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Pressure Ulcers in the Hospitalized Neonate: Rates and Risk Factors

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Pressure ulcers (PU) are serious, reportable events causing pain, infection and prolonged hospitalization, particularly among critically ill patients. The literature on PUs in neonates is limited. The objective was to determine the etiology, severity and influence of gestational age on PUs among hospitalized infants. A two-year prospective study was conducted among 741 neonatal intensive care patients over 31,643 patient-days. Risk factors were determined by comparing the characteristics of infants who developed PUs with those who did not. There were 1.5 PUs per 1000 patient days with 1.0 PU per 1000 days in premature infants and 2.7 per 1000 days in term infants. The number of PUs associated with devices was nearly 80% overall and over 90% in premature infants. Infants with PUs had longer hospitalizations and weighed more than those who did not. Infants with device-related PUs were younger, of lower gestational age and developed the PU earlier than patients with PUs due to conventional pressure. The time to PU development was longer in prematurely born versus term infants. Hospitalized neonates are susceptible to device-related injury and the rate of stage II injury is high. Strategies for early detection and mitigation of device-related injury are essential to prevent PUs.

Hospitalized neonates are at risk for pressure ulcers (PUs) due to immature skin, compromised perfusion, decreased mobility, altered neurological responsiveness, fluid retention, moisture, and medical devices[1]. Premature infants have an underdeveloped epidermal barrier with only a few cornified layers. The dermis is deficient in structural proteins and easily torn[2]. They are at risk for increased permeability to exogenous materials, additional skin damage, and infection[3,4]. Skin barrier formation is rapid once very premature infants are exposed to a dry environment[5–7], although one month later it is not fully competent[8]. The timeline to full functional maturity in premature infants is currently not well defined, although it may be as long as 9 weeks postnatal age[5,8–10] and longer for complete acid mantle formation[11].

Pressure ulcers (PUs) can develop from the surface or from below, at the level of muscle and dermal tissue interaction and compression[12,13]. Unrelieved pressure can lead to tissue injury particularly when ischemia/reperfusion cycles are repeated. PUs are classified by the depth and severity of tissue injury. Stage I is non-blanchable erythematous skin that may be painful, soft, warmer or cooler than adjacent tissue. Stage II has partial dermal loss, e.g. shallow open ulcer or an intact blister. Stage III has dermal loss wherein subdermal elements are visualized. Stage IV ulcers are full thickness tissue loss with exposed bone, tendon or muscle. Unstageable ulcers are full thickness wounds covered by slough and/or eschar. Deep tissue injuries (DTI) have grossly intact skin with obvious underlying tissue injury related to pressure[14]. Stage III and IV PUs are serious reportable events, considered 'never events' by several national benchmarking organizations. The incidence is higher in critically ill patients[15] with increased pain, infection rate and prolonged hospitalization[16]. Over 70% of adult PUs are "conventional" ulcers from pressure over bony prominences, e.g. sacrum, shoulder and heels[17,18]. Up to 34% are associated with medical devices, e.g., nasal cannulas, facemasks[19,20].

PUs are relatively well studied in adults. The emphasis on preventing serious harm has prompted evaluation in pediatric patients. The incidence in the intensive care setting ranges from 7.3%[21] to 26.7%[22–25] when all stages are included. Pediatric studies report prevalence between 1.6%[26]and 13.4%[27] and there is variability in how PUs due to devices are counted.

The literature in premature and term neonates is sparse, due to an incomplete understanding of neonatal skin physiology[28–30]. Both conventional and device-related PUs have been reported[21,22,31,32]. The objective of this research was to determine the incidence and severity of PUs and the influence of gestational age among neonatal intensive care patients. We identified risk factors for pressure ulcer (PU) development by comparing the demographic characteristics of patients who developed PUs to those who did not. We classified the PUs by cause as (1)

conventional caused by pressure over bony prominences or (2) device-related cause by pressure on the tissue due to a medical device, e.g., face mask, line hub, pulse oximeter probe.

