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Sarah Haider , [Kareem Ahmed](#) , [Babiker Rahamtalla](#) , [Badrelddeen Ahmed](#) , [Justin C. Justin](#) *

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Article

Identification of Risk Factors for Preterm Birth in a Regional Hospital in Northern Region of Sudan—A Prospective Study

Sarah Haider ¹, Kareem Ahmed ², Babiker Rahamtalla ³, Badreldeen Ahmed, ^{4,5,6} and Justin C. Konje ^{4,6,7,*}

- ¹ Omdurman Maternity Hospital, Omdurman, Sudan
- ² Medical Student, Medical School, University of Nicosia, 2417, Nicosia, Cyprus
- ³ Department of Community Medicine, University of Medical Sciences and Technology, Khartoum, Sudan
- ⁴ Feto Maternal Centre, Al Markiya Street, Doha, Qatar
- ⁵ Department of Obstetrics and Gynaecology, Qatar University, Doha Qatar
- ⁶ Weill Cornell Medicine, Doha Qatar
- ⁷ Department of Health Sciences, University of Leicester, University Road, Leicester, LE1 7RH UK
- * Correspondence: jck4@leicester.ac.uk

Abstract

Introduction: Preterm birth (PTB) (delivery< 37 completed weeks of gestation) is one of the leading causes of neonatal mortality and morbidity. Its aetiology is multifactorial but is unknown in many cases. Worldwide about 15 million babies are born preterm annually. Rates are higher in low and middle-income countries where several social, environmental and health factors interact. **Objectives:** The aim of this study was to identify factors associated with PTB in a metropolitan area of a low middle income country- Sudan. **Method:** This was a prospective cross-sectional hospital-based study carried out at Omdurman Maternity Hospital over a period of six months on women who received antenatal care and delivered at the hospital over the study period. After delivery, the cohort was then divided into those who delivered preterm and those who delivered at term, and a multivariate analysis performed to identify factors associated with PTB. Those who had elective CS were excluded from the study. **Result:** A total of 411 women received antenatal care and delivered over the study period and 384 formed the subjects of the study. The PTB rate was 7.4%. Factors identified that were associated with PTB included maternal age <20 years old (P=0.017), low family income (P=0.005), rarely receiving iron and folic acid supplementation (P=0.00001), infrequent antenatal care attendance (P=0.013), poor nutritional status (P=0.0000001), low maternal education (P=0.04) and short inter-pregnancy interval (<6 months) (P=0.04). Other factors included multiple birth (P=0.001), diabetes mellitus (P=0.004), antepartum haemorrhage (P=0.002), hypertension (P=0.004), previous PTB (P=0.0001) and urinary tract infections (P= 0.004). **Conclusion:** Various sociodemographic factors and complications during pregnancy increased the risk of PTB in this population. To reduce the risk, an interdisciplinary approach must be adopted. This should tackle factors pre-pregnancy and improve access. Healthcare providers should ensure folate and iron supplementation and identify complications such as diabetes and hypertensive disorders in pregnancy early and manage appropriately.

Keywords: preterm labour; perinatal morbidity; risk factors of preterm labour; complications of pregnancy

1. Introduction

Preterm birth defined as delivery < 37 completed weeks is the leading cause of neonatal morbidity and mortality world-wide, accounting for 18% of deaths among children less than 5 years

old and 35% of deaths among those aged less than 28 days [1]. The rate PTB varies from country to country with the highest rates in low-income countries and the lowest in high income countries. [2] It is estimated that there are approximately 15million preterm births every year for an average PTB rate of 11% [3]. The rates vary from 5%-9% in high income countries to about 18% in some low-income countries [4–6]. In sub-Sahara African the rate of PTB is high being for example 13.3% in Ethiopia [7] and 18.3% in Kenya [8]. In addition to negative health outcomes, the cost of PTB is exorbitant to families, society and governments [9]. The long-term health consequences include chronic lung diseases, cognitive impairment and cardiovascular disease [10].

Increasingly, PTB is not regarded as a single entity, but a complex condition best described as a syndrome caused by an interaction of multiple factors where these are known but in many cases these factors are unknown. There is now an acknowledgement that to better understand its pathophysiology, prevention and management, PTB should be phenotyped based on conditions present in the mother and conditions of the fetus and placenta at the time of birth [11]. Two classical phenotypes have been proposed [12,13]. Prevention of PTB can only be effective if its multifactorial aetiology is better understood.

