

Maternal Risk Factors and Neonatal Outcomes of Uncomplicated Spontaneous Preterm Birth in Ghana: A Multicentre Case–Control Study

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Abstract

Background

Spontaneous preterm birth (SPTB) remains a major contributor to neonatal mortality and long-term morbidity worldwide, yet its underlying aetiology continues to challenge clinicians and researchers. This study aimed to identify maternal predispositions to spontaneous preterm birth (SPTB) as well as neonatal outcomes of SPTB in the absence of other birth-related complications in Ghana.

Methods

A multicentre unmatched case-control study design involving 604 post-partum mothers with singleton births was conducted across six hospitals in Ghana. The cases comprised 277 mothers with SPTB neonates, while controls comprised 327 mothers with term neonates. Demographic and clinical data were obtained from health records and structured interviews. Neonatal measurements, including birth weight, head circumference, length, and Apgar scores, were assessed. Univariate and multivariate regression analyses identified maternal and neonatal factors associated with outcomes. The main outcome measures were: association of maternal demographic and clinical characteristics, and SPTB, comparison of term and SPTB neonatal clinical characteristics, foetal growth trajectory using the Olsen curve.

Results

Maternal age < 20 years and attending ≤ 3 antenatal visits independently increased the risk of SPTB by about twofold (aOR = 1.9, 95% CI [1.03–3.57]) and 2.5-fold (aOR = 2.55, 95% CI [1.31–5.11]), respectively. Maternal anaemia at booking also showed an independent borderline association with SPTB (aOR = 1.39, 95% CI [1.00–1.94]). Nulliparity, unmarried status, and early menarche (≤ 12 years) were linked to increased risk, although not independently. Preterm neonates had significantly lower neonatal anthropometries, and first- and fifth-minute Apgar scores compared with the term neonates ($p < 0.00001$). Neonatal anthropometric measures across gestational ages declined relative to the Olsen curve from 29 weeks' gestation onward.

Conclusions

Adolescent pregnancy, inadequate antenatal care, and maternal anaemia at booking increase the risk of SPTB among Ghanaian women. SPTB is linked to poorer neonatal growth outcomes. The Ghanaian intrauterine growth trajectory differs from the Olsen reference. The findings highlight the need for integrated multidisciplinary strategies to reduce SPTB, improve neonatal outcomes, and advance our understanding of foetal growth in Ghana.

Background

Over 13 million babies (1 in 10 births) are born preterm annually, contributing to nearly 1 million deaths and 35% of global neonatal mortality [1]. The occurrence of preterm birth in Ghana is alarming, with a prevalence of 18.9% recorded at the premier teaching hospital [2] and > 14% in the eastern region [3]. In Ghana, preterm birth complications are associated with approximately one neonatal death every hour, exceeding 8,000 deaths annually [4]. The national burden is likely underestimated because foetal viability is defined at 28 weeks compared with 22 weeks in high-income countries leading to misclassification [5]. Limited neonatal care for extremely preterm (< 28 weeks' gestation) further worsens outcomes, with survival rates below 10% in LMICs like Ghana compared with over 90% in high-income countries [6][7]. Preterm babies spend on average 13 days compared to 1.5 days for full-term neonates, resulting in a sevenfold increase in hospital care costs [8]. On average, Ghanaian families spend \$147.60, constituting 8.1% of annual income as out-of-pocket expenses on initial hospitalisation of preterm neonates [9]. The uncertainty surrounding the prognosis of preterm babies and the challenges within the health system place enormous psychological stress on affected families [10].

About two-thirds of preterm births are spontaneous (SPTB), while one-third are provider-initiated due to maternal or foetal complications. SPTB includes spontaneous preterm labour with intact membranes (SPTL) and preterm premature rupture of membranes (PPROM). SPTL, caused by uterine contractions leading to cervical effacement and dilation, accounts for most SPTBs [11]. PPRM arises from pathological weakening of foetal membranes before labour [12][13], driven by extracellular matrix degradation involving matrix metalloproteinases and apoptosis-related processes [14][15].

Studies on preterm birth are mostly conducted at health facilities in the southern part of Ghana [2][3][16][17]. Additionally, research specifically focusing on SPTB within the broader spectrum of preterm birth, and nationwide investigations of this condition remain exceedingly scarce. Focusing on SPTB is important because it represents the major contributor to preterm birth incidence and remains the least understood preterm birth phenotype. Furthermore, it is also essential to understand how different environmental and contextual factors collectively influence its risk dynamics. This is particularly crucial with WHO and the United Nations aiming to reduce preterm birth-related mortalities [18]. The objective of this study is to ascertain the maternal determinants of SPTB and neonatal outcomes in Ghana to inform public health policies and enhance clinical management of SPTB in the country.

Methods

Study design and setting

We conducted a multicentre unmatched case-control study which formed part of a broader study, Gh-PREGEN (Ghana Spontaneous PREterm Birth GENetics Study) at six health facilities across Ghana, (Fig. 1) comprising three tertiary referral hospitals, two secondary hospitals, and one district hospital. Maternal

and neonatal data were collected using a structured questionnaire to obtain demographic and clinical information for determining factors associated with SPTB.

