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Original article

Determinants of Elevated Gentamicin Trough Concentrations among Neonates Receiving Once-Daily Therapy: A Prospective Cohort Study in Tanzania

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Abstract
Neonatal sepsis remains a major cause of morbidity and mortality, particularly in low-resource settings. Gentamicin is widely used for treatment; however, its narrow therapeutic index and variable neonatal pharmacokinetics increase the risk of accumulation and toxicity. Therapeutic drug monitoring is rarely available in Tanzania. Identifying factors associated with elevated gentamicin concentrations may support safer antibiotic use where therapeutic drug monitoring is unavailable. This study aimed to identify factors associated with elevated gentamicin trough concentrations among term neonates receiving once-daily intravenous gentamicin. This sub-study was nested within a prospective observational cohort evaluating the pharmacokinetics and safety of once-daily intravenous gentamicin at doses of 4 mg/kg and 5 mg/kg among term neonates with sepsis. A total of 250 neonates receiving gentamicin were included. Trough concentrations were measured at steady state, five minutes before the fourth dose. An elevated trough concentration was defined as >2 µg/mL. Factors associated with elevated trough concentrations were assessed using multivariable logistic regression, with adjusted odds ratios and 95% confidence intervals. Elevated trough concentrations occurred in 27.2% of neonates. Independent factors associated with elevated trough concentrations included age <7 days (adjusted odds ratio, 4.41; 95% confidence interval, 2.16–8.99), weight <2.5 kg (adjusted odds ratio, 2.10; 95% confidence interval, 1.20–3.68), non-weight-based dosing (fixed-dose administration) (adjusted odds ratio, 3.41; 95% confidence interval, 1.45–8.05), vomiting (adjusted odds ratio, 2.65; 95% confidence interval, 1.22–5.74), diarrhea (adjusted odds ratio, 8.26; 95% confidence interval, 2.98–22.89), inability to suck (adjusted odds ratio, 3.82; 95% confidence interval, 1.26–11.56), and high-normal baseline serum creatinine (>100 µmol/L within the laboratory reference range of 44.22 - 132.63 µmol/L) (adjusted odds ratio, 2.21; 95% confidence interval, 1.03–4.73). More than one-quarter of neonates receiving once-daily gentamicin had elevated trough concentrations. Clinical and dosing-related factors may help identify neonates at risk of gentamicin accumulation and support safer antibiotic use where therapeutic drug monitoring is unavailable.
Keywords. Gentamicin, Term Neonates, Trough Concentrations, Neonatal Sepsis, Therapeutic Drug Monitoring.

Introduction

Neonatal sepsis remains a leading cause of morbidity and mortality during the first month of life, particularly in low- and middle-income countries. Despite substantial global progress in reducing neonatal mortality, from 38 per 1,000 live births in 1990 to 17 per 1,000 in 2021, neonatal infections continue to account for a substantial proportion of neonatal deaths, with sepsis contributing approximately 30–50% of these deaths [1,2]. In Tanzania, neonatal mortality is estimated at 20 per 1,000 live births, with sepsis contributing approximately 29% of these deaths [3]. Beyond mortality, neonatal sepsis is associated with prolonged hospitalization, increased healthcare costs, and long-term complications among survivors. Therefore, timely initiation of effective antimicrobial therapy remains critical for improving neonatal outcomes.

Gentamicin, an aminoglycoside antibiotic, remains an important component of empirical treatment for neonatal sepsis because of its potent bactericidal activity and synergistic effects when combined with β-lactam antibiotics [4-6]. Its pharmacokinetic characteristics, including high water solubility, low protein binding (10–30%), extracellular distribution, and predominant renal elimination, make serum concentrations highly sensitive to neonatal physiological factors such as body weight, renal maturation, fluid distribution, and clinical condition [7-9]. Once-daily gentamicin dosing (4–5 mg/kg) is widely recommended because it optimizes concentration-dependent bacterial killing, utilizes the post-antibiotic effect, and reduces the risk of toxicity [10,11]. However, gentamicin has a narrow therapeutic index; inadequate exposure may compromise treatment effectiveness, whereas excessive exposure may increase the risk of adverse effects, particularly nephrotoxicity and ototoxicity.