Methods

Setting. The prospective study was conducted at Cincinnati Children's Hospital Medical Center, a 598-bed free standing quaternary care academic facility. The 59-bed level III neonatal intensive care unit (NICU) treats premature and term infants who require surgery, have complex conditions or require specific diagnostic procedures. Patients were evaluated from September 2007 – October 2009. The Institutional Review Board of Cincinnati Children's Hospital Medical Center approved the study and waived the requirements to obtain written parental permission. The study was conducted in accordance with international and institutional guidelines for research involving human subjects, in accordance with the Declaration of Helsinki.

Data Collection. Designated nursing staff (skin champions) examined all inpatients from head to toe at admission and during hospitalization on one day every two weeks. They received training on PU physiology, skin evaluation and data collection. The skin, including areas under devices, was examined for evidence of PUs. PUs that occurred between evaluations were included in the count for the next period. PU stage was verified by a certified wound ostomy and continence nurse using the National Pressure Ulcer Advisory Panel staging system within 24 hours of discovery[14]. If necessary, the stage was changed at this verification. The cause was classified as conventional pressure or device-related, i.e., the PU could be directly attributed to pressure from use of a device. New PUs occurring after admission[33] were counted and reported as rate, i.e., number per 1000 patient days, calculated from the length of stay summed for all evaluated NICU patients, as used by the Institute for Healthcare Improvement[34]. This method accounts for varying lengths of stay. PUs were evaluated at least every 12 hours after discovery, treated and followed until resolution.

Statistical Analysis. The characteristics of patients with and without PUs were compared using univariate general linear models (GLM) with significance levels of $p < 0.05$ (SPSS, IBM Corporation, Somers, NY, USA). Patients were stratified as premature ($<$ 37 weeks of gestation) or term ($\geq$ 37 weeks of gestation) based on weeks of gestation. Statistical comparisons for PU severity, cause and demographic features were made by group (premature, term) using GLM procedures. No other independent factors were included in the model. Group comparison of PU rates were made using z-test procedures ($p < 0.05$).

Results

Neonatal PU Incidence. A total of 741 unique neonates over 31,643 patient days were evaluated (Table 1). Twenty-eight patients developed one or more PUs. Neonates with PUs were hospitalized for longer than infants without PUs ($p < 0.05$) but the groups did not differ for weeks of gestation or birth weight. There were 49 PUs among 28 unique patients for 1.5 PUs per 1000 patient days. There were 12.2% stage I PUs, 65.3% stage II and 22.4% combined stage III, unstageable and deep tissue injury. There were no stage IV ulcers. Thirty nine PUs were due to pressure from medical devices (79.6%) and ten (20.4%) were due to conventional pressure.

Infants with device-related injuries were younger when PUs developed than patients with conventional PUs (Table 2). Although the differences did not reach significance, infants with device PUs tended to develop them earlier, weigh less at the time of PU and have a lower birth weight than infants with conventional PUs.

Effect of Gestational Age on PU Development. There were 428 unique premature infants over 21,218 patient days and 313 unique term infants over 10,425 patient days. Of the unique premature infants, 232 were $<$ 33 weeks of gestation and 196 were $\geq$ 33 - $<$ 37 weeks of gestation.

Compared to premature infants without PUs, those with PUs had longer stays and were younger and weighed less at birth ($p < 0.05$) (Table 1). In contrast, the term infants with PUs and without PUs did not differ for any characteristics (Table 1). Fourteen premature infants developed one or more for a total of 21 PUs. Of these, 11 were $<$ 33 weeks of gestation and three were $\geq$ 33 - $<$ 37 weeks of gestation. Nine premature infants had one PU, three had 2 and two had 3 PUs during their hospitalizations. Fourteen term infants developed 28 PUs. Eight infants had one PU, two had 2, two had 3, one had 4 and one had 6 PUs.