Participants

The study participants involved postpartum mothers with singleton spontaneous vaginal deliveries, comprising 277 mothers with SPTB and their neonates (cases), and 327 mothers who had term births and their neonates (controls) receiving obstetric and neonatal care, respectively. Participants were identified in the labour ward before the onset of labour and then followed through to the post-natal ward, where they were observed until recovery from the delivery process before discharge.

Exclusion criteria and inclusion criteria

Clinical data and interviews were used to exclude participants with chronic health conditions such as pregnancy-induced hypertension, thyroid-related disease, pre-eclampsia, mental disorders, pre-gestational/gestational diabetes, heart-related disease, antepartum haemorrhage, placenta previa, abruptio placentae, HIV or AIDS, ascending infection, minor and major foetal malformations, lupus, uterine malformations, rheumatoid arthritis, Crohn's disease, ulcerative colitis, cancer and influenza. Additionally, mothers with multiple gestations, connective tissue diseases, medical conditions of pregnancy requiring induction of labour, peripartum Hb of < 10.5 g/dl, alcoholism, cigarette smoking and recreational drug use during pregnancy as well as women who conceived through assisted reproductive technology were also excluded.

All pregnancies meeting the inclusion criteria were intrauterine, had documented ultrasound examination from the first trimester (< 13 weeks) and had live births. The controls had gestational weeks between 37 and 42. For mothers with SPTB, gestational ages ranged from 24 weeks to 36 weeks and were diagnosed by an obstetrician- gynaecologist or a midwife.

Data collection technique and tools

Data were collected by research assistants, midwives, paediatric nurses and paediatricians trained on the use of the standardised data collection protocol. Maternal and foetal hospital health records were extracted using Microsoft excel spreadsheets with codified identifiers exclusive to each participant incorporated. The questionnaire was used to obtain information on maternal demographic and obstetric variables from their first antenatal visits (booking) through to the intrapartum and postpartum periods. Face-to-face and follow-up telephone interviews were used to obtain information on demographics and obstetric factors not documented in the health records.

The neonates' weight, length and head circumference (HC) were taken within the first hour after birth. The weights were measured using an electronic weighing scale (Seca) and recorded to the nearest 100th of a kilogram. All the scales used were checked daily for errors and tared to zero before all measurements were taken. Their lengths were measured to the nearest centimetre with an infantometer. Each neonate was carefully laid in a flat, supine position on the infantometer and the length was carefully recorded by positioning the device from the crown to heels, ensuring it was in contact with the body without compression [19]. The head circumference was measured by placing a non-stretchable flexible measuring tape around the occipitofrontal circumference of the neonate's skull [19]. The first- and fifth-minute Apgar scores were also recorded by trained personnel.

Data processing and analysis

Data were verified and cleaned in Microsoft Excel to ensure quality and then exported to R software for analysis. Frequencies of cases and controls were assessed to ascertain the completeness of each independent variable. Means of continuous variables (maternal age, Hb at booking, height and age at menarche) were compared using the Welch's t-test. A Chi-square analysis test of proportions was performed to determine the statistical significance between the risk factors (age, ethnicity, age at menarche, height, level of education, parity, marital status, number of antenatal care (ANC) visits, previous pregnancy outcomes and Hb status at booking) among mothers with SPTB and those with term deliveries. Univariate logistic regressions were carried out to demonstrate the strength of associations. Variables significantly associated with SPTB were entered into a multiple logistic regression model and analysed to determine significant independent risk factors. The medians of gestational age, birth weight, head circumference, length, first and fifth-minute Apgar Score of SPTB and term neonates were also compared using the Mann-Whitney U test. Statistical significance was set at a *p*-value of < 0.05. The medians for birth weight, head circumference and length were used to construct smooth curves and then compared with medians of Olsen's growth curves for birth weight, head circumference and length [20].

Results

Maternal characteristics

The ages of women with SPTB and term births ranged from 12–44 years and 16–46 years, respectively. The mean age of those with SPTB was 27.08 ($\pm$ 6.73SD), whereas that of controls was 28.63 ($\pm$ 6.27SD); the difference was statistically significant (*p* = 0.004). Likewise, the difference in the mean Hb in g/dl at booking for mothers with SPTB [10.94 ($\pm$ 0.93 SD)] and that of mothers with term birth [11.13 ($\pm$ 0.93SD)] was also statistically significant (*p* = 0.01). The means of height and age at menarche, did not differ significantly between cases and controls using Welch's T-test (**Table S1**).

Maternal age was further categorised into five age groups (< 20, 20–25, 26–30, 31–35, > 35) to explore the relationship between age and the risk of SPTB. Chi-squared test showed a significant difference ($\chi^2 = 12.69, p = 0.013$) in age groups between SPTB and term births.