Despite the advantages of once-daily dosing, gentamicin exposure remains highly variable during the neonatal period because of rapid physiological changes affecting drug distribution and elimination. In term neonates, reduced renal clearance may prolong the gentamicin half-life (6–12 hours), resulting in variable peak and trough concentrations [7–9]. Therapeutic peak concentrations of 5–12 µg/mL are generally targeted to achieve effective bacterial killing, whereas trough concentrations >2 µg/mL have been associated with an increased risk of toxicity and are commonly used as an indicator of potentially excessive exposure [6,12-14]. Because gentamicin is primarily eliminated through renal filtration, impaired renal function may result in drug accumulation and elevated trough concentrations. Therapeutic drug monitoring (TDM) is therefore recommended in many settings to individualize dosing and minimize toxicity.

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Although several factors, including younger age, low body weight, impaired renal function, and dosing practices, have been associated with altered gentamicin exposure among neonates, their clinical relevance may vary across healthcare settings. Much of the available evidence has been generated in environments where routine TDM, frequent laboratory monitoring, and individualized dose adjustment are readily available. In contrast, in Tanzania and other resource-limited settings, TDM for gentamicin is rarely accessible, and clinicians often rely on standardized dosing approaches despite substantial variability in neonatal characteristics that may influence drug clearance. [15,16] Furthermore, differences in neonatal populations, disease severity, nutritional status, clinical practices, and healthcare resources may influence the occurrence of elevated gentamicin concentrations. Consequently, evidence generated in other settings may not fully address the practical challenges faced in routine neonatal care in Tanzania.

There remains limited local evidence on readily available clinical and dosing-related factors that can identify neonates at increased risk of gentamicin accumulation. Identifying such factors may enable clinicians to recognize high-risk neonates and optimize antibiotic safety using information available during routine care. Therefore, this study aimed to determine clinical and demographic predictors associated with elevated gentamicin trough concentrations among term neonates receiving once-daily intravenous gentamicin therapy at a regional referral hospital in Tanzania, to identify readily available factors that may support safer antibiotic use in settings where TDM is limited.

Materials and methods

Study design and setting

This sub-study was nested within a larger prospective observational study evaluating the pharmacokinetics and safety of once-daily intravenous gentamicin in term neonates receiving either 4 mg/kg or 5 mg/kg as part of routine clinical care. The parent study included neonates treated with either gentamicin regimen and a comparison group receiving alternative antibiotics (ceftriaxone or cefotaxime). For this sub-study, all neonates who received gentamicin (n=250), irrespective of the prescribed dose, were included. Gentamicin trough concentrations were measured, and neonates were classified according to whether their trough concentration was elevated (>2 µg/mL) or not elevated (≤2 µg/mL). Clinical, demographic, and dosing-related factors associated with elevated gentamicin trough concentrations were then assessed.

The study was conducted from January to March 2025 in the neonatal unit of Mwananyamala Regional Referral Hospital (MRRH) in Dar es Salaam, Tanzania. The unit admits approximately 400 neonates per month, is staffed by pediatricians and trained healthcare personnel, and is supported by a laboratory capable of essential biochemical analyses.

