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Original Research Article

The impact of oscillometric blood pressure measurement on pain response in preterm neonates

Yerramada Narsimha Reddy[1], Surabhi H. Shamakrishna[2]*, Venkatesh Murthy Dammaningala Venkataramaiah[2], Rajanish Kanduri Vishwanatha Gupta[1]

[1]Department of Pediatrics, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India
[2]Department of Neonatology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India

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***Correspondence:**
Dr. Surabhi H. Shamakrishna,
E-mail: surabhi.hs90@gmail.com

ABSTRACT

Background: Preterm neonates admitted to neonatal intensive care unit (NICU) are subjected to numerous painful and potentially noxious procedures. Oscillometric blood pressure (BP) measurement, although classified as non-invasive, involves repeated application and inflation of a cuff on a fragile limb, and may elicit a significant pain response in this vulnerable population. The extent of this pain in preterm neonates, particularly in the Indian context, remains inadequately studied. Aim was to assess the pain response to non-invasive oscillometric BP measurement in preterm neonates using the premature infant pain profile-revised (PIPP-R).
Methods: A prospective observational study was conducted at the NICU of Rajarajeswari Medical College and Hospital, Bangalore, enrolling 50 preterm neonates (gestational age <36 weeks and post menstrual age <37 weeks). PIPP-R scores were recorded at three timepoints: baseline (T1), during BP measurement (T2), and 10 minutes after the procedure (T3). For within-group analysis, the Friedman test with post-hoc Wilcoxon signed-rank tests (Bonferroni correction) was used. Clinical characteristics were compared between neonates with pain and without pain using Mann-Whitney U and chi-square tests.
Results: Median PIPP-R scores were significantly higher during BP measurement (T2) compared to baseline (T1) and 10 minutes post-procedure (T3) (χ^2=38.99, p<0.001). Out of 50 neonates, forty two percent of neonates (n=21) had pain during the procedure. Neonates with pain had significantly lower gestational age, birth weight, post menstrual age. (p<0.05).
Conclusions: Oscillometric BP measurement causes clinically significant pain in a substantial proportion of preterm neonates, particularly those with lower gestational age and birth weight. Individualized monitoring strategies and non-pharmacological pain management should be considered in this population.

Keywords: Infant, Premature, Pain measurement, Blood pressure determination, Neonatal intensive care units, Premature infant pain profile, Pain, Procedural

INTRODUCTION

Preterm birth, which is defined as giving birth before 37 completed weeks of gestation, continues to be a major global cause of neonatal morbidity and mortality. India is one of the countries with the highest preterm birth rates in the world, with an estimated 13% preterm birth rate. In order to stabilise and sustain their developing organ systems, preterm neonates-especially those born at lower gestational ages or with very low birth weights-need specialised neonatal care and are often hospitalised to the NICU for extended periods of time.[1,2]

Preterm newborns are subjected to several diagnostic and therapeutic treatments every day while they are in the NICU. According to studies, a premature newborn may

have eight to seventeen unpleasant or stressful operations every day, which equates to hundreds of exposures during a normal NICU stay.[3] Untreated procedural pain in preterm newborns has far-reaching effects that go far beyond the first clinical encounter. The preterm brain is particularly sensitive to the effects of repetitive nociceptive stimulation at its most vulnerable stage of development and organization.[2,4]

Changes in pain sensitivity have been linked to repeated painful stimuli during this crucial time., abnormal neurodevelopmental trajectories, impaired cognitive and motor outcomes in childhood, and structural changes in the brain, including reduced cortical thickness in somatosensory areas and altered white matter organization. Furthermore, untreated pain in the neonate activates the hypothalamic-pituitary-adrenal axis, resulting in cortisol-mediated catabolic effects, disruption of sleep-wake cycles, and instability of vital parameters, all of which can have cascading effects on the preterm neonate's already precarious physiological homeostasis. The recognition of these long-term consequences has driven a paradigm shift in neonatal care, emphasizing the importance of systematic pain assessment and management as a core component of developmentally supportive NICU care.[5,6]

