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Early postnatal growth failure in infants <1500 g in a Ugandan referral hospital: a retrospective cohort study

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Abstract

Background Postnatal growth failure (PGF), a multifactorial condition is common in preterm infants and infants born weighing <1500 g and is associated with impaired neurodevelopmental and growth outcomes. In low-resource settings, like Uganda, parenteral nutrition and breastmilk fortifier are often unavailable, and preterm infants rely solely on their mother's expressed breastmilk, which can be inadequate. This retrospective cohort study, conducted in a level II neonatal unit in eastern Uganda, aimed to evaluate the incidence of and risk factors for postnatal growth failure among infants <1500 g.

Methods The study included infants with birthweight <1500 g, admitted within 24 h of birth, and who spent 7 or more days in the neonatal unit. Major congenital malformations or a diagnosis of hypoxic ischemic encephalopathy were exclusion criteria. PGF was defined as a decrease in weight Z score between birth and discharge of more than − 1.28. Data on feeding, anthropometry, co-morbidities, and clinical measures were extracted from medical records. Statistical analyses were performed using Stata 17.0 with crude and adjusted relative risks (RR) were reported.

Results One hundred and four infants were recruited, including 47 (45.2%) male and 57 (54.8%) female, with a mean birth weight of 1182 g (SD 18 g, 95% CI: 1140, 1210). Almost half were small for gestational age, most were singletons (66.3%), and most were born by spontaneous vaginal delivery (82.7%). PGF was observed at discharge in 75.9% (*N* = 79). Clinical risk factors for PGF included: small for gestational age (cRR 1.25, 95% CI: 1.01, 1.53), respiratory distress syndrome (aRR 1.30 95% CI: 1.01, 1.67), duration of bubble continuous positive airway pressure use (aRR 1.35, 95% CI: 1.10, 1.66), sepsis requiring second line (aRR 1.58, 95% CI: 1.22, 2.04) and third line treatment (aRR 1.46, 95% CI: 1.20, 1.77), prolonged time to achieve full feeds (aRR 1.30, 95% CI: 1.01, 1.66) and prolonged hospitalisation (aRR 1.85, 95% CI: 1.31, 2.61).

Conclusion PGF was common among infants <1500 g in this hospitalised cohort who were primarily fed on their mother's own milk. Urgent action is needed to enhance postnatal growth in this vulnerable patient group. Future research should focus on exploring multidisciplinary interventions that can improve growth outcomes in this population and understanding the long-term implications and need for care for these infants.

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Background

Postnatal growth in preterm infants is a key determinant of their long-term health and developmental outcomes. Failure to achieve adequate growth during the early postnatal period has been associated with a range of adverse consequences, including chronic health conditions, neurodevelopmental impairment, and an increased risk of mortality [1–4]. The prevalence of growth failure in LMICs is notably high, with many preterm infants experience postnatal growth failure (PGF) due to inadequate nutritional support, limited healthcare resources, and high rates of neonatal morbidity [5–8].

Very low birth weight (VLBW, 1000–1499 g) and extremely low birth weight (ELBW, <1000 g) infants have metabolic and gastrointestinal immaturity, compromised immune function, and a high incidence of comorbidities, such as necrotizing enterocolitis, respiratory distress syndrome and late-onset infections, all of which increase the risk of impaired postnatal growth [9, 10].

The nutritional goal for these infants is to replicate the growth trajectory that would have occurred in utero at the same postmenstrual age [11]. This requires matching the high rates of nutrient deposition typical during foetal development, which makes the nutritional needs of preterm infants inherently high [11, 12]. Therefore, achieving adequate postnatal growth and nutritional support in preterm VLBW and ELBW infants is challenging, not least that preterm birth is already the result of a compromised pregnancy [13, 14].

In high-resource settings, rapid advances in neonatal care have greatly improved the growth and survival of preterm infants [15]. Postnatal growth has been improved through optimising nutritional support, including early initiation of parenteral nutrition, increased protein administration, early initiation of enteral feeds, encouraging the use of human milk and the addition of human milk fortifier [16–18]. However, in low-resource settings, parenteral nutrition is neither affordable, safe nor feasible, breastmilk fortifier is prohibitively expensive, and donor human milk is not readily available. Therefore, preterm infants usually rely solely on their mother's own expressed breast milk. Many of the mothers have themselves been unwell and their access to adequate nutrition is also limited, culminating in a poor milk supply, and contributing to the poor postnatal growth of their infants [19–21].