Likewise, marital status (“married” or “not married”) and parity were also significantly different between SPTB and term births at $\chi^2 = 6.52, p < 0.01$ and $\chi^2 = 7.37, p = 0.03$, respectively. Though antenatal visit frequency categories ($\leq 3, 4-5, 6-7$, and ≥ 8) differed significantly between the SPTB and term births ($\chi^2 = 16.09, p < 0.001$), visits based on the WHO-recommended threshold (< 8, ≥ 8) did not differ statistically between the two groups ($\chi^2 = 3.19, p = 0.07$). A binary classification of maternal Hb at booking into anaemia (< 11 g/dl) and non-anaemia (≥ 11) status showed a significant difference between the SPTB and term births ($\chi^2 = 4.44, p < 0.04$). However, a further classification of the maternal Hb in g/dl at booking based on severity moderate (7.0–9.9), mild (10.0–10.9), Normal (11–13.5) and high (≥ 13.6) did not show a significant difference between SPTB and term births ($\chi^2 = 6.48, p < 0.09$).

Additionally, maternal ages at menarche into early menarche (< 12), on-time menarche (12–14), and late menarche (≥ 15) did not show a significant difference between SPTB and term births ($\chi^2 = 4.71, p < 0.09$). Similarly, other maternal characteristics such as ethnicity, height, level of education and previous pregnancy outcomes did not differ significantly between cases and controls ($p > 0.05$). Further details were provided in **Table S2**.

Multivariate logistic regression was performed to explore the differences observed further. The results demonstrated that mothers < 20 years had more than twofold increased risk of SPTB (OR = 2.40, 95% CI [1.35–4.37], $p < 0.003$) compared with mothers aged 26–30 years. The risk remained significant (aOR = 1.9, 95% CI [1.03–3.57], $p < 0.04$) even after adjusting for marital status and ANC visits. A WHO-recommended ANC attendance of ≥ 8 was not associated with SPTB compared with < 8 (OR = 1.83, 95% CI [1.00–3.48], $p < 0.06$). However, when the visit frequency was further categorised, ANC visits ≤ 3 increased the risk of SPTB by more than 2.5-fold (OR = 2.67, 95% CI [1.39–5.32], $p < 0.001$) and even after adjusting for parity and maternal age (aOR = 2.55, 95% CI [1.31–5.11], $p < 0.007$). Nulliparity compared to para (1–4) was associated with an increased risk of SPTB (OR = 1.64, 95% CI [1.14–2.37], $p < 0.007$), but this did not reach statistical significance after adjusting for ANC visits and maternal age (aOR = 1.33, 95% CI [0.84–2.11], $p < 0.23$). Additionally, maternal anaemia (< 11 g/dl) at booking compared with non-anaemia (≥ 11 g/dl) increased the risk of SPTB (OR = 1.44, 95% CI [1.04–2.00], $p = 0.03$). A borderline significance was observed even after adjusting for antenatal visits (aOR = 1.39 95% CI [1.00–1.94], $p = 0.05$). Focusing on the severity of maternal Hb status at booking, mothers with moderate anaemia at booking had over 2-fold increased risk of SPTB compared to mothers with normal Hb (OR = 2.16, 95% CI [1.08–4.45], $p = 0.03$) but failed to reach statistical significance after controlling for ANC visits (aOR = 1.85, 95% CI [0.91–3.87], $p < 0.1$). Similarly, mothers who were not married, compared to married women were associated with an increased risk of SPTB (OR = 1.71, 95% CI [1.15–2.57], $p < 0.008$), but this did not reach statistical significance after adjusting for maternal age and parity (aOR = 1.48, 95% CI [0.97–2.27], $p = 0.07$). (see Table 1 for more details).

Table 1
Association between Maternal characteristics and SPTB

Variable	SPTB Count	Term Count	OR	95% CI	p - value	_a OR	95% CI	p - value
Age group (years)^a								
< 20	43	23	2.40	1.35–4.37	0.003**	1.9	1.03–3.57	0.04*
20–25	72	83	1.12	0.72–1.72	0.62			
26–30	77	99	Ref	Ref				
31–35	50	78	0.82	0.52–1.31	0.41			
> 35	35	44	1.02	0.60–1.74	0.93			
Parity^β								
Nulliparity	89	73	1.64	1.14–2.37	0.007**	1.33	0.84–2.11	0.23
Para (1–4)	184	248	Ref	Ref				
Grand-multiparity	4	6	0.90	0.23–3.19	0.87			
Hb (g/dl) status at booking^δ								
Binary classification of Hb status								
< 11 (Anaemia)	126	120	1.44	1.04–2.00	0.03*	1.39	1.00–1.94	0.05
≥ 11 (Non-anaemia)	151	207	Ref					
Severity classification of Hb status								
Moderate (7.0–9.9)	22	14	2.16	1.08–4.45	0.03*	1.85	0.91–3.87	0.1
Mild (10–10.9)	104	105	1.35	0.96–1.90	0.08			
Normal (11–13.5)	147	202	Ref	Ref				
High (≥13.6)	4	6	1.10	0.27–4.22	0.89			
Antenatal visits^δ								
Visits based on WHO-recommended threshold								
< 8	261	294	1.83	1.00–3.48	0.06			
≥ 8	16	33	Ref					
Visit frequency categories								
≤ 3	97	75	2.67	1.39–5.32	0.001**	2.55	1.31–5.11	0.007**
4–5	102	115	1.83	0.96–3.52	0.07			
6–7	62	104	1.23	0.63–2.46	0.55			
≥ 8	16	33	Ref					
Age at menarche (years)								
Early (< 12)	30	21	1.70	0.95–3.10	0.08			
On-time (12–14)	208	248	Ref					
Late (≥ 15)	39	58	0.80	0.51–1.25	0.33			
Marital status^ε								
Not married	69	53	1.71	1.15–2.57	0.008**	1.48	0.97–2.27	0.07
Married	208	274	Ref	Ref				
OR- Odds Ratio; CI- Confidence Interval expressed as (lower limit – upper limit); OR - Odds Ratio; _a OR - adjusted Odds Ratio; *= p value < 0.05, shows statistical significance; Ref. : Reference category; ^a - marital status and antenatal visits; ^β - adjusted for antenatal visits and maternal age; ^δ - adjusted for antenatal visits; ^δ - adjusted for parity and maternal age; ^ε - adjusted for maternal age and parity								