Although the causes of PTB are known in some cases, they are poorly defined in many cases, but various risk factors have been identified [14]. Most of these risk factors are modifiable [15] and it has been estimated that more than 75% of PTB deaths are preventable without intensive care [16]. In sub-Sahara Africa and some South-East Asia [17,18] with limited resources, therefore a more pragmatic approach to reducing PTB would be identifying the modifiable factors and taking appropriate steps to mitigate them. These factors vary from individual, social and medical, to care provided antenatally. Identification of these factors and addressing them either pre-pregnancy or during pregnancy may significantly reduce the risk of PTB. Some of these factors which if addressed have been shown to reduce the rate of PTB include smoking [10], short interpregnancy intervals, maternal age (<20years and >35 years) [19,20], anaemia, urinary tract infections, previous preterm birth and medical disorders of pregnancy [11,20] and infections [21].

That the WHO and the United Nations' 2010 goal of reducing mortality due to PTB by 50% before 2025 has unfortunately not been achieved in most countries is reflective of failure of multidisciplinary concerted efforts to address modifiable factors that increase the risk of PTB. In Sudan for example, a country that is currently experiencing one of the most destructive civil strife, most studies on PTB have been retrospective and few have investigated modifiable factors such as nutritional status, periodontitis [22] number of antenatal clinical visits and regularity of iron and folate supplementation during pregnancy [23]. In a previous study from Omdurman, Sudan, the rate of live preterm birth was surprisingly 3.8%, significantly lower than rates reported from all of the region. The study did identify a few preventable factors (interpregnancy interval of <18 months and low or high BMI), hence was not comprehensive, and furthermore the economic changes in the country partly because of the civil strife and poverty have undoubtedly increased the number and prevalence of preventable factors [24]. That study [24] could be criticised on many counts, the most important being that the cohort was not reflective of the country (the rate was too low). In another study in North Ethiopia, age, rural residency, lack of antenatal care, multiple pregnancy and malaria infections were identified as preventable factors associated with PTB [7]. The aims of this study were therefore to comprehensively investigate and identify the modifiable/preventable factors (including intrinsic maternal factors like nutrition and extrinsic factors) and determine whether they are similar to those reported from other sub-Sahara countries and middle- and high-income countries in the hope of overcoming the weaknesses in the previous and retrospective studies. Identifying these factors should provide healthcare policy makers a list to address in any multidisciplinary attempt to reduce the rate and burden of PTB in Sudan.

2. Materials and Methods

Study design and setting

This was a prospective study at Omdurman Maternity Hospital, located in Khartoum State for the period June to December 2022 - a period of political instability and population displacement that preceded the ongoing civil war. All pregnant mothers who received antenatal care and their pregnancies progressed beyond 26 weeks of gestation and delivered in the hospital were recruited. We excluded those who miscarried or had an elective caesarean section (normally performed at term). For each woman studied, a set of variables were extracted from their records onto a spread sheet. These included age, family income, level of education, antenatal folic acid and iron supplementation, number of antenatal visits, obstetric history (including previous deliveries, miscarriages and gestational age at delivery), medical history, social variables (smoking, alcohol and drugs) and any complications during pregnancy. All information was collected on a spreadsheet.

The family income was estimated from the combined earnings of the woman and her husband. Education level was categorised into

The women who delivered before 37 weeks were analysed as the preterm group while those whose pregnancies progress to at least 37 weeks of gestation were analysed as the term group.

Preterm birth was defined as delivery between before 37 completed weeks of gestation. 26 weeks is the gestational age cut-off for fetal viability in viability in Sudan.

Nutritional status was assessed at the first antenatal visit using Mid-Upper Arm Circumference (MUAC). Status was categorized as 'poor' (MUAC < 23 cm), 'normal' (MUAC 23-28 cm), or 'good/excellent' (MUAC > 28 cm) [25,26].

Iron and folate supplementation was categorized as 'regular' if the woman reported taking prescribed supplements for more than 75% of her pregnancy days, and 'rare' if taken for less than 50%.

Antenatal care (ANC) attendance was considered 'regular' if the woman attended at least 4 scheduled antenatal visits prior to delivery, as per WHO recommendations. Attendance of fewer than 4 visits was deemed 'inadequate'.