Study population and sample size estimation

The study enrolled term neonates (gestational age ≥37 weeks), as determined by the last menstrual period, who had a clinical diagnosis of neonatal sepsis on admission, were aged 1 to 28 days, and for whom written informed consent was obtained from the mother or caregiver. Term neonates who were severely ill or in decompensated states, including respiratory distress, lethargy, coma, or shock, and those with hyperbilirubinemia or requiring calcium-containing intravenous fluids were excluded. Also excluded were term neonates with severe congenital malformations; exposure to nephrotoxic or ototoxic medications (for example, vancomycin, furosemide, acyclovir, amphotericin B, and ibuprofen) or drugs with potential pharmacokinetic interactions with gentamicin (such as phenobarbital, erythromycin, and phenytoin) within 72 hours prior to admission; serum creatinine above the upper limit of the laboratory reference range (>132.63 µmol/L); evidence of hearing loss at baseline; and prior gentamicin therapy within the 72 hours preceding study enrollment. Baseline serum creatinine concentrations within the laboratory reference range (44.22 - 132.63 µmol/L) were not an exclusion criterion. For the analysis of factors associated with elevated gentamicin trough concentrations, baseline serum creatinine > 100 µmol/L was categorized as high-normal while remaining within the laboratory reference range.

The sample size for the parent study was calculated using the Fisher and Leslie formula. After adjusting for a 10% attrition rate, the required sample size was 125 neonates per study group. The parent study enrolled three groups: neonates receiving gentamicin 4 mg/kg once daily (n=125), gentamicin 5 mg/kg once daily (n=125), and an alternative antibiotic regimen (n=125), giving a total sample size of 375 neonates. For this sub-study, all neonates who received gentamicin (n=250), comprising 125 neonates receiving 4 mg/kg and 125 receiving 5 mg/kg, were included in the analysis irrespective of dosing group. The sub-study therefore evaluated clinical, demographic, and dosing-related factors associated with elevated gentamicin trough concentrations among the complete gentamicin-treated cohort.

Gentamicin treatment and blood sampling

Eligible neonates were consecutively enrolled upon admission. Antibiotic treatment decisions were made by attending clinicians according to routine clinical practice. Each participant was assigned a unique study identification number.

Gentamicin was administered intravenously once daily at either 4 mg/kg or 5 mg/kg according to the prescribed regimen. Other antibiotics were administered according to standard neonatal sepsis treatment protocols and clinician judgment.

Serum gentamicin trough concentrations were measured using blood samples collected five minutes before administration of the fourth intravenous gentamicin dose, representing steady-state conditions. A 0.5 mL blood sample was collected by heel prick into serum separator tubes.

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Samples were stored at –20°C at Mwananyamala Regional Referral Hospital and transported within one hour under controlled temperature conditions (2–8°C) to the Central Pathology Laboratory at Muhimbili National Hospital. Serum samples were centrifuged at 3,000 × g for 10 minutes and stored at –80°C until analysis.

Measurement of gentamicin trough concentrations

Gentamicin concentrations were quantified using chemiluminescent microparticle immunoassay technology (ARCHITECT iGentamicin assay, Abbott Diagnostics, Illinois, USA) on an ARCHITECT ci4100 analyzer. The assay demonstrated acceptable accuracy, precision, and linearity across the therapeutic concentration range according to standard validation procedures.

An elevated gentamicin trough concentration was defined as >2 µg/mL. Neonates were therefore categorized into two groups according to their measured trough concentration: elevated (>2 µg/mL) and non-elevated (≤2 µg/mL). These categories formed the outcome variable for the analysis of factors associated with elevated gentamicin trough concentrations.

Data Analysis

Data were analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Normally distributed variables were summarized as mean ± standard deviation (SD), while non-normally distributed variables were summarized as median and interquartile range (IQR). Categorical variables were summarized as frequencies and percentages.

Gentamicin trough concentrations were normally distributed and were compared using independent-samples t-tests. Categorical variables were compared using chi-square or Fisher's exact tests, as appropriate.

Variables with p-values <0.20 in univariate analysis and those considered clinically relevant were included in multivariable logistic regression analysis. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were used to identify independent predictors of elevated gentamicin trough concentrations. Model diagnostics included assessment of multicollinearity using variance inflation factors (VIFs) and evaluation of model fit using the Hosmer–Lemeshow goodness-of-fit test. Two-sided p-values <0.05 were considered statistically significant.