Neonatal outcomes

The total number of neonates assessed was 604, comprising 277 SPTB neonates and 327 term neonates, matching the number of mothers studied. When SPTB neonates were categorized as extreme preterm (< 28), very preterm (28–33 weeks) and late preterm (34–36) categories, late preterm neonates constituted 49.8% (138/277), while the proportion of extremely preterm neonates was (7.9%) (22/277) as shown in Fig. 2, **panel A**. In terms of SPTB type, a higher proportion (~ 61%) of cases had SPTL compared with ~ 39% of cases with PPRM (Fig. 2, **panel B**). Neonatal anthropometric characteristics including birth weight, length, head circumference as well as Apgar score (1st minute and 5th minute Apgar scores) assessed to determine the impact of shortened duration due to SPTB on neonatal outcomes clearly demonstrated the growth and development disparity between the two groups of neonates. Results showed that term neonates had significantly higher medians for all measured characteristics compared with the SPTB neonates ($p < 0.00001$), as shown in **Figure S1**. The median gestational ages for SPTB and term neonates were 33 and 39 weeks, respectively (**Figures S1, panel A**), and ranged from 24 to 36 weeks for SPTB and 37 to 42 weeks for the term neonates (**Table S3**). Regarding birth weight, the median for the SPTB was 1.9 kg, significantly lower than the 3.09 kg of term neonates, as shown in **Figure S1, panel B**. The birth weight for SPTB ranged from 0.5 to 3.2 kg while that of the term neonates ranged from 2.2 to 4.31 kg (**Table S3**). Invariably, the median head circumference for SPTB neonates was 29.8 cm and 33.6 cm for term neonates, significantly different from each other as illustrated in **Figure S1, panel C**. The head circumference ranged from 21.7 cm to 35.9 cm among the SPTB neonates and 29.5–37.4 among the term neonates (**Table S3**). Additionally, the SPTB neonates had a median birth length of 43.3 cm, significantly lower than 49.5 cm for the term neonates, as shown in **Figure S1, panel D**. The length also ranged from 29.2–52.6 cm and 41.8–55.6 cm among the SPTB and the term neonates, respectively (**Table S3**). The first- and fifth-minute Apgar scores for the SPTB and term neonates were apparently dichotomous, with the term neonates exhibiting better developmental attributes compared with SPTB neonates. The median first-minute Apgar Score of 6 for the SPTB was significantly lower than the 8 for the term neonates as shown in **Figure S1, panel E**, and ranged from 2 to 8 for SPTB and 6 to 9 for the term neonates. Likewise, the median fifth-minute Apgar Scores for SPTB and term neonates, as shown in **Figure S1, panel F**, were 7 and 9, respectively, and were significantly different ($p < 0.00001$). The fifth-minute Apgar Score also ranged from 1 to 9 for SPTB and 7 to 9 cm for the term neonates (**Table S3**).

When the distribution of the neonates' first- and fifth-minute Apgar scores was categorised into 7–10 (reassuring or good to excellent health), 4–6 (fair or moderately abnormal), and 0–3 (very low) Apgar scores, over 67% (407/604) had Apgar scores between 7 to 10 in the first minute. However, the proportion of neonates in this Apgar score range increased to nearly 80% (479/604) by the 5th minute. In contrast, among neonates with 0–3 (very low) Apgar scores, the proportion of neonates decreased from 7% (43/604) in the first minute to 3.5% (21/604) in the fifth minute (**Figure S2**).

Additionally, based on the neonatal anthropometric indicators, a foetal growth analysis was carried out using scatter plots overlaid with smooth curves, harnessing the medians of birth weight, HC, and length, along with their corresponding completed gestational weeks at delivery. Coincidentally, all three anthropometric indices peaked at the 41st week of gestation (Fig. 3).

