-term morbidity may occur [1]. On the other hand, extremely preterm birth which accounts for about 5% of all preterm deliveries is associated unacceptably high frequency of early

Table 2
Characteristics of women with preterm births categories at KBTH.

Indicator	< 28 weeks n (%)	28–31 weeks n (%)	32–36 weeks n (%)	Total n (%)
Age (years)				
< 20	8 (9.3)	11 (12.8)	67 (77.9)	86 (5.8)
20–34	47 (4.6)	168 (16.3)	816 (79.1)	1031 (69.8)
= > 35	13 (3.6)	56 (15.5)	292 (80.9)	361 (24.4)
Parity[a]				
Nullip	28 (6.0)	87 (18.5)	355 (75.5)	470 (32.3)
Para 1-4	37 (3.9)	138 (14.6)	768 (81.4)	943 (64.8)
Grand multip	1 (2.4)	4 (9.5)	37 (88.1)	42 (2.9)
Marital status Single	12 (4.1)	57 (19.6)	222 (76.3)	291 (19.7)
married	56 (4.7)	178 (15.0)	953 (80.3)	1187 (80.3)
Education[b]				
Primary/None	14 (4.6)	44 (14.5)	245 (80.9)	303 (20.8)
Secondary	42 (4.5)	148 (16.0)	734 (79.4)	924 (63.4)
Tertiary	11 (4.8)	38 (16.5)	181 (78.7)	230 (15.8)
BMI[c]				
< 18.5	0 (0.0)	0 (0.0)	19 (4.7)	19 (3.6)
18.5–24.9	16 (7.4)	40 (18.5)	160 (74.1)	216 (40.5)
25.0–29.9	10 (6.3)	36 (22.8)	112 (70.9)	158 (29.6)
= > 30.0	7 (5.0)	22 (15.7)	111 (79.3)	140 (26.3)
ANC visits[d]				
Good	24 (3.1)	83 (10.9)	657 (86.0)	764 (54.1)
Poor	42 (6.5)	138 (21.3)	468 (72.2)	648 (45.9)
HDP	13 (3.4)	78 (20.3)	293 (76.3)	384 (26.0)
No HDP	55 (5.0)	157 (14.4)	882 (80.6)	1094 (74.0)
PROM	6 (4.3)	29 (20.9)	104 (74.8)	139 (9.4)
No PROM	62 (4.6)	206 (15.4)	1071 (80.0)	1339 (90.6)

[a] 23 (1.6%) missing.
[b] 21 (1.4%) missing.
[c] 945 (63.9%) missing.
[d] 66 (4.5%) missing; BMI: body mass index (kg/m^2); ANC: antenatal care; HDP: hypertensive disorders in pregnancy.

neonatal deaths with resultant long-term multi-systemic sequelae in majority of the survivors [24,25]. In this study preterm births were categorized using the WHO classification with extremely, mild and moderately preterm deliveries occurring in 4.6%, 15.9% and 79.5% respectively. The use of WHO classification system in this study is considered as a strength of the study as it permits direct comparison of specific preterm rates with other institutions both locally and internationally although the lower limit of defining preterm birth still remains debatable. The main disadvantage of the WHO classification is the non-existence of specified lower limit for defining preterm birth as it includes all live births [1].

This study has also determined specific determinants associated with preterm birth in the hospital with maternal age, poor antenatal care, hypertensive disorders and PPROM being the major contributors as reported by other studies [19,26–28]. In China, Zhang et al. determined that obesity, maternal hypertension, unbalanced diet, poor prenatal care and placental previa are specific risk factors for preterm birth [27]. It is worth emphasizing the some of these determinants such as maternal hypertension and antenatal care are modifiable. Other factors that showed significant potential of positive association are maternal age less than 20 years, grandmultiparity, unmarried status and underweight but these did not reach statistical significance. Further prospective studies with improved methodological quality and power are needed in these settings to either support or refute these clinically important etiological associations.

Intruigingly, maternal overweight/obesity was found to be protective in the epidemiology of preterm births in our study. This represents a sharp distinction to reports by some researchers [27,29] but consistent with other studies [30,31]. A systematic review by Torloni et al. showed that overweight/obesity may have different effects on various types of preterm births with type 1 obesity/overweight being protective for spontaneous PTB whiles type 11 and 111 increasing the risk for preterm births in general [32]. In a case-control study, Torloni and colleagues determined no significant differences between preterm births and obesity categories when different ethnic groups were considered composite. However, there was a significant reduction in the

Table 3
Risk factors for preterm births at KBTH.