These challenges underscore the urgent need for targeted interventions to prevent PGF and support the healthy growth and development of preterm infants, particularly in resource-limited settings. Improving our understanding of postnatal growth of ELBW and VLBW infants, will allow more appropriate interventions to be developed to improve the growth and development of these infants.

Aims and objectives

The aim of this study was to evaluate the incidence of and risk factors for PGF among infants<1500 g in a level II neonatal unit in eastern Uganda.

The specific objectives were:

- To assess the postnatal growth from birth until discharge.
- To identify clinical and nutritional risk factors associated with PGF.
- To determine what proportion of preterm infants had not regained their birth weight by day 28 of life.
- To examine the relationship between growth velocity, birth weight, nutritional practices, and illnesses.

Methods

Study design

This was a retrospective cohort study using in-patient records of infants with a birthweight<1500 g admitted between 1 Jan 2018 and 31 Dec 2018 to a level II neonatal unit (NNU) in eastern Uganda.

Study population

Infants that were admitted to the NNU with a birthweight<1500 g, within 24 h of birth and spent≥7 days in NNU were included in the study. Infants with major congenital malformations or a diagnosis of hypoxic ischaemic encephalopathy were excluded as they were expected to have PGF secondary to these co-morbidities. In addition, those infants with incomplete growth parameters and unknown gestational age were excluded.

Study setting

The study was conducted in a government hospital in eastern Uganda. The hospital serves a population of about 4.5 million people, and hundreds of lower-level health facilities. The labour ward has approximately 10,000 deliveries a year. The NNU also admits infants referred from district hospitals and health centres beyond its catchment area. In addition a high rate of home deliveries still occur in rural Uganda and some of these infants are brought directly from home [22]. The NNU provides level II neonatal care, for which the facilities have been previously described [23]. There are approximately 2500

neonatal admissions annually, including an estimated 270 infants with a birthweight<1500 g.

Fluid and nutrition policy

The NNU had a standardised protocol for feeding and fluid administration for infants<1500 g. Intravenous fluids began with 75 ml//kg/day of 10% dextrose on the day of birth changing to 0.225% sodium chloride and 10% dextrose 48 h after birth. Enteral feeds were normally initiated at 25 ml/kg/day 24 h after birth using expressed breast milk (EBM). Feeds were progressively increased by 25 ml/kg/day depending on the tolerance and condition of the infant, as well as the availability of EBM from the mother. Feeds were advanced to a minimum of 150 ml/kg/day and increased beyond this by 25 ml/kg/day until the infant was documented to be gaining weight. Enteral feeds were initiated using nasogastric tube feeding and once full feeds were achieved, and weight gain was documented, the infant was slowly transitioned to cup and spoon-feeding as tolerated. Almost all infants were fed exclusively with EBM. Breastmilk fortifier and preterm formula were not available. A multivitamin supplement was initiated once the infant was on full feeds and iron supplementation was started at day 14.

Growth measurements

Birth weight was recorded on admission to the NNU by an electron weighing scale (SECA 354). Nude body weight was recorded daily until discharge. Weight-for-age Z-scores were calculated using the INTERGROWTH-21st (IG-21st) standard [24]. Small for gestational age (SGA) was defined as a weight-for-age Z-score at birth <-1.28 [25, 26]. Infant growth was monitored through daily weight measurements during the inpatient stay. PGF was determined by calculating the delta change in z-score based on the IG-21st standards, between admission (at birth) and the last review prior to inpatient discharge (Inpatient discharge ages varied for each infant depending on their clinical course). PGF was defined as a decline in weight Z score between birth and discharge of more than −1.28 [27].

Head circumference was measured weekly during the in-patient admission using a non-elastic tape measure held above the eyebrows and ears. Length was not recorded as part of routine clinical care and these data were not available for analysis.

Gestational age and birth weight

Gestational age was estimated using New Ballard Score examination [28]. Preterm infants were classified as extremely preterm (EPT, <28 weeks), very preterm (VPT, 28 to <32 weeks) and moderate to late preterm (32 to <37 weeks). Birth weight was classified as extremely low birth weight (ELBW, <1000 g) and very low birthweight (VLBW, 1000–1499 g) [29].