The difference in birth weight between males and females was not evident between the 24th and 29th weeks of gestation. However, from the 30th week till the 42nd week, a difference between the two sexes became apparent, with the males exhibiting a higher weight-for-gestational age than their female counterparts. The median birth weight for the male neonates increased from 0.66 kg at the 24th gestational week and peaked at 3.31 kg at the 41st week, while that of the females increased from 0.70 kg at 24 weeks of gestation to 3.20 kg at the 41st week (Fig. 3, **panel A**) or **Table S4** and **Table S5**. A noticeable sex difference was observed in the growth trajectory of the head circumference HC from the 25th week, with the males' curves lying above the females. The median HC for the male neonates increased from 22.25 cm at the 24th gestational week and peaked at 34.25 cm at the 41st week. For the female neonates, their HC increased from 22.45 cm at the 24th gestational week and peaked at 33.80 cm at the 41st week (Fig. 3, **panel B**) or **Table S6** and **Table S7**. The birth length for the male neonates increased from 31.1 cm at the 24th gestational week and peaked at 50.6 cm at the 41st week. The length of female neonates increased from 31.4 cm at the 24th gestational week and also peaked at 50.1 cm at the 41st week (Fig. 3, **panel C**) or **Table S8** and **Table S9**.

Discussion

This multicentre case–control study conducted across six ethnically diverse sites in Ghana supports the multifactorial aetiology of SPTB. Maternal age < 20 years and < 4 antenatal visits were independent risk factors, whereas nulliparity, unmarried status, and moderate anaemia were not independent predictors. Ghanaian neonates showed consistently lower anthropometric measures from around 29 weeks' gestation when compared with the Olsen foetal growth chart.

The association between adolescent pregnancy and SPTB is consistent with findings from studies conducted in the USA [21][22]; Wales [23]; Turkey [24]; Nepal [25] and Ukraine [26], although a Zambian study reported no significant relationship [27]. The increased risk among adolescents may result from biological immaturity, competition between maternal and foetal nutrient requirements [22][28]–[30], oxidative stress, and inflammation that can shorten gestation [31]–[33]. Socio-economic challenges like stigmatisation and reduced access to healthcare can further heighten the risk [34][35]. Lifestyle factors including smoking and illicit drug use, common among adolescents and associated with SPTB[13][36], were excluded from this study.

Inadequate ANC visits emerged as another important determinant of SPTB. Although attending fewer than the WHO-recommended eight ANC visits [37] showed a suggestive association with SPTB, attending < 4 visits independently increased the risk. Similar findings have been reported in Indonesia [38], Gaza [39], Nigeria [40], Bangladesh [41], and Ghana [2], [42]–[44]. ANC provides opportunities for monitoring maternal and foetal health, and delivering preventive interventions to reduce adverse pregnancy outcomes [37][45][46]. Nulliparity was associated with a 64% increased risk of SPTB in the unadjusted analysis, but this association lost significance after adjustment for maternal age and ANC visits. Previous population-based studies from the Netherlands [47] and United States [21] have similarly reported increased SPTB risk among nulliparous women. Since adolescent mothers are more likely to be nulliparous [48][49], these factors may interact to elevate risk. Unlike some studies [47][50], this study observed no association between grand multiparity and SPTB. This was likely due to the relatively small number of grand multiparous participants in this study. Unmarried maternal status was also associated with increased SPTB risk in unadjusted analyses, but the association weakened after adjustment for maternal age and parity, and remained only suggestive. This finding aligns with studies from the United States [51][52], Poland [53], and Bulgaria [54]. Psychosocial stress [55], unintended pregnancies [56], and reduced social and

financial support may contribute to the elevated risk among unmarried women. Marriage has been shown to offer protective effects against preterm birth, potentially through enhanced emotional, financial, and practical support during pregnancy [53], [57]–[60]. Maternal haemoglobin (Hb) concentration at booking was significantly lower among women with SPTB than those with term births. While mild anaemia was not associated with increased risk, moderate anaemia appeared to elevate the likelihood of SPTB. Similar observations have been reported in studies from Saudi Arabia [61] and Malaysia [62]. A difference between our study and the Malaysian study is that the latter study defined 7 – < 9 g/dl as moderate anaemia and 9 – <11 g/dl as mild anaemia. Findings from the multinational SCOPE study [63] and a Zambian study [27] did not demonstrate such an association between early pregnancy Hb and SPTB. Differences in study outcomes may also reflect variations in recruitment criteria, including earlier booking gestational age (< 13 vs. <15 weeks) between our study and the SCOPE study [63], and exclusion of women with peripartum Hb < 10.5 g/dl. Additionally, the Zambian study [27] did not specify the maximum gestational weeks before booking. These factors may have affected intervention duration and maternal–foetal exposure to anaemia. Several biological mechanisms may link anaemia to SPTB. Reduced oxygen-carrying capacity impairs foetal nutrient and oxygen supply [64][65], causing hypoxia, stress responses, and activation of pathways that trigger SPTB [66]. Anaemia may also impair maternal immunity and increase susceptibility to infections, another risk factor for SPTB [67][68]. However, symptomatic infection was unlikely, as women with hospital records of infection were excluded. Our study did not record women with severe anaemia (Hb < 7.0 g/dl) at booking. Their Hb concentrations may have remained below our peripartum inclusion threshold of ≥ 10.5 g/dl. The mean age at menarche did not differ significantly between mothers with SPTB and term births. Although early menarche (< 12 years) was not significantly associated with SPTB, the findings suggested a possible trend. This contrasts with studies from China [69] and the USA [70] that linked early menarche to preterm birth. The discrepancy may reflect differences between the aetiology of SPTB and the broader preterm birth spectrum [69][70] used in the referenced studies. Biologically, early menarche may increase exposure to oestradiol, promoting uterine contractility and labour [71][72]. However, findings from Japan suggest that very early menarche (≤ 9 years) may have distinct underlying mechanisms [73].