Indicator	Preterm del n (%)	OR (95%CI)	p value	aOR[a] (95%CI)	p value
Age (years)					
< 20	86 (24.2)	1.468 (1.141–1.888)	0.003	1.040 (0.633–1.703)	0.071
20–34	1031 (17.9)	Ref		Ref	
= > 35	361 (21.5)	1.255 (1.097–1.435)	0.001	1.454 (1.139–1.856	0.003
Parity					
Nullip	470 (18.8)	0.982 (0.868–1.110)	0.768	1.041 (0.814–1.330)	0.749
Para 1-4	943 (19.0)	Ref		Ref	
Grand multip	42 (16.8)	0.859 (0.612–1.205)	0.378	0.521 (0.261–1.040)	0.064
Marital status					
Single	291 (21.8)	1.241 (1.074–1.434)	0.003	0.789 (0.599–1.039)	0.091
married	1187 (18.4)	Ref		Ref	
Education					
Primary/None	303 (21.9)	1.177 (1.017–1.362)	0.029	0.956 (0.736–1.242)	0.735
Secondary	924 (19.2)	Ref		Ref	
Tertiary	230 (15.2)	0.751 (0.642–0.879)	< 0.001	1.117 (0.835–1.495)	0.457
BMI (kg/m^2)					
< 18.5	19 (26.0)	1.767 (1.027–3.014)	0.040	1.723 (0.938–3.165)	0.080
18.5–24.9	216 (16.6)	Ref		Ref	
25.0–29.9	158 (13.8)	0.806 (645–1.007)	0.057	0.766 (0.597–0.984)	0.037
= > 30.0	140 (12.4)	0.713 (0.566–0.896)	0.004	0.609 (0.467–0.793)	< 0.001
ANC visits					
Good	764 (14.3)	Ref		Ref	
Poor	648 (30.0)	2.574 (2.284–2.902)	< 0.001	5.172 (4.057–6.594)	< 0.001
HDP	384 (33.7)	2.593 (2.256–2.979)	< 0.001	3.335 (2.625–4.236)	< 0.001
No HDP	1094 (16.4)	Ref		Ref	
PROM	139 (37.7)	2.750 (2.210–3.422)	< 0.001	3.143 (2.155–4.584)	< 0.001
No PROM	1339 (18.0)	Ref		Ref	

[a] Adjusted for all variables in the table; aOR = adjusted Odds Ratio; ANC: antenatal care; HDP: hypertensive disorders in pregnancy; CI = confidence interval; BMI: body mass index (kg/m^2).

Table 4
Maternal and perinatal outcomes term and preterm births at KBTH.

Indicator	Total n(%)	Preterm births n(%)	Term births n(%)	OR (95%CI)	p-value
Cesarean section	3324 (42.6)	624 (42.2)	2700 (42.7)	0.996 (0.975–1.018)	0.748
LBW (< 2.5 kg)	1414 (18.4)	808 (56.2)	606 (9.7)	11.956 (10.460–13.666)	< 0.001
Stillbirth	286 (3.7)	156 (10.6)	129 (2.0)	1.821 (1.602–2.070)	< 0.001
MSB	164 (2.1)	93 (6.6)	71 (1.1)	1.904 (1.597–2.269)	< 0.001
FSB	121 (1.6)	63 (4.5)	58 (0.9)	1.719 (1.427–2.071)	< 0.001
ENND	34 (0.5)	21 (1.6)	13 (0.2)	1.682 (1.604–1.764)	< 0.001
Perinatal death	320 (3.8)	177 (12.0)	142 (2.2)	1.856 (1.641–2.099)	< 0.001
Apgar at 1 min < 7	1522 (21.4)	455 (37.9)	1067 (18.1)	2.764 (2417–3.161)	< 0.001
Apgar at 5 min < 7	382 (5.4)	178 (14.9)	204 (3.5)	4.889 (3.956–6.042)	< 0.001
Male fetus	4016 (51.5)	737 (49.9)	3279 (51.9)	0.985 (0.964–1.006	0.174
NICU admission	1544 (20.1)	721 (46.7)	823 (13.0)	2.161 (1.409–3.313)	< 0.001

FSB: fresh stillbirth; MSB: macerated stillbirth; ENND: Early neonatal deaths; NICU: neonatal intensive care unit; LBW: low birth weight.