Data analysis

The IBM Statistical Package for Social Sciences software, version 27 of 2019, was used for analysis. Data are presented as means and standard deviation if normally distributed and median and range if not. Normal distribution was tested by the Kolmogorov Smirnov test. Comparisons between the groups were made using Chi square Test or Fisher's Exact Test. Binary logistic regression Test was used to identify risk factors associated with PTB. The statistical analysis was undertaken by a statistician (Dr Rami Yousif Hasabelrasul Mohamed)

Ethical consideration

Ethics approval for the study was obtained from the Sudan Medical Specialization Board (SMSB), council of family medicine, Khartoum state ministry of health research department on 25th May 2022. Each woman who was included in the study gave a signed informed consent to participate in the study. Each study participant was assigned a study number, and the data were extracted and analysed anonymously.

3. Results

Over the study period, a total there were a total of 411 deliveries, and 384 pregnant women were recruited (20 excluded as these were elective term CSs and 11 delivered between 24 and 26 weeks) and followed up. Table 1 shows the demographics of the cohort. The mean (SD) age was 27 (6) years (range 16-45 years). Most of the women were housewives (88.8%) and more than three quarters were from families that owned their houses (75.5%). 177 (46.1%) of the women were primigravida. In the multigravida group (207), 31 (8.1%) had previously delivered preterm. There were 50 (13%) multiple pregnancies. The education level of the women varied. 62% had secondary school, university or postgraduate education and 32% were either illiterates or had only completed primary

schooling. 69.5% of the husband's had either secondary, university or postgraduate education and 30.5% were either illiterates or had only primary schooling. Approximately, two-third (66.7%) of husband's were self-employed and non-smokers (75.8%). With regards to the income of the household from which the women came, 4.4% had a total monthly income of <30.000-50.000 Sudanese pound (SDG)[50-85 USD], 18.0% >50.000-70.000 SDG[85-120 USD], 46.1% >70.000-100.000 SDG[120-170 USD], and 31.5% >100,000 SDG[>170 USD].

Table 1. Demographic variables.

Variables	Number	Percent
Mother's age groups		
<20 years	61	15.9
20–25 years	111	28.9
26–30 years	88	22.9
31–35 years	83	21.6
>35 years	41	10.7
Previous preterm delivery		
Yes	31	8.1
No	353	91.9
Housing		
Owned	290	75.5
Hired (Rent)	67	17.4
Others	27	7.0
Mother's educational level		
Illiterate/Primary	146	30.0
Secondary	113	29.4
University/postgraduate	125	32.6
Mother's occupation		
Housewife	341	88.8
Employee	41	10.7
Husband's educational level		
Illiterate/Primary	117	30.5
Secondary	90	23.4
University/postgraduate	177	46.1
Husband's occupation		
Unemployed	8	2.1
Self-employed	256	66.7
Professional/employed	120	31.3
Husband's lifestyle (smoking)		
Yes	93	24.2
No	291	75.8

Table 2 shows the inter-pregnancy interval, nutritional status at first visit, regularity of antenatal visits and micronutrient supplementation. The inter-pregnancy interval was less than 6 months in 21 (10.1%) of cases, 6–12 months in 34 (16.4%), >1-2 years in 57 (27.5%) and more than 2 years in 95 (46.0%) cases. About 64.1% (246) of mothers received folate and iron supplementation regularly

while 60.4% (232) attended antenatal care regularly. More than half of the mothers' nutrition during pregnancy was judged as either excellent or good in 63.3% (N=243) of cases and poor in 6.8% (N=26) of cases.

Table 2. Inter-pregnancy interval, nutritional status at first visit, rate of antenatal visits and micronutrient supplementation.

Variables	Number	Percent
*Interpregnancy interval (IPI) (N=207)		
<6 months	21	10.1
6–12 months	34	16.4
2 years	57	27.5
>2 years	95	45.9
Received iron and folic acid (N=384)		
Regular	246	64.1
Sometimes	127	33.1
Rarely/never	11	2.8
Antenatal care attendance (N=384)		
Regular (4 or more)	232	60.4
Sometimes (2-3)	133	34.6
Rarely/never (0-1)	19	4.9
Nutrition during pregnancy (N=384)		
Excellent	53	13.8
Good	190	49.5
Reasonable	115	29.9
Poor	26	6.8

*IPI excluding primigravidas (n=177).

The complications reported in the pregnancy are shown in Table 3. The most common were hypertensive disorders of pregnancy (15.6%), diabetes mellitus (17.4%) and urinary tract infections (16.9%). Malaria was diagnosed in 3.9% of cases.

Table 3. Antenatal complications.