Neonatal health was assessed using birthweight, head circumference (HC), length, and Apgar scores. Term-born infants had significantly higher values for all anthropometric measures than those born preterm, reflecting shortened intrauterine growth time in SPTB. Males generally showed higher birthweight, HC, and length than females. These sexual dimorphic differences are attributed to factors including variations in placental development, umbilical oxygen delivery [74][75], and greater responsiveness to growth factors such as insulin-like growth factor 2 (IGF2) in males [76]. When the medians of anthropometric measures were compared with the Olsen foetal growth chart [20], the Ghanaian cohort showed consistently lower values from around 29 weeks' gestation. The Olsen chart was preferred because it is based on a large singleton birth cohort, approximately 15% of whom were of Black ancestry, and is designed for neonatal size classification at birth, similar to the present study. This divergence in growth trajectory may reflect genetic differences [77] as well as maternal and socioeconomic factors, including the nutritional insecurity common in Sub-Saharan Africa [78]. The proportion of neonates with very low 1-minute Apgar scores (7%) was similar to another Ghanaian tertiary hospital (6.5%) [79], with the slight increase possibly due to inclusion of very early preterm infants (24–27 weeks). Low Apgar scores are linked to increased mortality, neurodevelopmental impairment, cardiovascular risk in later life, and ADHD [80]–[82]. Ghana's high preterm birth prevalence suggests many infants experience shortened gestation, limiting optimal growth and development.

Strengths and Limitations

The strengths of the study include its broad geographic coverage across Ghana. The six study centres were distributed across the country to capture people of varying socio-economic, cultural and geographic backgrounds, which enhanced the representativeness of the Ghanaian population. Additionally, robust exclusion and inclusion criteria were adopted to increase the authenticity of the study outcome. Data were collected by highly experienced healthcare professionals to ensure the reliability of the data.

However, certain limitations must be acknowledged. The study was constrained by a low sample size among neonates with early gestational duration, especially those born before 28 weeks.

Conclusions

This study demonstrates that SPTB is driven by a multifactorial interplay of maternal health behaviours, clinical characteristics, and prenatal care utilization. Key among them were adolescent maternal ages, poor antenatal visits, and maternal anaemia, while other factors such as nulliparity, moderate haemoglobin levels at booking, unmarried status, and early menarche (≤ 11 years) showed contributory but non-independent associations. SPTB was further associated with adverse neonatal outcomes, evidenced by reduced birth weight, head circumference, length, and Apgar scores, reflecting compromised neonatal adaptation. The Ghanaian neonates studied demonstrated a distinct foetal growth pattern compared with the Olsen reference population.

These findings highlight the critical need for targeted public health interventions focusing on adolescent reproductive health, improved antenatal care attendance, and the early detection and management of maternal anaemia. Furthermore, the diverse ethnic and sociocultural backgrounds of Ghanaian women suggest that susceptibility to spontaneous preterm birth (SPTB) may be influenced by a combination of genetic and environmental factors. Therefore, comprehensive genomic and environmental investigations aimed at identifying SPTB-associated markers in Ghanaian women could provide valuable insights for the development of diagnostic and therapeutic tools. Collectively, these efforts underscore the importance of a multidisciplinary and integrated approach to reduce the burden of SPTB, improving neonatal outcomes, and enhance our understanding of foetal growth in Ghana.

Abbreviations

SPTB spontaneous preterm birth

SPTL spontaneous preterm labour

PPROM preterm premature rupture of membranes

LMIC lower-to-middle income country

HIV human immunodeficiency virus

AIDS acquired immunodeficiency syndrome

ANC antenatal care

HC head circumference

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from: Ghana Health Service (GHS-ERC 009/02/21), Korle Bu Teaching Hospital Institutional Review Board (KBTH-IRB/00003/2020), Komfo Anokye Teaching Hospital Institutional Review Board (KATH-IRB/AP/022/20), University of Ghana Ethics Committee for Basic and Applied Sciences (ECBAS 007/19-20). Approval was also granted by the management study sites. All patients gave written informed consent. The study complied with the Declaration of Helsinki.

Consent for publication

Not applicable.