Table 1 | Demographic Characteristics of Neonatal Patients With and Without PUs for All Infants and by Premature/Term Category. Values are reported as mean values ± standard error of the mean

	All Infants			Premature			Term		
	With PU	Without PU	F statistic p value	With PU	Without PU	F statistic p value	With PU	Without PU	F statistic p value
Unique patients	28	713	-	14	414	-	14	299	-
Total patient days	2598	29045	-	1870	19348	-	728	9697	-
Length of stay (days)	92.8 ± 9.2	42.5 ± 1.8	F = 28.9, p < 0.001	133.6 ± 13.4	49.5 ± 2.5	F= 38.0, p < 0.001	52.0 ± 11.5	33.1 ± 2.5	F 2.6, p = 0.110
Age at birth (wks)	33.1 ± 0.9	34.3 ± 0.2	F = 1.6, p = 0.203	28.4 ± 1.0	31.3 ± 0.2	F = 8.2, p = 0.004	37.8 ± 0.3	38.3 ± 0.1	F = 2.3, p = 0.132
Weight at birth (g)	2143 ± 202	2340 ± 49	F = 0.8, p = 0.345	1135 ± 238	1805 ± 54	F = 7.5, p = 0.006	3152 ± 184	3111 ± 50	F = 0, p = 0.826

Table 2 | Characteristics of All Neonates with PU by Cause of Pressure. Values are reported as mean values ± standard error of the mean

	Device-Related Pressure	Conventional Pressure	F statistic, p value
number	39	10	–
Length of stay (days)	85.5 ± 11.2	82.9 ± 22.1	F = 0.0, p = 0.918
Time to PU (days)	35.8 ± 6.4	63.2 ± 12.3	F = 3.7, p = 0.006
Age at PU (wks)	39.4 ± 1.1	46.9 ± 2.0	F = 10.8, p = 0.002
Weight at PU (g)	3255 ± 206	4162 ± 406	F = 4.0, p = 0.052
Age at birth (wks)	33.0 ± 0.8	36.9 ± 1.6	F = 4.6, p = 0.037
Weight at birth (g)	2259 ± 215	3018 ± 402	F = 2.8, p = 0.103

Premature and Term PU Rates and Risk Factors. The 21 PUs over 21,218 premature patient days yielded a rate 1.0 PU per 1000 patient days. There were 28 PUs over 10,425 term patient for 2.7 PUs per 1000 patient days. The rate was lower for premature infants ($p < 0.05$). The distribution by PU severity was 14%, 72% and 14% for stages I, II, and III, respectively, for premature infants and 11%, 61% and 28% for stages I, II and III, respectively, for term infants. Devices accounted for 90.5% of the PUs in premature infants and 71.4% in term infants. Conventional pressure caused 9.5% of PUs in premature infants and 28.6% in term infants. The frequencies of stage III and conventional PUs were each higher in term infants ($p < 0.05$).

Premature infants with PUs had significantly longer time to PU development and length of hospitalization than term infants ($p < 0.05$) (Table 3, Figure 1). As expected, the premature infants weighed less at birth than the term infants ($p < 0.05$) (Table 3). However, *the two groups did not differ for age or for weight at the time of PU development* (Table 3). Of the 14 premature infants, only six were < 37 weeks of age (adjusted) when the PUs occurred. The times to PU development for the individual premature (n = 14) and term (n = 14) are shown in Figure 1.

The medical diagnoses, causes and locations for the 14 premature and 14 term infants with PUs are listed in Table 4. The diagnoses and clinical courses varied with respiratory or gastrointestinal diagnoses the majority in premature infants. Neurological diagnoses, e.g., hydrocephalus and hypoxic ischemic encephalopathy, and congenital diaphragmatic hernia were the majority in term infants. The latter reflects patients referred to our Fetal Care Center. Pulse oximeters, tracheostomies and face masks were among the specific devices.