Ethical considerations

Ethical approval was obtained from the University of Dodoma Institutional Research Review Ethics Committee (IRREC) (MA.84/261/74/38), and permission to conduct the study was granted by Mwananyamala Regional Referral Hospital. Written informed consent was obtained from mothers or legal guardians before enrolment of neonates. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

During the study period, 493 neonates were screened for eligibility. Of these, 118 (23.9%) were excluded, with the majority (84; 71.2%) having received gentamicin prior to admission at Mwananyamala Regional Referral Hospital (MRRH). A total of 375 neonates (76.1%) met the eligibility criteria and were enrolled. Among these, 250 received gentamicin and were categorized into the 5 mg/kg group (n=125) and the 4 mg/kg group (n=125). These 250 neonates were included in the present analysis to identify clinical, demographic, and dosing-related factors associated with elevated gentamicin trough concentrations (Figure 1). No participants withdrew consent, died, or were lost to follow-up.

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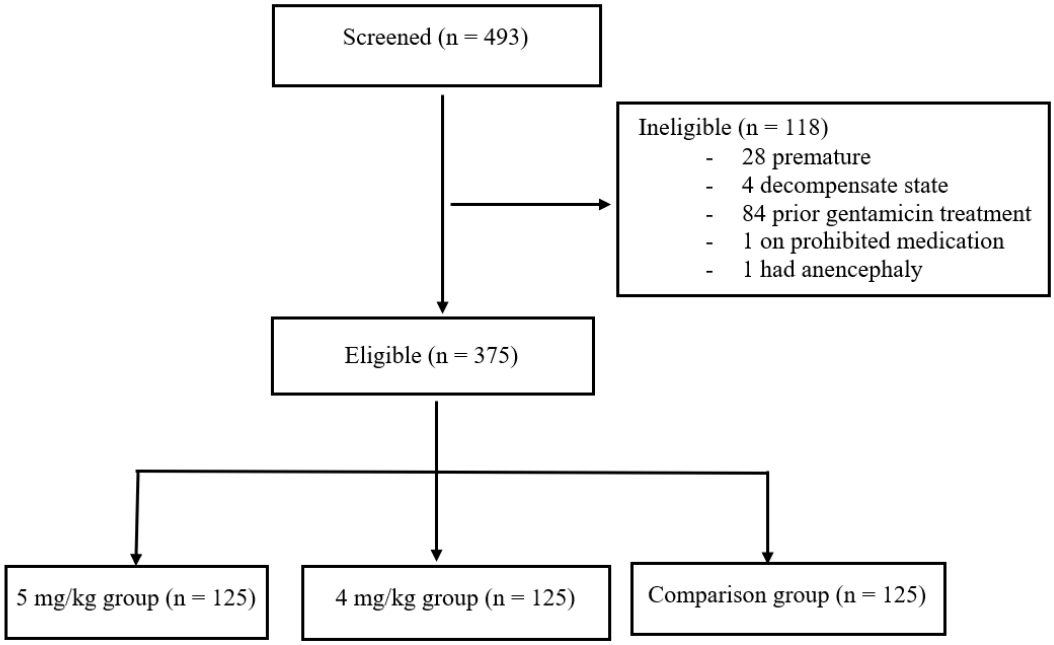

Figure 1. Participants' screening, eligibility and recruitment

Sociodemographic and clinical characteristics by dosing group

Most participants had normal birth weight and normal weight at enrolment, with no significant differences between the 4 mg/kg and 5 mg/kg groups. Age distribution and APGAR scores were also comparable between the groups. However, diarrhea was significantly more common among participants receiving 5 mg/kg than among those receiving 4 mg/kg, whereas the prevalence of vomiting did not differ significantly between the groups. The majority of neonates in both groups were able to suck, with no significant difference in the proportion unable to suck. Overall, baseline characteristics were comparable between the two dosing groups, including renal function profiles, and no participants had pre-existing hearing impairment, consistent with the study eligibility criteria (Table 1).