Data Availability Statement

Data underlying the findings of this study is in the manuscript. However, any other information about the data can be obtained from the corresponding author (L.P.) upon reasonable request. Public access is restricted to protect participant confidentiality and comply with ethical requirements. Access will be granted for research purposes only. Access to the data will be granted after a standard Data Use Agreement (DUA) has been completed.

Competing interests

The authors declare no conflict of interests.

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Authors' contribution

P.N-A., K.A-B., S.G., E.T.D., L.A. and L.P. conceptualised the project, methodology and project administration. P.N-A., J.A.Y., S.G, R.A., E.A., Y.O. and L.P. data acquisition. F.D., C.M.M. and P.N-A. performed the data curation and analysis. P.N-A and L.P. drafted the first version of the manuscript. P.N-A., K.A-B., J.A.Y., S.G, R.A., E.A., Y.O., F.D., C.M.M., E.T.D., L.A., L.P. reviewed and edited subsequent version of the manuscript and approved final version.

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Figures

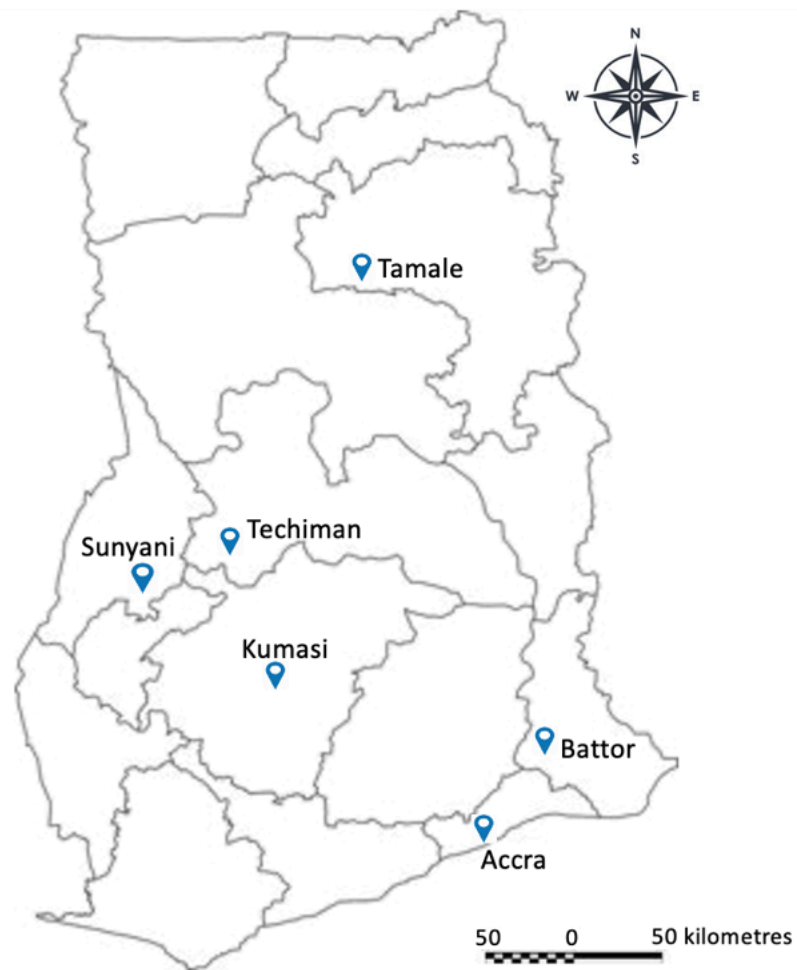


Figure 1

Distribution of the study centres in Ghana. Three tertiary referral hospitals, namely: Korle-Bu Teaching Hospital, Accra; Komfo Anokye Teaching Hospital, Kumasi; and Tamale Teaching Hospital, Tamale – are located in the southern, middle, and northern parts of Ghana, respectively, and receive referrals from across the country. Bono Regional Hospital, Sunyani, and Holy Family Hospital, Techiman, are secondary hospitals, while Battor Catholic Hospital is a district hospital.