Non-invasive BP measurement is an indispensable component of routine hemodynamic monitoring in the NICU. Oscillometric BP measurement involves placement of an appropriately sized cuff around the upper arm or lower limb, followed by rapid inflation and controlled deflation while the device detects oscillations in arterial pressure. In preterm neonates, the limb circumferences are small, the skin is thin and delicate, and the subcutaneous tissue is minimal, rendering even the mechanical pressure of cuff inflation a potentially noxious mechanical stimulus.[7,8] A validated, context-sensitive, multidimensional pain assessment instrument designed especially for preterm and term infants is called the PIPP-R. In order to give a composite pain score, it takes into account gestational age as a contextual modifier and evaluates six behavioural and physiological signs, including brow bulge, eye squeeze, nasolabial furrow, heart rate, oxygen saturation, and sleep-wake state.[9]

The evolving recognition that non-invasive monitoring procedures can be painful prompted Aktas and colleagues to demonstrate that echocardiographic examination caused significant pain responses in preterm infants, as evidenced by significant rises in PIPP scores during the procedure.[10] Subsequently, Kavurt and colleagues in Turkey conducted the first dedicated prospective study examining oscillometric BP measurement as a pain stimulus using the PIPP-R, finding that 34% of preterm neonates with a gestational age under 34 weeks had PIPP-R scores ≥7 during the procedure, with pain being significantly more common among those with lower gestational ages.[11] In the Indian context, Ganguly and colleagues conducted a PIPP-based assessment of ten routine NICU procedures in a western Indian centre and reported a mean PIPP score of 4.5 for non-invasive BP measurement, underscoring that BP monitoring causes at least mild pain in Indian preterm neonates.[12]

Given the lack of South Indian data, the clinical significance of undertreated procedural pain in preterm neonates, and the universal practice of routine oscillometric BP measurement in all NICU settings, it is imperative to quantify the pain burden associated with this specific procedure in a South Indian preterm population. Thus, the current study was carried out to determine clinical predictors linked to a significant pain response and to evaluate the pain response to oscillometric BP measurement in preterm neonates admitted to the NICU of a tertiary care center in Bangalore using the PIPP-R scale.

METHODS

Study design and setting

Over the course of three months, this prospective observational research was carried out at the NICU of Rajarajeswari Medical College and Hospital in Bangalore, a tertiary care teaching facility. The Institutional Ethics Committee approved the research, and all enrolled infants' parents or legal guardians provided written informed permission.

Preterm neonates (gestational age <36 weeks and post menstrual age <37 weeks) admitted to the NICU, haemodynamically stable, requiring routine non-invasive BP monitoring, and whose parents provided written informed consent were enrolled in the study.

Neonates with major congenital anomalies (including congenital heart disease or chromosomal abnormalities), neurological conditions likely to alter pain response (grade III/IV intraventricular haemorrhage or hypoxic-ischaemic encephalopathy), or those who had received sedatives, opioids, or analgesics within 12 hours prior to the procedure were excluded. Neonates who had undergone any invasive procedure within same day preceding the observation, or those requiring respiratory support at the time of assessment, neonates with central or peripheral canula are also excluded.

Sample size

A sample size of 50 preterm neonates were enrolled in the study.

Procedure and data collection

Each enrolled neonate's baseline clinical and demographic information, such as gestational age, sex, method of delivery, birth weight, postnatal age at the time of the trial, and postmenstrual age (PMA), was documented at the time of recruitment along with 1-minute and 5-minute APGAR scores at birth.

Oscillometric BP measurement was performed using a standard, validated digital oscillometric device with an appropriately sized cuff applied to the upper arm as per standard NICU protocol.

PIPP-R

Pain was assessed using PIPP-R, a validated multidimensional behavioral and physiological pain scoring tool for preterm and term neonates. Behaviour state and gestational age are considered if subtotal score (facial indicators and physiological) is more than zero.

Scores were recorded at three pre-defined timepoints:

T1 (Baseline)

Before measurement of BP.

T2 (During)

During the oscillometric BP measurement.

T3 (Recovery)

Ten minutes after completion of the BP measurement.

A PIPP-R score of 0-6 was classified as no pain, 7-12 as moderate pain, and >12 as severe pain.

Table 1: Premature Infant Pain Profile-Revised (PIPP-R) scale.