Risk factors

Data on sex, gestational age, multiple birth, place of birth, mode of delivery, anthropometry, feeding history, co-morbidities and neonatal clinical outcomes were extracted from the medical records. Data were extracted regarding the feeding including, the method of administration, the type of milk used, the age that feeding was initiated, and the age that full feeds were achieved.

Due to the limited access to suitable investigations, many of the co-morbidities diagnosed in this study relied on clinical features. The following definitions for co-morbidities were used:

- Necrotising enterocolitis (NEC): lethargy and temperature instability plus one or more of abdominal distension, vomiting, bloody stools, bilious or bloody aspirate.
- Respiratory distress syndrome (RDS): presence of tachypnoea, sub-costal recessions, and nasal flaring within the first 4 h after birth.
- Patent ductus arteriosus (PDA) was suspected in the presence of a characteristic murmur with bounding peripheral pulses after 72 h of age. The presence of a haemodynamically significant PDA (hsPDA) was confirmed on echocardiogram and defined by the presence of left atrium: aortic root diameter ≥ 1.5 in presence of continuous left to right shunting.
- Apnoea: a pause in breathing requiring stimulation or bag-mask ventilation.
- Feeding intolerance: frequent regurgitation or emesis of milk with or without abdominal distension.
- Sepsis: one or more of hypothermia not responsive to kangaroo care, fever > 37.5 °C, lethargy, tachypnoea, sub-costal recession, apnoea.
- Moderate hypothermia: <35.5 °C.
- Severe hypothermia: <32 °C.

Statistical analysis

Growth from birth to discharge was assessed as both a continuous variable (delta change Z-score value) and a binary variable (a negative change in Z-score of more than 1.28). Descriptive statistics and bivariable risk ratios were reported. We computed mean and median of continuous variables (as appropriate) and presented frequencies and percentages for categorical variables. In the bivariable risk ratio analysis, the following independent variables were included: sex, SGA, duration of bubble continuous positive airway pressure (bCPAP), RDS, PDA, NEC, jaundice requiring treatment, sepsis requiring second-line treatment, sepsis requiring third-line treatment,

hypothermia, time to first feed, time to achieve full feeds, and duration of hospitalisation. The risk ratios were adjusted for sex, SGA and hypothermia using the Cochran Mantel–Haenszel method. All analyses were carried out using Stata 17. We also modelled a linear regression (supplementary results) as a form of sensitivity analysis with the aim of exploring if the direction of coefficients and interpretation would remain consistent.

Results

A total of 274 infants <1500 g were admitted to the NNU during the study period (Fig. 1). Of these, 113 were excluded for the following reasons: 35 were admitted more than 24 h after birth; 78 had hospital stays of less than 7 days (including 5 who were discharged against medical advice and 73 who died within 7 days); and 57 were excluded due to other factors (9 with major congenital abnormalities, 22 with incomplete growth data, and 26 with unknown gestational age). This resulted in a final cohort of 104 infants, which included 89 (85.6%) very low birth weight (VLBW) infants and 15 (14.4%) extremely low birth weight (ELBW) infants, being included in the study.

Of the 104 infants, 57 were females (54.8%) and 47 males (45.2%). The mean birth weight was 1182 g (SD 18 g, 95% CI: 1140, 1210), and the birth weight ranged from 730 g to 1490 g. A large proportion, 43 infants (41.3%), were classified as SGA, with the likelihood of being SGA increasing by 2.13 times with each unit rise in gestational age (95% CI [1.52, 2.98]).

At admission, there were 104 participants with a mean IG-21st z-score of -0.90 (95% CI [-1.15, -0.66]). At inpatient discharge, for the 81 infants with available data, the mean z-score was −3.19 (95% CI [-3.58, -2.80]). The mean nadir weight for infants without postnatal growth failure (PGF) was 1115 g (95% CI [1039, 1191]), while for infants with PGF, it was 948 g (95% CI [910, 986]). The mean time to reach nadir weight was 8.3 days (95% CI [7.3, 9.2]). The mean duration of inpatient hospitalization was 11.0 days (95% CI [9.0, 13.0]) for those without PGF and 29.3 days (95% CI [24.5, 34.1]) for those with PGF. The mean time to regain birth weight was reported in only 66 participants due to deaths in the cohort ($n=17$) and missing data ($n=21$). Among those without PGF, the mean time to regain birth weight was 19.2 days (95% CI [11.7, 26.6]), while in those with PGF, it was 26.4 days (95% CI [22.8, 30.0]).