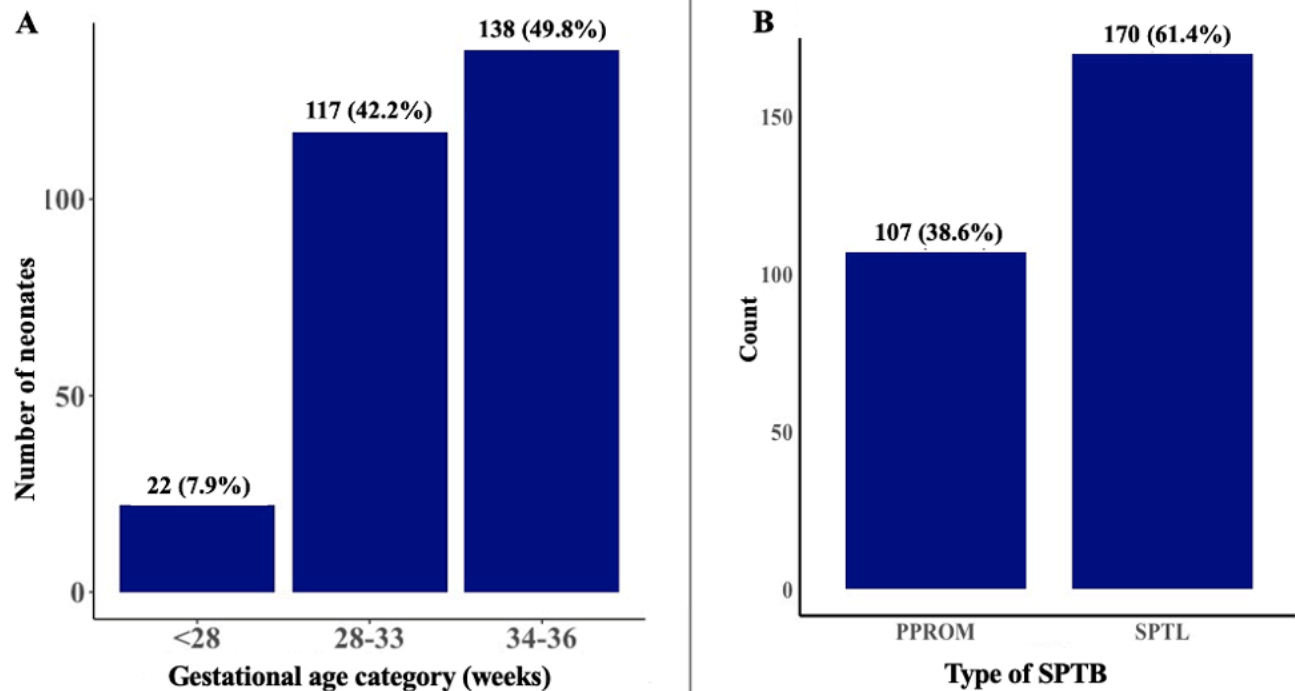


Figure 2

Distribution of gestational age categories and SPTB sub-types among neonates. Neonates delivered from 34-36 gestational weeks constituted 49.8%, while those delivered <28 weeks made up 7.9% (Panel A). About 6 out of 10 participants with SPTB had SPTL (Panel B).

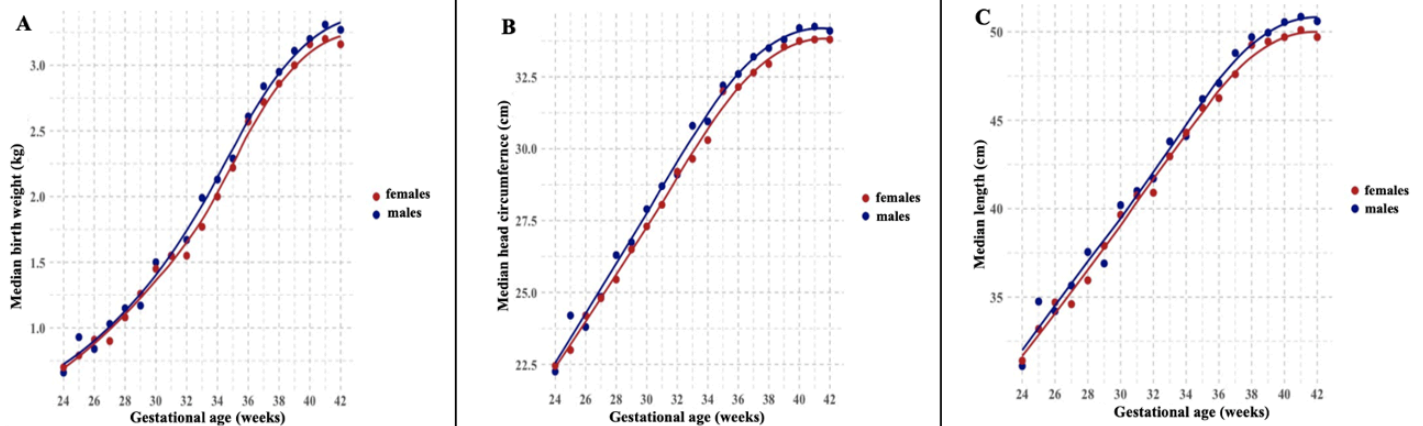


Figure 3

Neonatal anthropometric indicators. The medians of all three indicators, measured from 24 to 42 gestational weeks are represented with scatter plot and smooth curve overlay. The median birth weight for males rose from 0.66 kg at 24 weeks and peaked at 3.31 kg at 41 weeks. That of females was 0.70 kg at 24 weeks but peaked at 3.20 kg at 41 weeks (**panel A**). The median head circumference for both males and females was 22.25 cm and 22.45 cm, respectively, at 24 weeks but topped out at 34.25 cm and 33.80 cm, respectively at 41 weeks (**panel B**). Invariably, the median lengths were 31.10 cm and 31.4 cm for males and females, respectively at 24 weeks, and peaked at 50.58 cm and 50.10 cm for males and females, respectively at 41 weeks (**panel C**).

Supplementary Files

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