Table 5
Pregnancy outcomes of preterm births at Korle-Bu Teaching Hospital.

Indicator	< 28 weeks (n = 68)	28–31 weeks (n = 235)	32–36 weeks (n = 1175)	Total (n = 1478)
Cesarean section	26 (38.2)	113 (48.1)	485 (41.3)	624 (42.2)
Vaginal delivery	42 (61.8)	122 (51.9)	690 (57.8)	854 (57.8)
PPROM	6 (8.8)	29 (12.3)	104 (8.9)	139 (9.4)
No PPROM	62 (91.2)	206 (87.7)	1339 (91.1)	1339 (90.6)
Birth weight < 2.5 kg	56 (84.8)	188 (83.9)	564 (49.1)	808 (56.2)
Birth weight ≥ 2.5 kg	10 (15.2)	36 (16.1)	584 (50.9)	630 (43.8)
Livebirth	65 (95.4)	179 (76.2)	1078 (91.7)	1322 (89.4)
Stillbirth	3 (4.4)	56 (23.8)	97 (8.3)	156 (10.6)
MSB	1 (1.5)	35 (14.9)	57 (4.9)	93 (6.3)
No MSB	67 (98.5)	200 (85.1)	95 (95.1)	1385 (93.7)
FSB	2 (3.0)	21 (8.9)	40 (3.4)	63 (4.3)
No FSB	66 (97.1)	214 (91.1)	1135 (96.6)	1415 (95.7)
Perinatal death	6 (8.8)	60 (25.5)	111 (9.4)	177 (12.0)
No perinatal death	62 (91.2)	175 (74.5)	1064 (90.6)	1301 (88.0)
Apgar at 1 min < 7	42 (75.0)	95 (62.5)	318 (32.0)	455 (37.9)
Apgar at 1 min ≥ 7	14 (25.0)	57 (357.5)	676 (62.1)	747 (62.1)
Apgar at 5 min < 7	29 (52.7)	57 (37.7)	92 (9.3)	178 (14.9)
Apgar at 1 min ≥ 7	26 (47.3)	94 (62.3)	897 (90.7)	1017 (85.1)

Apgar score at 1 min (276 excluded comprising 156 stillbirths and 120 missing data).
Apgar score at 5 min (283 excluded comprising 177 perinatal deaths and 106 missing data).
Birth weight [40 (2.7%) missing data]; PPROM: preterm premature rupture of membranes; FSB: fresh stillbirth; MSB: macerated stillbirth. Values in the Table are presented as number (percentage).

Table 6
Birth weight distribution and perinatal outcomes among preterm neonates at KBTH.

Indicator	< 1.0 kg (n = 116)	1.0–1.49 kg (n = 163)	1.5–2.49 kg (n = 529)	≥ 2.5 kg (n = 630)	Total 1438
Livebirth	95 (81.9)	120 (73.6)	470 (88.8)	608 (96.5)	1293
Stillbirth	21 (18.1)	43 (26.4)	59 (11.1)	22 (3.5)	145
MSB	16 (13.8)	23 (14.1)	33 (6.2)	13 (2.1)	85
FSB	5 (4.3)	20 (12.2)	26 (4.9)	9 (1.5)	60
ENND	6 (6.3)	2 (1.7)	9 (1.9)	4 (0.7)	21
Perinatal	27 (23.3)	45 (27.6)	68 (12.9)	26 (4.1)	166
Apgar 1 < 7	62 (77.5)	87 (81.3)	182 (42.8)	114 (19.9)	455
Apgar 5 < 7	41 (53.9)	44 (41.5)	59 (13.9)	28 (4.9)	172
Male baby	59 (50.9)	72 (44.9)	251 (47.4)	334 (53.0)	716

FSB: fresh stillbirth; MSB: macerated stillbirth; ENND: Early neonatal deaths. Values in the Table are presneted as number (percentage).

odds for early preterm birth among obese African-Americans with reference to normal weight women in the same ethnicity and the converse was true for the Caucasian counterparts [33].