For the infants who experienced weight gain, the mean growth velocity was 5.2 g/day (95% CI [3.9, 6.4]). In contrast, those who experienced weight loss had a mean growth velocity of -12.0 g/day (95% CI [-14.4, -9.6]). Infants without PGF had a mean percentage weight loss of -5.2% (95% CI [-9.8, -0.5]), whereas infants with PGF had a mean percentage weight loss of 4.0% (95% CI [-1.8, 9.8]).

Most infants, 64.4% ($n=67$), were born between 28 and 32 weeks of gestation. Additionally, those born between 32 and 37 weeks comprised 31.7% ($n=33$), while a smaller number, representing only 3.8% ($n=4$), were born before 28 weeks. Of the mothers, 4% were HIV positive ($n=15$), 53.8% were HIV negative ($n=56$), and the status of 31.8% mothers was unknown ($n=33$). Feeding practices primarily involved nasogastric tubes (NGT), used in 74.0% infants ($n=77$), and mother's own milk was the primary type of milk provided, utilised for 95.2% infants ($n=99$). The mean age to achieve a feeding volume of 150 ml/kg/day was 8.2 days (SD 2.5). The patient characteristics are described in Table 1.

Risk factors for postnatal growth failure

We identified several statistically significant risk factors for PGF among the 104 infants. Infants with SGA had a higher risk of PGF compared to those without SGA (cRR 1.25, 95% CI [1.01, 1.53], p value 0.04). Additionally, infants who required bCPAP for >7 days had a higher risk of PGF (aRR 1.35, 95% CI [1.10, 1.66], p value 0.33).

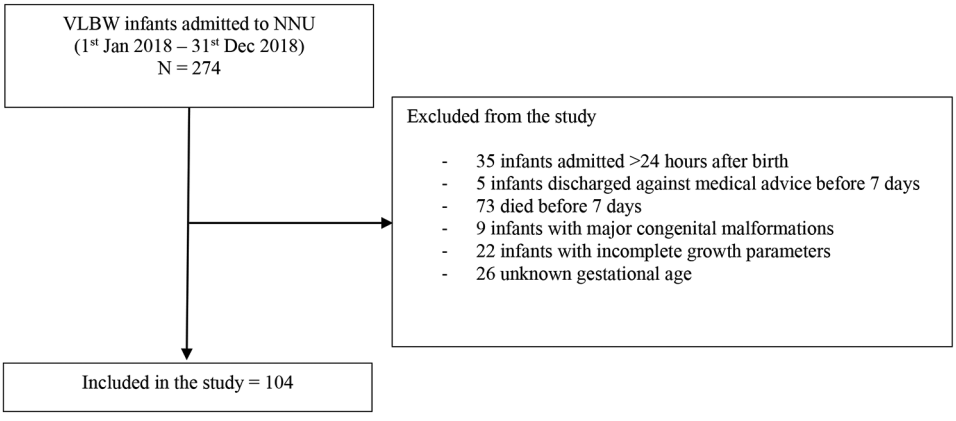

Fig. 1 Flow chart of study participants

Table 1 Patient characteristics of <1500 g infants admitted to neonatal unit during the study period