Variables	Number	Percent
Antepartum Haemorrhage		
None	373	97.1
Yes	11	2.8
Multiple pregnancy		
Yes	50	13
No	334	87
Hypertension during pregnancy		
Yes	60	15.6
No	324	84.4
Diabetes during pregnancy		
Yes	67	17.4
No	317	82.6
UTI during pregnancy		
Yes	65	16.9

Periodontal infection during pregnancy	No	319	83.1
	Yes	7	1.8
Malaria during pregnancy	No	377	98.2
	Yes	15	3.9
Toxoplasmosis	No	369	96.1
	Yes	3	0.8
	No	381	99.2

In this cohort there were 30 preterm deliveries for a rate of 7.8% and 4 neonatal deaths. A comparative analysis (Table 4) was undertaken of variables in the cohort - divided into those who had preterm birth and those who delivered at term. Sociodemographic factors that were significantly more common in the preterm group included younger mothers age (P=0.017), area of residence (P=0.013), and poor housing (P=0.007).

Table 4. Association between preterm and term delivery with sociodemographic data.

Variables		Delivery outcome				Pearson Chi-Square
		Preterm (N=30)		Term (N=354)		P value
		Number	%	Number	%	
Mother's age groups	<20 years	10	33.3	51	14.4	0.017
	20-25 years	10	33.3	101	28.5	
	26-30 years	2	6.7	86	24.3	
	31-35 years	7	23.3	76	21.5	
	>35 years	1	3.3	40	11.3	
Residence	Urban	24	80.0	333	94.1	0.013
	Rural	6	20.0	21	5.9	
Housing	Owned	19	63.3	271	76.6	0.007
	Renting	4	13.3	63	17.8	
	Others*	7	23.3	20	5.6	
Mother's educational level	Illiterate	6	20.0	52	14.7	0.300
	Primary	9	30.0	79	22.3	
	Secondary	7	23.3	106	29.9	
	University	7	23.3	114	32.2	
	Post graduate	1	3.3	3	0.8	
Mother's occupation	Housewife	27	90.0	314	88.7	0.999
	Employee	3	10.0	38	10.7	
	Heavy physical laborer	0	0.0	2	0.6	
Husband's educational level	Illiterate	6	20.0	50	14.1	0.240
	Primary	6	20.0	55	15.5	
	Secondary	10	33.3	80	22.6	
	University	8	26.7	163	46.0	
	Postgraduate	0	0.0	6	1.7	
Husband's occupation	Unemployed	0	0.0	8	2.3	0.146
	Self Employed	25	83.3	231	65.3	
	Professional/employed	5	16.7	115	32.5	
Husband's life style (smoking)	Yes	8	26.7	85	24.0	0.744
	No	22	73.3	269	76.0	

*sharing with other families/friends.

Table 5 shows the relationship between pregnancy complications and preterm and delivery. Multiple pregnancy, hypertensive disorders of pregnancy, diabetes mellitus, and toxoplasmosis in pregnancy were all associated with a statistically increased risk of preterm birth. Of all the antenatal complications, urinary tract infection had the highest impact on the risk of preterm birth (P=0.000001 OR - 5.685 (95%CI 1.752-18.447) followed by previous preterm birth (P=0.0001, OR=35.094, (95%CI 5.983-205.856) and antepartum haemorrhage (P=0.002; OR 29.085 (95%CI 3.325-254.431). Interestingly malaria infection was not a risk factor for preterm birth, but the number of confirmed infections was very small.

Table 5. Relationship between antenatal complication and preterm or term delivery.

Variables		Delivery outcome				Pearson Chi-Square
		Preterm (N=30)		Term (N=354)		P value
		Number	%	Number	%	
Antepartum hemorrhage	No	26	86.7	347	98.0	0.002
	Once	2	6.7	7	2.0	
	Multiple	2	6.7	0	0.0	
Multiple birth	Yes	11	36.7	39	11.0	0.001
	No	19	63.3	315	89.0	
Hypertension during pregnancy	Yes	11	36.7	49	13.8	0.003
	No	19	63.3	305	86.2	
Diabetes during pregnancy	Yes	11	36.7	56	15.8	0.004
	No	19	63.3	298	84.2	
Previous preterm delivery	Yes	7	23.3	24	6.8	0.0001
	No	23	76.7	330	93.2	
UTI during pregnancy	Yes	15	50.0	50	14.1	0.000001
	No	15	50.0	304	85.9	
Periodontal infection during pregnancy	Yes	2	6.7	5	1.4	0.097
	No	28	93.3	349	98.6	
Malaria during pregnancy	Yes	2	6.7	13	3.7	0.330
	No	28	93.3	341	96.3	
Primary Toxoplasma gondii infection in pregnancy	Yes	2	6.7	1	0.3	0.017
	No	28	93.3	353	99.7	