Variables	0	1	2	3	Score
Gestational age (at that time in weeks)	≥36	32 to 35+6	28 to 31+5	≤28	
Behaviour	Awake/active	Awake/quiet	Sleep/active	Sleep/quiet	
Oxygen saturation	Decrease in 0% to 2.4%	Decrease in 2.4% to 4.9%	Decrease in 5% to 7.4%	Decrease in ≥7.5%	
Heart rate	Increase in 0 to 4 bpm	Increase in 5 to14 bpm	Increase in 15 to 24 bpm	Increase in ≥25 bpm	
Nasolabial fold	None, 0% to 9% of time (3 sec)	Minimum (10% to 39% of time (3 to <12 sec)	Moderate 40% to 69% of time (≥12 to <21 sec)	Maximum 70% of time or more (≥ 21 sec)	
Brow buldge	None, 0% to 9% of time (3 sec)	Minimum, (10% to 39% of time (3 to <12 sec)	Moderate 40% to 69 % of time (≥12 to <21 sec)	Maximum 70% of time or more (≥21 sec)	
Eye squeeze	None, 0% to 9% of time (3 sec)	Minimum, (10% to 39% of time (3 to <12 sec)	Moderate, 40% to 69% of time (≥12 to <21 sec)	Maximum, 70% of time or more (≥21 sec)	

Statistical analysis

SPSS version 23.0 was used to input and evaluate the data. The Shapiro-Wilk test was used to determine if continuous data were normal. PIPP-R scores are shown as mean±standard deviation and median (25^{th}-75^{th} interquartile range) since they were not normally distributed. The Friedman test was used to compare repeated PIPP-R values throughout the three timepoints. The Wilcoxon signed-rank test with Bonferroni correction was used for post-hoc pairwise comparisons (significance threshold: $p<0.017$ for three comparisons). The Mann-Whitney U test was used to assess continuous data for group comparisons between the pain and no-pain groups, and the Chi-square test or Fisher's exact test was used for categorical variables. For every group comparison, $p<0.05$ was deemed statistically significant.

RESULTS

Fifty preterm neonates were included throughout the research period. Of them, 22 (44%) were female and 28 (56%) were male. The median birth weight was 1810 gm (IQR: 1465-2315), and the median gestational age at delivery was 33.6 weeks (IQR: 32.6-35.3). At the time of examination, the median PMA was 35.1 weeks (IQR: 33.9-36.3) and the median postnatal age was 9 days (IQR: 7-15). Eighteen (36%) newborns were delivered vaginally, while thirty-two (64%) were delivered via lower segment caesarean section (LSCS). Table 2 provides a summary of the clinical features of the included neonates.

At baseline (T1), during oscillometric BP measurement (T2), and ten minutes after the procedure (T3), the PIPP-R score was measured. At baseline, none of the newborns had a PIPP-R score higher than zero. With a mean of 3.0±4.0, the median PIPP-R score during BP measurement was 0 (IQR: 0-7). Ten minutes following the procedure, the scores went back to 0 (IQR: 0-0).

PIPP-R ratings varied statistically significantly across the three time periods, according to the Friedman test ($\chi^2=38.99$, $p<0.001$). PIPP-R scores during BP measurement were significantly higher than baseline ($p<0.001$) and significantly higher than at 10 minutes

after the procedure (p<0.001), according to pairwise comparisons using the Wilcoxon signed-rank test with Bonferroni correction; scores at 10 minutes after were also significantly higher than at baseline (p=0.004), suggesting a brief but statistically significant pain response. Table 3 goes into depth about these results.

Of the 50 neonates, 21 (42%) recorded a PIPP-R score of ≥1 during BP measurement and were categorised as the pain group, while the remaining 29 (58%) with a score of 0 constituted the no-pain group. Neonates in the pain group had a significantly lower gestational age at birth (median 32.9 vs. 34.6 weeks; p=0.002) lower birth weight (median 1560 g vs. 1980 g; p=0.016), lower postnatal age at examination (median 11 vs. 8 days; p=0.013), lower post-menstrual age (median 33.9 vs. 36.0 weeks; p=0.002), lower current weight at examination (median 1400 g vs. 1900 g; p=0.028).

There was no significant difference between the two groups in terms of sex distribution, manner of delivery, or APGAR scores at one and five minutes (p>0.05). Table 4 provides a thorough comparison of the two groups' clinical features.