Characteristic (*N* = 104)	*N* (%)
Maternal HIV serostatus	
Negative	56 (53.8)
Positive	15 (14.4)
Unknown	33 (31.8)
Birth	
Single	69 (66.3)
Twin	31(29.8)
Triplet	4 (3.8)
Place of delivery	
In-born	55 (52.9)
Out-born	
District hospital	5 (4.8)
Health centre	25 (24.0)
Private clinic	14 (13.5)
Home	1 (1.0)
On the way to hospital	4 (3.8)
Mode of delivery	
SVD	86 (82.7)
Breech	1 (1.0)
Elective caesarean section	2 (1.9)
Emergency caesarean section	12 (11.5)
Unknown	3 (2.9)
Sex	
Male	47 (45.2)
Female	57 (54.8)
Birthweight (g)	
Mean (SD)	1182 (18)
Range (min, max)	730–1490
1000–1499 g	89 (85.6)
<1000 g	15 (14.4)
Gestational age at admission	
<28 weeks	4 (3.8)
28–32 weeks	67 (64.4)
32-<37 weeks	33 (31.7)
Head circumference (cm)	
Mean (SD)	26.5 (1.5)
Range	22.0–29.5
< -2SD for gestational age (microcephaly), n (%)	17 (16.3)
Admission observations	
Temperature (°C), Mean (SD)	34.8 (1.4)
Range of temperature (°C)	< 32.0–37.0
Heart rate (beats per minute), Mean (SD)	132 (22)
Oxygen saturations (%), Mean (SD)	86 (13)
Maximum respiratory support provided during admission to NNU	
No respiratory support provided	27 (26.0)
Free flow oxygen only	20 (19.2)
bCPAP	57 (54.8)
Co-morbidities diagnosed during admission to NNU	
RDS	61 (58.7)
Apnoea	32 (30.8)
NEC	9 (8.7)
Haemodynamically significant PDA	31 (29.8)
Anaemia requiring transfusion	12 (11.5)
Sepsis requiring 2nd line Antibiotics	52 (50.0)
Sepsis requiring 3rd line Antibiotics	20 (19.2)
Moderate hypothermia at admission (< 35.5 °C)	92 (88.4)
Severe hypothermia at admission (< 32.0 °C)	3 (3.12)
Feeds	
Initial method of feeding	
Cup and spoon	27 (26.0)
NGT	77 (74.0)
Median age to initiate enteral feeds (IQR)	2.0 (2.0, 3.0)
Mean age to achieve 150 ml/kg/day (SD)	8.2 (2.5)
Feeding intolerance documented	31 (29.8)
Type of milk given	
Mothers own milk	99 (95.2)
Donor milk	4 (3.8)
Formula milk	1 (1.0)
In-patient outcome	
Survived	81 (77.9)
Died	17 (16.3)
Self-discharged	6 (5.8)

Bubble Continuous Positive Airways Pressure (bCPAP), Nasogastric tube (NGT), Respiratory distress syndrome (RDS), Patent ductus arteriosus (PDA), Necrotizing enterocolitis (NEC)

Infants with RDS were also at a higher risk of PGF (aRR 1.30, 95% CI [1.01, 1.67], p value 0.88). Furthermore, infants who required second-line antibiotics for sepsis had a higher risk of PGF (aRR 1.58, 95% CI [1.22, 2.04] p value 0.09), as did those who required third-line antibiotics (aRR 1.46, 95% CI [1.20, 1.77], p value 0.08). Infants who took>7 days to achieve full feeds of 150 ml/kg/day had a higher risk of PGF (aRR 1.30, 95%CI [1.01, 1.66], p value 0.29). Infants with PGF also had a longer duration of hospitalisation compared to those without PGF (aRR 1.85, 95% CI [1.31, 2.61], p value 0.32). The risk factors are described in Table 2.

Discussion

We found a high rate of 75.9% of PGF during inpatient hospitalisation of <1500 g infants in a level II neonatal unit. The study revealed several significant risk factors associated with PGF. Notably, infants with SGA demonstrated a 1.25-fold increased risk of PGF, while those affected by RDS exhibited a 1.36-fold higher risk.

Additionally, prolonged duration of bCPAP use was associated with an increased risk of PGF (aRR 1.36), while sepsis requiring second-line treatment had an increased risk (aRR 1.55), and sepsis requiring third-line treatment also showed a higher risk (aRR 1.49). Delayed achievement of full feeds (aRR 1.32) and extended

Table 2 Risk factors associated with postnatal growth failure during inpatient hospitalisation