Table 1. Baseline characteristics of the study participants

Variable	Study group			p – value
	5mg/kg (n = 125)	4mg/kg (n = 125)	Comparison group	
Median age (IQR) (days)	8 (6, 11)	8 (6, 11)	8 (6, 9)	0.378
Sex, n (%)				
Male	78 (62.4)	72 (57.6)	54 (43.2)	0.007
Female	47 (37.6)	53 (42.4)	71 (56.8)	
Median gestational age (weeks) (IQR)	38 (37, 38)	38 (37, 38)	38 (37, 38)	0.962
Median birth weight in Kg (IQR)	3.0 (2.8, 3.5)	3.0 (2.6, 3.4)	3.0 (2.6, 3.4)	0.427
Median weight at enrolment in Kg (IQR)	3.10 (2.4, 3.2)	3.04 (2.4, 3.6)	3.07 (2.3, 3.8)	0.49
Weight at enrolment category, n (%)				
Normal (≥ 2.5 kg)	100 (80.0)	96 (76.8)	101 (80.8)	0.712
Low (< 2.5 kg)	25 (20.0)	29 (23.2)	24 (19.2)	
Median height in cm (IQR)	50.0 (48.5, 52.0)	50.0 (48.0, 52.3)	50.0 (48.0, 52.8)	0.696
Median Apgar score (IQR)	8.0 (7.0, 9.0)	8.0 (7.0, 8.5)	8.0 (7.0, 8.5)	0.222
Diarrhea, n (%)				
Yes	24 (19.2)	11 (8.8)	7 (5.6)	0.002
No	101 (80.8)	114 (91.2)	118 (94.4)	
Vomiting, n (%)				
Yes	27 (21.6)	24 (19.2)	26 (20.8)	0.892
No	98 (78.4)	101 (80.8)	99 (79.2)	
Unable to suck, n (%)				
Yes	10 (8.0)	14 (11.2)	15 (12.0)	0.548
No	115 (92.0)	111 (88.8)	110 (88.0)	
Median creatinine (µmol/L) (IQR)	79.0 (56.9, 99.1)	80.0 (60.0, 100)	78.5 (62.9, 100)	0.819
Median urinary KIM-1 (ng/mL) (IQR)	0.38 (0.28, 0.51)	0.39 (0.29, 0.50)	0.39 (0.30, 0.45)	0.594
Median AABR threshold (dB) (IQR)	7.0 (5.0, 9.0)	7.0 (4.0, 9.0)	6.0 (4.5, 9.0)	0.389
Median baseline eGFR (IQR)	25.9 (20.2, 34.5)	24.4 (19.9, 33.1)	25.6 (20.7, 33.3)	0.854

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Steady state trough serum gentamicin concentrations

The mean steady-state trough serum gentamicin concentration was higher in the 5 mg/kg group (2.52 ± 0.93 µg/mL) than in the 4 mg/kg group (1.46 ± 0.36 µg/mL; p<0.001, independent-samples t-test) (Table 2). Sixty-five of 125 neonates (52.0%) in the 5 mg/kg group had trough concentrations above the safety threshold (>2 µg/mL), compared with 3 of 125 neonates (2.4%) in the 4 mg/kg group (p<0.001, chi-square test). Thus, elevated trough concentrations were substantially more frequent among neonates receiving 5 mg/kg than among those receiving 4 mg/kg.