In Ghana, the nationwide preterm birth rate is estimated at 14.5% [34] which is higher than the average of 11.9% for African continent [6]. The unusually high frequency of preterm births with disproportionately high spontaneous PTB rate maybe explicable by the tertiary status of the hospital where high-risk pregnancies are referred to and managed under direct supervision of consultant obstetricians. Most cases of threatened preterm labor are referred to KBTH to optimize neonatal survival in the tertiary hospital. Although the NICU at KBTH is considered the most endowed in the country, there are specific limitations in the management of extremely preterm neonates mainly due to lack of surfactant in the country. The unavailability of surfactant is a major limitation to improving outcomes of preterm birth in the country and partly accounts for the high mortality index and long-term respiratory sequelae characteristic of prematurity. Generally, surfactant replacement therapy is recommended for intubated and ventilated preterm neonates with respiratory distress syndrome because of the associated evidence-based clinical benefit for affected newborns [35,36].

In the developing world, spontaneous and provider-initiated preterm births are equally important as the two entities present proportionate clinical challenges to obstetricians and neonatologists. There is evidence that, more than 50% of all provider-initiated preterm births between 34 and 36 weeks gestation in the United states are not convincingly justified clinically [16]. Maternal and fetal indications are classical clinical conditions underlying medically-indicated preterm birth including severe preeclampsia, placental abruption, uterine rupture, fetal distress and fetal growth restriction [37]. In such situations expectant management is not normally entertained with the main objective of safeguarding maternal survival primarily with neonatal outcome considered secondary. This clinical rule of thumb “maternal life first” is applicable to most obstetric emergencies especially in resource poor settings with resultant increase in the burden of prematurity, the treatment of which is poorly tolerated in the developing world. In these areas, direct neonatal death from prematurity has become extremely common on daily basis displaying unacceptably excessive disparity in the neonatal health indicators compared to the resource rich world.

In this study, there was no significant difference between the preterm and term births regarding the route of childbirth and cesarean section was proportionately distributed. Generally, vaginal birth is recommended unless there is another convincing obstetric indication other the preterm labor. To buttress this, the WHO recently stated that routine cesarean section with the primary aim of improving the neonatal outcome of preterm birth is not recommended irrespective of the fetal presentation [35]. In this study, all the poor perinatal outcome indicators such as low birth weight, stillbirths and neonatal death and NICU admission rates were worse in the preterm neonates compare to their term counterparts.

Moving forward, maternal interventions aimed at optimizing neonatal outcomes of preterm birth such as antenatal corticosteroids, magnesium sulfate and antibiotic prophylaxis (for prolonged PPROM) are indispensably recommended and these strategies are best considered in terms of primary, secondary and tertiary prevention [1,38]. Generally, dexamethasone is the drug of choice administered to women with threatened preterm labor before 34 weeks to improve fetal lung maturity because betamethasone (preferred option) is non-existent in the country. In most cases, effective medication for managing preterm birth and prematurity are either unavailable or too expensive for the populace. There is the need for a global concerted effort from both governmental and non-governmental organizations (NGOs) in providing evidence-based measures in the prevention and treatment of preterm birth and prematurity in resource limited settings.

The strength of the study relies on the implementation of the WHO classification in the categorization of preterm birth in a tertiary hospital in Ghana and the relatively large sample size included in the analysis. The limitation of the study is inclined to the retrospective nature of the study restricting access to relevant clinical indicators of preterm birth coupled with significant incomplete data excluded from the analysis. However, the findings are significant and maybe applicable to similar settings in the sub-region.

Conclusion: Preterm birth is highly prevalent (18.9%) with significant adverse outcomes among singleton gestations at Korle-Bu Teaching Hospital in Ghana, with disproportionately higher spontaneous etiology (59.5%) compared to provider-initiated phenotype (40.5%). The frequencies of extremely, very and moderate or late preterm were 4.6%, 15.9% and 79.5% respectively. The major determinants of preterm delivery include advance maternal age of over 35 years, poor antenatal care, hypertensive disorders and PPROM with maternal obesity being protective. Moving forward, a paradigm shift in clinical management of preterm births/prematurity is urgently required with proactively dedicated multidisciplinary team and involvement of the global community. Further large prospective study of moderately high methodological superiority with intervention-oriented focus is strongly recommended in similar settings to guide the development of evidence-based locally appropriate clinical guidelines for the management of preterm births and prematurity in the country.

Conflicts of interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.placenta.2019.01.007.

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