A logistic regression was undertaken to predict which factors had the greatest impact on the risk of preterm birth. Mother's age <25 years (P=0.04; OR 2.5; 95% CI 1.042-6.003) and interpregnancy interval of <6 months (P=0.04, OR 0.59; 95% CI 0.356-0.997) were associated with an increased risk of preterm birth while excellent or good nutrition (P=0.003; OR 4.069; 95%CI 1.631-10.151) was associated with a decreased risk of PTB. Table 6 shows the association between timing of delivery and family income, regularity of antenatal attendance, nutritional status at first visit to the hospital and interpregnancy intervals. Low family income was significantly associated with an increased in the risk of preterm birth (P=0.005) while regular iron and folate supplementation in pregnancy (P=0.00001), regular attendance of antenatal clinics (P=0.013) and having an excellent or good nutrition (P=0.0000001) were factors that significantly reduced the risk of preterm.

Table 6. Association between timing of delivery (term or preterm) and antenatal care variables, interpregnancy-interval and Family monthly income.

Variables	Delivery outcome				Pearson Chi-Square
	Preterm (N=30)		Term (N=354)		P value
	Number	%	Number	%	

Family Income per month	<30.000-50.000 SDG	0	0.0	17	4.8	0.005
	>50.000-70.000 SDG	12	40.0	57	16.1	
	>70.000-100.000 SDG	14	46.7	163	46.0	
	>100,000	4	13.3	117	33.1	
Spacing interval for this pregnancy	Primigravida	17	56.7	160	45.2	0.413
	≤1 years	5	16.7	50	14.1	
	1-2 years	4	13.3	53	15.0	
	>2 years	4	13.3	91	25.7	
Receive iron and folic acid during this pregnancy	Regular	11	36.7	235	66.4	0.00001
	Sometimes	15	50.0	112	31.6	
	Rarely	2	6.7	2	0.6	
	Never	2	6.7	5	1.4	
Antenatal care attendant	Regular	12	40.0	220	62.1	0.013
	Sometimes	14	46.7	119	33.6	
	Rarely	1	3.3	9	2.5	
	Never	3	10.0	6	1.7	
Type of nutrition during pregnancy	Excellent	0	0.0	53	15.0	0.0000001
	Good	7	23.3	183	51.7	
	Reasonable	15	50.0	100	28.2	
	Poor	8	26.7	18	5.1	

4. Discussion

The preterm delivery rate in our cohort was 7.4%. Factors which were more prevalent in those who delivered preterm included maternal age <20 years, low levels of maternal education, interpregnancy interval of <6 months low family income, inadequate folate and iron supplementation throughout pregnancy, irregular antenatal visits, poor nutritional status at booking, and previous preterm delivery. Pregnancy complications such as antepartum haemorrhage, diabetes mellitus, hypertensive disorders of pregnancy, multiple pregnancy and, and urinary tract infections increased the risk of preterm birth. An interpregnancy interval of at 1-2 years was associated with the lowest risk of PTB.

The PTB rate of 7.4% in this cohort is much higher than that from previous studies in Sudan which were 3.8% in 2010 and 4.7% in 2012 [27,28]. By using a cut-off of 26 weeks, we might have under-estimated the PTB rate. Including the 7 deliveries between 24 and 26 weeks would have given a much higher PTB rate of 9.0%. The problem of variable cut-offs for defining viability are well recognised when comparing not only perinatal mortality but PTB rates across the globe [29]. Lack of high-level neonatal care facilities mean survival before 26 weeks is almost impossible in Sudan and indeed most low-income countries compared to high-income countries with viability varying from 22-24 weeks. [30,31]. There has been a consistent rise in the PTB rate in Sudan, and this is most likely to have risen exponentially with the ongoing civil war. For low and middle-income countries, this rate is in the middle of the range (5% to 19%) [3,32]. Our rate is however, comparable to those from some middle and high-income countries such as the USA with the latest reported rate of 9.6% and 5%-9% in European countries [4]. We feel that this rate does not truly reflect the magnitude of the problem in the country for two reasons - firstly, our numbers are very small and secondly, the population that comes this this hospital may be skewed toward the middle/higher income category. In our cohort, about two thirds of the women and the men had either received secondary, university or postgraduate education and just over 90% of the men were either self-employed or employed. This reflects the income for the household and therefore better nutritional status, more compliance with antenatal visits and supplementation.