Table 2. Steady state trough serum gentamicin concentration

Variable	5 mg/kg (n=125)	4 mg/kg (n=125)	p-value
Mean steady-state trough serum gentamicin (µg/mL)	2.52 ± 0.93	1.46 ± 0.36	<0.001
Proportion of neonates with trough >2 µg/mL (%)	52.0	2.4	<0.001

Factors associated with elevated serum gentamicin trough concentrations

Among the 250 neonates who received intravenous gentamicin at either 5 mg/kg or 4 mg/kg, 68 (27.2%) had elevated steady-state trough serum gentamicin concentrations (>2 µg/mL). Multivariable logistic regression analysis was performed using the pooled gentamicin-treated cohort to identify clinical, demographic, and dosing-related factors independently associated with elevated trough concentrations.

Neonatal age below seven days was significantly associated with increased odds of elevated trough concentrations (aOR=4.41, 95% CI: 2.16–8.99, p<0.0001), as was low body weight (<2.5 kg) (aOR=2.10, 95% CI: 1.20–3.68, p=0.009). Non-weight-based dosing was also independently associated with elevated trough concentrations (aOR=3.41, 95% CI: 1.45–8.05, p=0.005). Gastrointestinal symptoms were associated with increased odds of elevated concentrations, including vomiting (aOR=2.65, 95% CI: 1.22–5.74, p=0.013) and diarrhea (aOR=8.26, 95% CI: 2.98–22.89, p<0.0001). Inability to suck was also significantly associated with elevated trough concentrations (aOR=3.82, 95% CI: 1.26–11.56, p=0.0177). High-normal baseline serum creatinine (>100 µmol/L), while remaining within the laboratory reference range of 44.22 - 132.63 µmol/L, was associated with increased odds of elevated gentamicin trough concentrations (aOR=2.21, 95% CI: 1.03–4.73, p=0.042) (Table 3).

Table 3. Binary logistic regression analysis for factors associated with elevated steady state trough serum gentamicin concentrations

Variable	Crude OR (95%CI)	p-value	Adjusted OR (95% CI)	p-value
Age < 7 days	5.73 (3.14–10.46)	<0.001	4.41 (2.16–8.99)	<0.001
Body weight < 2.5 kg	2.76 (1.47–5.21)	0.002	2.10 (1.20–3.68)	0.009
Non–weight-based dosing	3.93 (1.11–7.78)	0.003	3.41 (1.45–8.05)	0.005
Vomiting	4.84 (2.52–9.28)	<0.001	2.65 (1.22–5.74)	0.013
Diarrhea	10.00 (4.47–22.38)	<0.001	8.26 (2.98–22.89)	<0.001
Unable to suck	2.33 (1.07–5.91)	0.035	3.82 (1.26–11.56)	0.018
High-normal baseline serum creatinine (> 100 µmol/L)	2.65 (1.46–4.84)	0.002	2.21 (1.03–4.73)	0.042

Discussion

In this cohort of 250 term neonates receiving once-daily intravenous gentamicin (5 mg/kg or 4 mg/kg), 27.2% (n=68) had elevated steady-state trough concentrations (>2 µg/mL). A marked difference was observed between dosing groups, with 65 (52.0%) neonates in the 5 mg/kg group compared with 3 (2.4%) in the 4 mg/kg group having elevated trough concentrations (p<0.001). These findings demonstrate substantially greater gentamicin exposure among neonates receiving the 5 mg/kg regimen in this population.

Multivariable logistic regression identified several clinical, demographic, and dosing-related factors associated with elevated gentamicin trough concentrations, highlighting the complex interplay between neonatal physiology, dosing practices, and clinical condition.

Neonatal age below seven days was among the strongest predictors of elevated trough concentrations (aOR=4.41; 95% CI: 2.16–8.99; p<0.0001). This finding is consistent with the established understanding that immature renal function, particularly reduced glomerular filtration, influences aminoglycoside elimination [8,17]. The prolonged elimination half-life during the first postnatal week may contribute to gentamicin accumulation, as reported by Avent et al. [18]. De Hoog and Van den Anker [19] reported a higher prevalence of supratherapeutic gentamicin concentrations among neonates within 72 hours of birth, while Fuchs et al. [20] observed reduced clearance among neonates with perinatal complications. Our findings further support the importance of age-related physiological changes when optimizing gentamicin dosing during the early neonatal period.