Risk factor	*N* = 104 (%)	Postnatal Growth failure (Inpatient)		Bivariable cRR (95% CI)	aRR[#] (95% CI)
		No	Yes		
Sex					
Male	47 (45.2)	8 (32)	39 (49.4)	1	-
Female	57 (54.8)	17 (68)	40 (50.6)	0.82 (0.64, 1.05)	-
SGA (z-score<-1.28 at birth)					
No	61 (58.7)	19 (76.0)	42 (53.2)	1	-
Yes	43 (41.3)	6 (24.0)	37 (46.8)	1.25 (1.01, 1.53)	-
Hypothermia < 35.5 °C					
No	9 (8.7)	4 (16.0)	5 (6.3)	1	-
Yes	95 (91.3)	21 (84.0)	74 (93.7)	1.40 (0.77, 2.54)	-
Duration of bCPAP > 7 days					
No	69 (66.3)	22 (88.0)	47 (59.50)	1	1
Yes	35 (33.7)	3 (12.0)	32 (40.5)	1.34 (1.11, 1.62)	1.35 (1.10,1.66)
RDS					
No	43 (41.3)	16 (64.0)	27 (34.2)	1	1
Yes	61 (58.7)	9 (36.0)	52 (65.8)	1.36 (1.05, 1.74)	1.29 (1.01. 1.67)
PDA					
No	73 (70.2)	20 (80.0)	53 (67.1)	1	1
Yes	31 (29.8)	5 (20.0)	26 (32.9)	1.16 (0.94,1.42)	1.15 (0.92, 1.44)
NEC					
No	95 (91.3)	24 (96.0)	71 (89.9)	1	1
Yes	9 (8.7)	1 (4.0)	8 (10.1)	1.19 (0.92, 1.54)	1.16 (0.89, 1.52)
Jaundice requiring treatment					
No	10 (9.6)	4 (16.0)	6 (7.6)	1	1
Yes	94 (90.40)	21 (84.0)	73 (92.4)	1.29 (0.77, 2.17)	1.32 (0.79, 2.19)
Sepsis requiring second line					
No	52 (50.0)	21 (84.0)	31 (39.2)	1	1
Yes	52 (50.0)	4 (16.0)	48 (60.8)	1.55 (1.22, 1.96)	1.58 (1.22, 2.04)
Sepsis requiring third line					
No	84 (80.8)	25 (100.0)	59 (74.7)	1	1
Yes	20 (19.2)	0 (0.0)	20 (25.3)	1.42 (1.24, 1.64)	1.46 (1.20, 1.77)
Time to first feed > 24 h					
No	61 (58.7)	17 (68.0)	44 (55.7)	1	1
Yes	43 (41.3)	8 (32.0)	35 (44.3)	1.13 (0.91, 1.39)	1.17 (0.94, 1.45)
Time to achieve full feeds (150 ml/kg/day) > 7days*					
No	49 (51.04)	18(85.71)	31 (41.33)	1	1
Yes	47 (48.96)	3(14.29)	44 (58.67)	1.37 (1.08, 1.74)	1.29 (1.01, 1.67)
Duration of hospitalisation					
< 14 days	39 (37.50)	19 (76.0)	20 (25.3)	1	1
> 14 days	65 (62.5)	6 (24.0)	59 (74.7)	1.77 (1.29, 2.43)	1.85 (1.31, 2.61)
Outcome					
Alive	87(83.65)	22 (88.0)	65 (82.28)	1	1
Dead	17 (16.35)	3 (12.0)	14 (17.72)	1.09 (0.85,1.41)	1.04 (0.82, 1.33)

*Missing data for 8 participants; crude risk ratio, cRR; adjusted risk ratio, aRR, [#]The risk ratios were adjusted for sex and SGA using the Cochran Mantel–Haenszel method

hospitalization (aRR 1.78) were also independently associated with elevated risks of PGF.

Growth outcomes: insights from low-resource and high-resource settings

Our findings align with existing research from various regions, highlighting similar risk factors. In Taiwan, risk factors such as being SGA or ELBW, and having extrauterine growth retardation (EUGR) at discharge were identified as significant predictors of post-discharge growth retardation [30], closely mirroring the prolonged hospitalization and delayed feeding initiation observed in our cohort. Studies from Uganda and Indonesia further support these findings with a PGF prevalence of