Maternal age < 20 years old was found to be significantly associated with an increased risk of preterm birth. This finding is similar to that from other studies (high income and low/middle income

countries). In Taiwan for example this was significantly associated with PTB [33]. Age above 35 years was not a risk factor for PTB in our series. This finding is at odds with findings from other studies especially from high income countries such as Taiwan and Canada [33,34]. Several reasons could be responsible for this - our numbers are small and furthermore our older women were multiparous having previously delivered at term which, in itself lowers the risk of PTB.

Central to maternal health is availability of not only healthcare resources but also ensuring that these are economically affordable. Family income and education status are important determinants for this. It was therefore not surprising that area of residence, housing, education and family income were all significantly associated with preterm birth in our series. Similar findings were reported from other studies [35–38]. These sociodemographic factors are interlinked and whether education is the core factor or family income is difficult to decipher. What is important is that by addressing these factors it should be possible to improve not only access but appropriate utilisation of services. In fact, regularly attending antenatal care and complying with supplementation was associated with a lower risk of preterm birth in our study. Never or rarely attending antenatal care was also significantly associated with more preterm birth. In China a study showed that those who had not attended antenatal care, had an OR of 5.19 of having a preterm birth OR = 95% CI: 3.77 - 7.14) [39].

The finding of an increased risk of preterm birth with multiple pregnancy, hypertensive disorders of pregnancy diabetes mellitus and urinary tract infections was expected as this has been widely reported [37,40–43]. While some of these may be iatrogenic, we believe that a significant number may be spontaneous. The risk of preterm birth increases with a previous PTB and this increase is exponential after 2 [9].

In low- and middle-income countries where women are likely to have several babies' inter-pregnancy interval is critical in not only ensuring that nutrients are replenished but that breastfeeding is enough to support the baby. An inter-pregnancy interval of <6 months and >2 years are considered risk factors for PTB [15,44]. In our series, IPI of <6 months was associated with PTB but not >2 years. Interestingly in the previous study from this same region [24], interpregnancy interval of <18 months was associated with an increased risk of PTB. These contrasting findings make a strong case for large cohort studies.

Preterm pre-labour (PPROM) and chorioamnionitis are well recognised precedents of PTB. These and other factors such as bleeding in pregnancy/threatened miscarriage were not investigated as these are not modifiable (at least in the context of a low-income country). Where facilities are available, microbiology of samples from those presenting in preterm labour will help isolate infective organisms and enable preventative treatment. This is an important cause of PTB that may be modified with antibiotics. While we could not do this in this study there is increasing evidence the antibiotics to women presenting in threatened preterm may reduce the risk of PTB. [21]

5. Conclusions

In our small series, the PTB rate was 7.4% which, while better than from most low-income countries is still considerably higher than most of the rates in high-income countries. We have shown that the traditional risk factors (pre-pregnancy and pregnancy) that have been associated with PTB also apply to Sudan, however, we have in addition shown that regular attendance at antenatal clinics and compliance with folate and iron supplementation can reduce the risk of PTB. Starting pregnancy with a good/excellent nutritional status is another factor that is associated with a lower risk for PTB. Within the context of Sudan therefore, a multi-prong approach that involves, healthcare workers, epidemiologists, nutritionist public health planners and educationists is likely to tackle most of the identifiable factors that are preventable. This is more important since neonatal facilities are poor meaning those babies delivered preterm are less likely to survive.

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editing, KA, BA, BR and JCK visualization, supervision, BR. All authors have read and agreed to the published version of the manuscript.”

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Data Availability Statement: Data available on request.

Strengths and limitations: The main strength of our study is that it was a prospective study in which most of the data would have been accurately collected. Most previous studies were retrospective with all the limitations of such studies. However, a major limitation of the study is the small numbers and the regionalised location of the study. The findings cannot therefore be generalised for the population. It is possible that in more rural areas, the rate of PTB may be higher and the factors that increase the risk may be different. That we did not include indications for iatrogenic PTB such as fetal growth disorders is another limitation of our study as this would have allowed for a better understanding of the potential additive impact of PTB on perinatal mortality and morbidity.

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