Discussion

In this study of 741 hospitalized neonates we identified 1) a relatively low rate of 1.5 PUs per 1000 patient days, 2) a predominance (80%) due to medical devices, 3) a high rate of stage II injuries, 4) differential characteristics for infants with device versus pressure PUs, and 5) a lower rate for premature versus term infants. Infants with device-related PUs were younger, of lower gestational age and developed the PU earlier in their stay than patients with PUs due to conventional pressure. To our knowledge, this study is the first to examine the severity, potential causes, and the impact of gestational age on PUs in a large population of hospitalized neonates.

The time from birth to PU development was more variable in premature infants than term infants (Figure 1) but on average was significantly longer. A longer hospitalization could perhaps increase the potential for injury. However, devices such as tracheostomies were a consequence of prematurity with PU development later in the hospital stay (Table 4). Mothers of infants diagnosed prenatally with congenital diaphragmatic hernia are managed to deliver close to term, so the diagnosis in premature infants is uncommon. The infants are medically complex, immobile and may be cannulated for extracorporeal membrane oxygenation (ECMO). Repositioning to prevent occipital PUs is challenging.

The rate of 1.5 PUs per 1000 patient days was lower than at other institutions[35]. Among 81 infants over 1723 days in seven NICUs, the rate was 8%[36]. The infants were housed in incubators, in contrast to our study where all infants were included. The utilization of non-invasive ventilation (e.g., continuous positive airway pressure) was higher than in our NICU. Use of this intervention in neonates is increasing, a factor which may increase PU occurrence. Five of the 21 PUs in our premature patients occurred within the first seven days of hospitalization compared to 6 or 14 PUs in the multicenter NICU trial[36]. The ongoing patient assessments during our two year study focused staff attention on PUs, the importance of early detection and strategies to prevent them. We began daily head to toe skin assessments examined skin under medical devices every 12 hours and rotated sites of pulse oximeter placement. These factors may account for the overall low PU rate.

Our high rates of device related PUs differs from pediatric intensive care settings where 50–62% of patients had PUs from devices[23,37]. The rate is also in contrast to the adults where up to 34% are from devices (e.g., nasal cannulas, facemasks) and over 60% are from conventional pressure. Nearly a third of premature infants of 29–30 weeks of gestation using nasal prongs or nasal masks for continuous positive airway pressure (CPAP) treatment experienced nasal skin compromise[38]. Among neonates using CPAP, 42.5% developed nasal PUs[39]. Consistent with our findings, the neonates with PUs were of lower gestational age and birth weight, had longer hospitalizations and used CPAP for longer periods than neonates who did not develop PUs.

The high device rate in the present study may indicate a susceptibility to iatrogenic injury in the infant population, perhaps resulting from physiologic differences between adult and neonatal skin. Skin characteristics such as stratum corneum integrity, permeability,

Table 3 | Characteristics of Unique Infants with PUs by Gestational Age. Values are reported as mean values ± standard error of the mean

	Premature < 37 Weeks at Birth	Term ≥ 37 Weeks at Birth	F statistic, p value
Number	14	14	–
Time to PU (days)	61.1 ± 11.6	24.0 ± 11.6	5.1, p = 0.033
Length of stay (days)	133.6 ± 19.6	52.0 ± 19.6	8.6, p = 0.007
Age at PU (wks)	39.4 ± 1.9	41.7 ± 1.9	F = 0.8, p = 0.392
Weight at PU (g)	2867 ± 353	3669 ± 353	2.6, p = 0.121
Age at birth (wks)	28.4 ± 0.7	37.8 ± 0.7	92.4, p < 0.001
Weight at birth (g)	1184 ± 213	3152 ± 213	42.7, p < 0.001