36.4% and 50%, and identifying delayed initiation of enteral feeds, the presence of sepsis, and a history of invasive ventilation as critical factors influencing PGF [5, 31]. In Uganda, particularly, the timing of the first feed and the duration of hospitalization have been highlighted as pivotal in determining growth outcomes, with early feeding and shorter hospital stays being crucial for promoting recovery and growth. While the risk factors for PGF may be similar across the globe, the ability to effectively address these risks is often shaped by the differences in healthcare resources, infrastructure, and systemic support available in various regions. In high-resource settings, patterns of growth in preterm infants have changed dramatically with advances in medical and nutritional care, which often involves a combination of total parenteral and supplementary enteral nutrition [33–35]. Research across several of these settings observed that rates of growth failure have declined in the past decade [35]. Preterm infants in high-resource settings now regain their birth weight sooner and experience higher rates of weight gain. For instance, a study in California found that from 2005 to 2012, the odds of a weight Z-score decrease by more than 1 during hospital admission dropped from 47 to 38%, and the likelihood of being discharged below the 10th weight-for-age centile also decreased [36], reflecting significant improvements in growth outcomes over time. Additionally, in Israel, the odds of severe PGF decreased by 46% and mild PGF by 32% among VLBW infants with major neonatal morbidities born between 2014 and 2018 compared to those born from 2009 to 2013. Similarly, infants without morbidities saw a 38% reduction in severe PGF and a 29% reduction in mild PGF during the same period [37], revealing an improvement in growth velocity and postnatal growth failure (PGF) in contrast to our study which observed slower growth, a longer time to regain birth weight, and higher PGF rates.

PGF still poses a substantial challenge for infants weighing<1500 g, especially in low-resource settings, where access to parenteral nutrition and breastmilk fortifiers is limited. In such settings, the primary source of nutrition for these infants is often only the mother's own milk, with few alternatives available. A prospective study from India on VLBW infants, who received enteral nutrition supplemented with human milk fortifiers and parenteral nutrition, reported a mean weight gain of 22.58 g/day, indicating steady growth during hospitalization [38]. In contrast, our study found a significantly lower mean growth velocity, with infants gaining only 5.2 g/day and those experiencing weight loss showing a mean growth velocity of -12.0 g/day. This study also noted that many VLBW infants did not achieve intrauterine growth rates, particularly among SGA infants, leading to PGF. Similarly, our study identified a high prevalence of PGF, with 75.9% of infants experiencing growth failure at discharge and a 1.25 times higher likelihood of PGF among those who were SGA. Additionally, a retrospective study from 2018, in a tertiary care centre in India found that unfortified breast milk can support the recommended growth rate when provided at higher feeding volumes of 220 ml/kg/day [39], achieving a satisfactory growth rate and quicker time to regain birth weight. In contrast, our study reported slower growth, a longer time to regain birth weight, and a higher incidence of PGF. In our study, we followed unit protocols by monitoring feeds up to 150 ml/kg/day but did not document any further increases in feeding volume during the inpatient stay. This conservative approach differed from the more aggressive feeding practices outlined in the 2018 study. The findings from both Indian studies suggest that more intensive feeding strategies, including higher feeding volumes and nutritional supplementation, even within resource-limited settings, could potentially lead to better growth outcomes. However, further research is needed in our context to explore the feasibility and impact of these approaches.

Nutritional strategies and supportive care for preventing pgf in preterm infants

Effective nutritional care during the neonatal period is crucial for achieving optimal outcomes and minimising the risk of both short-term and long-term adverse effects. The risk of PGF and postnatal malnutrition in these vulnerable infants arises from several factors, including limited nutrient reserves at birth, underdeveloped organs, diminished nutrient absorption capabilities, underlying health conditions, the accurate identification of malnutrition, and the timing of appropriate nutrient provision, leading to suboptimal growth or even postnatal growth failure [40, 41]. The prevention of PGF is vital to prevent potential long-term consequences, including suboptimal brain development due to undernutrition and impaired neurodevelopment [42, 43]. Also, the study identified worrying clinical status of referred infants such as hypothermia at admission. Kangaroo Mother Care (KMC) is recommended by the WHO for early and prolonged use in preterm and low-birth-weight infants [44]. Research shows that KMC reduces the incidence of nosocomial sepsis and enhances vital sign stability, including temperature regulation and weight gain [45]. A widescale implementation of KMC is needed as an effective, low-cost approach. There is an urgent need to improve pre-referral care and practices for these vulnerable infants. A widescale implementation of KMC is essential, as it is one of the urgent needs to improve pre-referral care and practices for vulnerable infants, alongside supportive nutritional practices, and effective management of early preterm complications to prevent PGF.