Among the 50 neonates, 29 (58%) recorded no pain (PIPP-R score=0) during oscillometric BP measurement. Of the remaining 21 neonates (42%) who experienced pain, 7 (14%) had mild pain (score 1-6), 12 (24%) had moderate pain (score 7-12), and 2 (4%) had severe pain (score >12). The distribution of PIPP-R score categories during BP measurement is illustrated in Figure 1.

The trend in mean PIPP-R scores across the three time periods is depicted in Figure 2. Ten neonates were found to have PIPP score above zero at the third assessment. The mean score was 0.0±0.0 at baseline, rose significantly to 3.0±4.0 during BP measurement, and subsequently declined to 0.7±1.5 at 10 minutes after the procedure. This pattern confirms transient yet statistically significant procedural pain response associated with oscillometric BP measurement in preterm neonates.

Table 2: Clinical characteristics of included infants.

Variables	Value [Median (IQR)]	Range
Gestational age at birth (in weeks)	33.6 (32.6-35.3)	28.4-36.4
Birth weight (gm)	1810 (1465-2315)	840-2750
Current weight at examination (gm)	1720 (1385-2220)	900-2640
Postnatal age at examination (in days)	9 (7-15)	4-30
Post-menstrual age at examination (in weeks)	35.1 (33.9-36.3)	31.9-36.9
APGAR score		
at 1 minute	6.5 (6.0-8.0)	4-9
at 5 minutes	8.0 (8.0-9.0)	6-10
Gender		
Male sex	28 (56%)	-
Female sex	22 (44%)	-
Mode of delivery		
LSCS	32 (64%)	-
Normal	18 (36%)	-

Table 3: PIPP-R scores at three time periods.

Variables	Baseline (T1)	During BP (T2)	10 min after (T3)	T1 vs T2, p value	T2 vs T3, p value	T1 vs T3, p value
Median (IQR)	0 (0-0)	0 (0-7)	0 (0-0)	<0.001*	<0.001*	0.004*
Mean±SD	0.0±0.0	3.0±4.0	0.7±1.5	-	-	-
Min-Max	0-0	0-13	0-5	-	-	-

*Friedman test: χ^2=38.99, p<0.001. Pairwise comparisons by Wilcoxon signed-rank test with Bonferroni correction (significance threshold p<0.017).

Table 4: Distribution of PIPP-R score categories during BP measurement.

PIPP-R category	N	Percentage
No pain (Score=0)	29	58.0%
Mild pain (Score 1-6)	7	14.0%
Moderate pain (Score 7-12)	12	24.0%
Severe pain (Score>12)	2	4.0%

*Statistically significant (p<0.017 after Bonferroni correction). All 50 neonates had PIPP-R score=0 at baseline.

Table 5: Comparison of clinical characteristics between infants with pain vs no pain during BP measurement.

Variables	Pain group, (n=21)	No pain group, (n=29)	P value
Gestational age at birth (in weeks), median (IQR)	32.9 (29.4-34.1)	34.6 (33.1-35.4)	0.002*
Birth weight (gm), median (IQR)	1560 (1100-2240)	1980 (1700-2320)	0.016*
Postnatal age at examination (days), median (IQR)	11 (8-20)	8 (6-11)	0.013*
Post-menstrual age at examination (in weeks), median (IQR)	33.9 (33.3-35.4)	36.0 (34.4-36.4)	0.002*
Current weight at examination (gm), median (IQR)	1400 (1240-2030)	1900 (1640-2240)	0.028*
Gender			
Male	6 (42.9%)	22 (61.1%)	0.395
Female	8 (57.1%)	14 (38.9%)	0.395
Mode of delivery			
LSCS	13 (92.9%)	19 (52.8%)	0.020*
Normal	1 (7.1%)	17 (47.2%)	0.020*
APGAR score at 1 min, median (IQR)	6.0 (6.0-7.0)	7.0 (6.0-8.0)	0.301
APGAR score at 5 min, median (IQR)	8.0 (7.0-8.0)	8.0 (8.0-9.0)	0.085

*Statistically significant ($p<0.05$), data presented as median (25^{th}-75^{th} percentile IQR) for continuous variables.