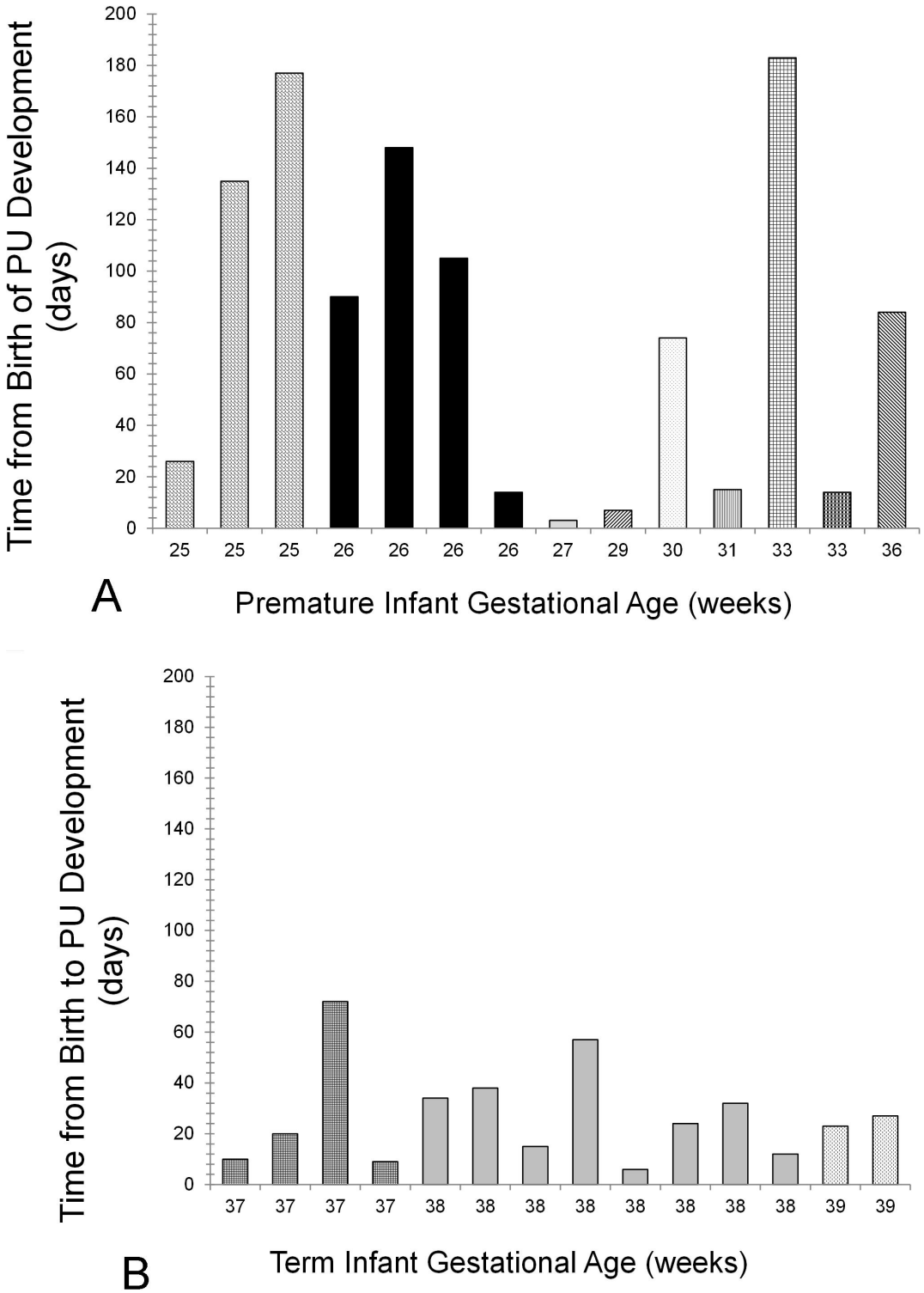

Figure 1 | Time to PU Development for Premature and Term Infants. The time to PU development is shown for the 14 premature (A) and 14 term (B) infants with PUs. The time was significantly longer for premature infants ($p < 0.05$) and may be related to the longer hospitalizations, particularly in extremely young patients who develop complications over time. The shorter time in term infants may reflect the acuity of these particular patients.

hydration, and fully formed dermal architecture vary substantially for months after birth in premature infants[2,11,28,30,40–42].