Controversies in neonatal practice

The definition and assessment of PGF are subjects of ongoing debate in neonatal practice, particularly due to the variability in percentile cut-offs, z-score thresholds, and timing of measurements [46]. These inconsistencies make it challenging to identify and compare PGF across different settings. Growth charts such as the Fenton and IG-21st further illustrate this issue; although both classify SGA infants at birth similarly, they differ significantly in reporting the prevalence of growth failure. The Fenton chart often indicates a higher prevalence of growth failure, potentially prompting more aggressive nutritional interventions that may carry long-term health risks, such as metabolic syndrome. Conversely, the IG-21st chart, developed using a healthier and more diverse preterm cohort, appears to be more closely associated with poor neurodevelopmental outcomes, possibly offering a more accurate reflection of optimal postnatal growth [47]. These differences raise critical questions about which growth assessment tool should be adopted in clinical practice, as each can significantly influence management strategies for preterm infants and their long-term health trajectories. In our study, we utilized the IG-21st standards and defined PGF as a decline in weight Z-score of more than −1.28. The choice was influenced by the characteristics of our population, the clinical relevance of this threshold in predicting adverse outcomes, and the need for standardized measures that facilitate comparison with other comparable research in similar settings.

Limitations

The study had several limitations, such as a small sample size which reduces its statistical power and generalisability. The single-centre design might have introduced selection bias; furthermore, the retrospective nature of the study resulted in excluding some participants due to incomplete data and limited accuracy due to incomplete data on variables that may confound the findings. Finally, the duration of hospitalisation may have been a limitation for longitudinal growth follow-up in the early postnatal period, as more than a third of the infants spent less than two weeks in the hospital, potentially affecting the assessment of these outcomes.

Future directions

In low-resource settings like Uganda, where access to specialised nutritional support may be limited, collaborative and innovative strategies are needed to prevent PGF in VLBW infants.

Future research should focus on evaluating novel and innovative approaches such as hospital-based lactational support; low-cost human milk banks, standardised growth monitoring; and educational and supportive programs on optimal breastfeeding practices and early child development. In addition, data are needed on the body composition of these VLBW infants and their long-term neurodevelopmental outcomes. Together this will inform contextually relevant evidence-based practices and policies aimed at reducing the burden of PGF in this vulnerable population.

Conclusion

PGF was common among infants<1500 g in this hospitalised cohort who were primarily fed on their mother's own milk. Urgent action is needed to enhance postnatal growth in this vulnerable patient group. Future research should focus on exploring multidisciplinary interventions that can improve growth outcomes in this population and understanding the long-term implications and need for care for these infants.

Abbreviations

bCPAP	Bubble continuous positive airway pressure
EBM	Expressed breastmilk
EPT	Extreme Preterm
hsPDA	hemodynamically significant patent ductus arteriosus
HIV	Human Immunodeficiency Virus
IG-21st	INTERGROWTH 21st growth standards
LBW	Low Birth Weight
NEC	Necrotizing enterocolitis
NGT	Nasogastric tube
NNU	Neonatal Unit
NMR	Neonatal Mortality Rate
PDA	Patent Ductus Arteriosus
PGF	Postnatal Growth Failure
RDS	Respiratory Distress Syndrome
SGA	Small for gestational age
VLBW	Very Low Birth Weight
VPT	Very Preterm

Supplementary Information

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Supplementary Material 1: Supplement 1. Linear regression: Risk factors associated with postnatal growth failure during inpatient hospitalization.

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Author contributions

NRAO: Study design, processing of ethical approvals, data collection, project administration, data analysis, manuscript writing for publication. KB: Primary mentorship, project administration, study design conceptualization, data analysis, revision of the manuscript. IMSE: Mentorship and supervision, data analysis, drafting and revision of the manuscript. POO: Mentorship, co-supervision, resources, and revision of manuscript. FO: Data analysis and revision of manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This retrospective observational study received approval from Mbale Regional Referral Hospital Research and Ethics Committee (MRRH REC 0041/2019) and registered with the Uganda National Council of Science and Technology (UNCST HS3295ES) and Regional Committee for Medical Research Ethics Western Norway (REK West 634003). A waiver for informed consent was approved by the Mbale Regional Referral Hospital Research and Ethics Committee.

Consent for publication
Parental consent was not required as the study was classified as an audit.

Competing interests
The authors declare no competing interests.

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