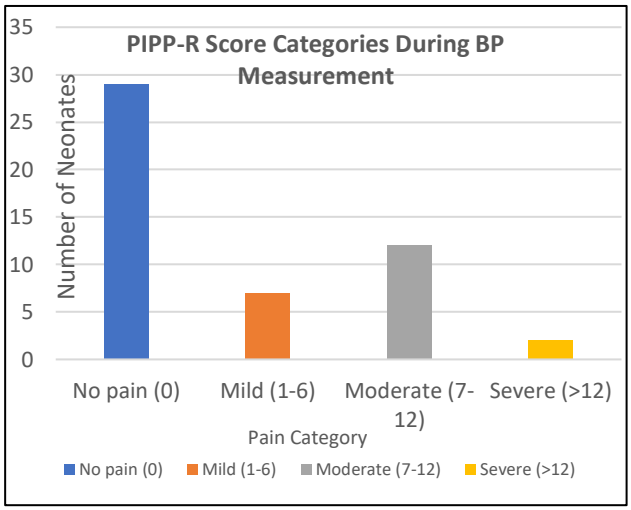

Figure 1: PIPP-R score categories during BP measurement.

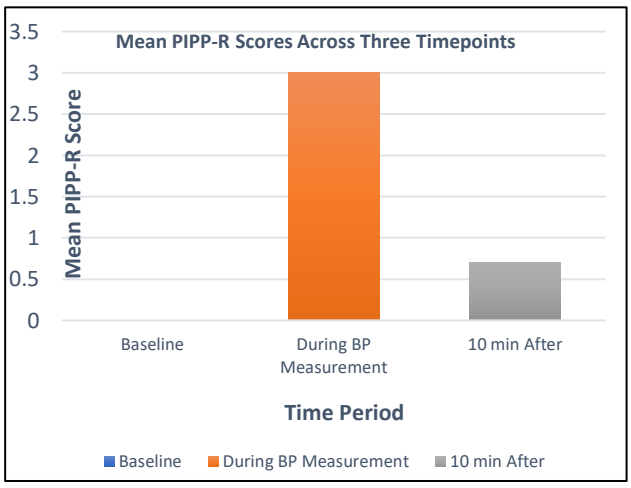

Figure 2: PIPP-R score distribution at three time periods.

DISCUSSION

Oscillometric BP measurement is an integral component of haemodynamic monitoring in the NICU, yet its potential to cause pain in preterm neonates has received limited attention in routine clinical practice.[10] The present study systematically assessed pain responses to this procedure using the PIPP-R in 50 preterm neonates at a tertiary care NICU in Bangalore.

The results of the present study closely parallel those of Kavurt et al who conducted the first dedicated prospective study on this subject in a Turkish cohort of 100 preterm neonates (GA<34 weeks, PMA<36 weeks), reporting a median PIPP-R of 5 (IQR 0-7) during BP measurement and a pain rate of 34% (PIPP-R≥7).[11] The marginally lower pain prevalence of 28% in the present cohort is likely attributable to the inclusion of a broader gestational age range (GA<36 weeks), encompassing more mature late preterm neonates who exhibit comparatively lower nociceptive sensitivity. The temporal pattern, with scores peaking during the procedure and returning to near-baseline within 10 minutes was identical in both studies, suggesting that BP measurement produces an acute, transient, but reproducible pain response.

Comparison with Indian data also demonstrates consistency. Ganguly et al assessed PIPP scores across ten routine NICU procedures in 132 neonates at a Gujarat tertiary centre and reported a mean PIPP score of 4.5 (SD=2.34) for non-invasive BP measurement, comparable to the mean PIPP-R of 3.0 (SD=4.0) in the present study. The slightly higher mean reported by Ganguly et al may reflect their lower gestational age threshold (>26 weeks), which included extremely preterm neonates with heightened pain sensitivity. Notably, Ganguly et al also observed that several routinely performed non-stressful procedures including weight and

temperature measurement generated unexpectedly high PIPP scores, collectively challenging the prevailing clinical assumption that non-invasive monitoring is inherently benign.[12]