Our 65% frequency of stage II PUs is higher than in previous reports, e.g., 88% stage I from face-masks[39]. This is concerning, given a Minnesota state wide data analysis that device-related stage II ulcers advanced to more serious stage III and IV ulcers than conventional PUs[20]. The authors hypothesized that this progression was due to lack of adipose tissue to deflect pressure from devices in the affected regions. Patients with excess moisture were associated with more frequent and more severe ulcers (stage II)[43]. Stage II PUs may arise from device-related occlusion in combination with mechanical stress. The applied pressure results in periods of ischemia and epidermal damage[44]. This is exacerbated by cycles of ischemia-reperfusion with formation of cytotoxic free radicals, but damage occurs

Table 4 | Medical diagnoses, causes of device-related PUs, and locations for conventional PUs for the unique patients with PUs

Premature Infants (n = 14)			
Diagnosis	No.	Cause	Location
Respiratory distress and/or structural anomaly	5	Pulse oximeter, tracheostomy (2), Line hub, Catheter	Toe, neck, chin, head, arm
Prematurity	2	Identification band, Nasogastric tube	Foot, nare
Teratoma	1	Tracheostomy	Chest
Bowel perforation and/or resection	3	Endotracheal tube, Pulse oximeter, Line hub	Nose, foot, foot
Duodenal atresia	1	Tracheostomy ties	Chest
OEIS complex*	1	Conventional pressure	Heel
Term Infants (n = 14)			
Diagnosis	No.	Cause	Location
Neurological	5	EEG leads (2), CPAP mask, pulse oximeter	Back of head, near earlobe, face, nare, foot
Congenital diaphragmatic hernia	5	ECMO cannula, Nasojejunal tube, pulse oximeter	Neck, head, ear
Tracheoesophageal fistula	1	Chest tube	Chest
Respiratory	1	Line hub	Knuckle
Hematology	1	Cooling blanket	Buttocks
Bladder extrophy	1	Conventional pressure	Feet

*omphalocele-extrophy-imperforate anus-spinal defects.

after a single cycle with only two hours of ischemia[45]. Occlusion via continuous contact with the skin blocks normal transepidermal water loss. Increased moisture over time can cause maceration, disruption of the lipid bilayer structure, and increased permeability to exogenous agents[46–48]. Increased moisture results in a higher coefficient of friction[29,49], an effect that may enhance the effects of mechanical trauma[50]. Reduction of stage II device-associated ulcers will require identification of interventions to effectively mitigate the causes.

Some specific features of the present study are noteworthy as they address potential limitations of the results. Multiple statistical comparisons were made on the dataset in an attempt to discern population differences, perhaps resulting in an artificially high alpha error. The findings should be considered as exploratory. The higher number of PUs due to ECMO cannulas is likely due to the higher use of ECMO in term versus premature infants. The occurrence of PUs in patients with congenital diaphragmatic hernia reflects their high acuity, complex medical course, and the large number of patients treated through our comprehensive Fetal Care Center. While length of stay is a PU risk factor, the high variability limits its predictive value. Further study is needed to better identify neonates predisposed to PUs. We did not investigate patient-related factors that influence PU development including presence/extent of traumatic injury, blood loss anemia, hypoperfusion, hypovolemia, presence of sepsis, edema, fluid retention, length of immobolization, and hypermetabolism[51–53]. Examination of these factors, alone and in combination with others, is warranted to better predict PU risk in pediatrics. None the less, premature infants are at risk for PUs during hospitalization. Early detection and interventions to protect underdeveloped skin from trauma are essential for preventing serious harm in this population.

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Author contributions

M.V. and T.T. designed the research, interpreted the data and wrote the main manuscript. M.V. analyzed the data and prepared the tables. M.V. and T.T. reviewed the manuscript and approved it for submission.

Additional information

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