The pain elicited by oscillometric BP measurement in the present study, however, was substantially lower in magnitude compared to that reported during echocardiographic examination. Ahsan et al reported a mean PIPP-R score of 8.18 (SD=2.6) during targeted neonatal echocardiography in 88 neonates at a Mumbai NICU, nearly three times the mean observed in the present study. Preterm neonates demonstrated significantly higher PIPP-R scores than term neonates in that study (8.76 vs. 6.81, $p<0.001$), consistent with the present study's finding that lower gestational age was the strongest independent predictor of pain during BP measurement.[13] The foundational demonstration that non-invasive diagnostic procedures can cause significant pain in preterm neonates was first provided by Aktas et al who documented significant NIPS score elevations during echocardiography in a Turkish NICU cohort, establishing the conceptual basis that has guided subsequent investigations including the present study.[10]

The significant associations between lower gestational age, lower birth weight, lower post-menstrual age, lower current weight, and pain response observed in the present study are well-corroborated by the existing literature. Shah et al in a prospective observational study at a Gujarat NICU demonstrated that preterm neonates had significantly higher PIPP-R scores than term neonates across six assessed procedures, and that small-for-date neonates were disproportionately sensitive, attributing this to the immaturity of descending inhibitory pain modulation pathways and a relative excess of excitatory neurotransmission in the underdeveloped neonatal brain.[14]

These pathophysiological mechanisms also explain the finding in the present study that neonates with higher postnatal age, who were by definition smaller and less mature in corrected age relative to procedure timing, had greater pain responses. The significant association with LSCS mode of delivery warrants further investigation, as this association has not been described in prior comparable studies and may reflect selection bias or differences in sedation exposure at delivery.

Chauhan et al in a randomised clinical trial evaluating analgesic interventions during heel prick in preterm neonates (GA 28-36 weeks) at a Vadodara NICU, demonstrated that baseline PIPP scores were higher in lower birth weight neonates, and that without analgesic intervention, PIPP scores rose significantly from baseline, reinforcing the need for routine pain management even for procedures perceived as minor.[15] Shinde et al at a Pune tertiary centre highlighted that a majority of NICU healthcare workers lacked formal training in neonatal pain assessment and did not routinely use validated pain scoring tools, contextualising why the pain associated with BP monitoring remains systematically underappreciated and to undertreated in the Indian NICUs.[16]

On a global scale, Cistone et al through a quality improvement initiative at a US NICU, specifically identified cuff BP measurements as a potentially noxious, cumulative stimulus in extreme preterm infants and demonstrated that reducing measurement frequency in haemodynamically stable infants was feasible and safe, recommending that future research correlate the quantity of BP measurements with long-term neurodevelopmental outcomes.[17] Luo et al in a large Chinese single-centre study of 957 neonates across 15 clinical NICU procedures using the NIPS advocated for systematic pre-procedural non-pharmacological analgesia for all procedures with a predictable pain profile.[18] Campbell-Yeo et al in a comprehensive practice update, provided robust evidence that untreated procedural pain in preterm neonates is associated with lasting adverse consequences including impaired cortical growth, altered functional brain connectivity, and epigenetic changes, underscoring that even mild procedural pain such as that from BP monitoring must not be disregarded.[4]

The primary limitations of the present study include its single-centre observational design, modest sample size, and the absence of long-term neurodevelopmental follow-up. The lack of an intervention arm means that the efficacy of analgesic measures during BP monitoring was not evaluated. However, the study carries important strengths: it is the first study from South India to specifically assess oscillometric BP measurement as a nociceptive stimulus using PIPP-R, utilising a standardized single-observer methodology that minimised inter-observer variability. Clinically, the results support the integration of non-pharmacological comfort interventions like facilitated tucking, oral sucrose, or non-nutritive sucking prior to BP measurement, all of which have been shown to be effective in lowering PIPP-R scores in preterm neonates, as demonstrated by earlier studies. They also support the individualisation of BP monitoring frequency in preterm neonates, especially those with lower gestational age.[19,20]

CONCLUSION

Oscillometric BP measurement causes clinically significant pain in a substantial proportion of preterm neonates, particularly those with lower gestational age, lower birth weight, and lower post-menstrual age at the time of measurement. Pain response is transient but reproducible, reinforcing the need to reconsider the classification of BP monitoring as a painless procedure. Routine implementation of validated pain assessment tools and evidence-based non-pharmacological analgesic measures prior to BP measurement should become an integral component of developmentally supportive NICU care.

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