Low body weight (<2.5 kg) was also independently associated with elevated trough concentrations (aOR=2.10; 95% CI: 1.20–3.68; p=0.009), consistent with previous evidence linking body weight to variability in gentamicin distribution and clearance. [14, 18] Differences in body composition and renal maturation may contribute to altered gentamicin

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disposition among smaller neonates. Pacifici [14] reported reduced gentamicin clearance among low-birth-weight neonates, emphasizing the importance of appropriate weight-based dosing. Although WHO guidelines recommend once-daily gentamicin at 5 mg/kg for term neonates, our findings suggest that neonates with lower body weight may require particular attention to dose selection and monitoring.

Non-weight-based dosing (fixed-dose administration) was independently associated with elevated gentamicin trough concentrations (aOR=3.41; 95% CI: 1.45–8.05; p=0.005). In this setting, neonates with different body weights within the same dosing category could receive the same absolute gentamicin dose rather than an individually calculated dose based on actual body weight. Consequently, smaller neonates may receive a higher effective dose when expressed in mg/kg, potentially increasing gentamicin exposure and accumulation. This finding is consistent with the pharmacokinetic variability reported under fixed-dose regimens [21] and highlights the importance of maintaining individualized weight-based dosing when administering gentamicin to neonates.

Gastrointestinal symptoms, including vomiting (aOR=2.65; 95% CI: 1.22–5.74; p=0.013) and diarrhea (aOR=8.26; 95% CI: 2.98–22.89; p<0.0001), were strongly associated with elevated trough concentrations. Although these symptoms are not established direct pharmacokinetic determinants of gentamicin exposure, they may indicate dehydration, reduced circulating volume, or impaired renal perfusion, potentially affecting gentamicin clearance [14, 16]. The particularly strong association observed with diarrhea suggests that acute clinical conditions that may alter hydration and renal function should be considered when assessing the risk of gentamicin accumulation.

Inability to suck was also independently associated with elevated trough concentrations (aOR=3.82; 95% CI: 1.26–11.56; p=0.0177). Inability to suck may serve as a readily identifiable marker of systemic illness or neurological impairment and may coexist with physiological disturbances that affect renal perfusion and drug elimination. This finding complements observations by Pacifici [7,14] regarding the relationship between poor feeding, neonatal illness, and altered drug pharmacokinetics. Although inability to suck is not itself a direct pharmacokinetic determinant, its association with elevated trough concentrations suggests that feeding ability may provide a clinically useful indicator for identifying neonates who require closer assessment during gentamicin therapy.

High-normal baseline serum creatinine (>100 µmol/L), while remaining within the laboratory reference range of 44.22 - 132.63 µmol/L, was associated with elevated trough concentrations (aOR=2.21; 95% CI: 1.03–4.73; p=0.042). This finding suggests that variation in renal function within the normal reference range may still be relevant to gentamicin elimination in neonates. Because gentamicin is predominantly eliminated by renal filtration, relatively higher creatinine concentrations may reflect lower renal clearance and consequently greater drug exposure. Previous evidence has similarly demonstrated an association between renal function and aminoglycoside clearance [22]. These findings emphasize the potential value of considering baseline renal function, even when serum creatinine remains within the accepted reference range, when optimizing gentamicin therapy.

Study strengths and limitations

A major strength of this study is its prospective cohort design, which enabled systematic collection of clinical, demographic, dosing, and pharmacokinetic data under routine clinical practice conditions. The inclusion of all 250 neonates receiving gentamicin from the parent cohort allowed factors associated with elevated trough concentrations to be evaluated across both the 4 mg/kg and 5 mg/kg dosing groups. The identification of readily available clinical and dosing-related factors may enhance the practical applicability of the findings, particularly in resource-limited settings where routine therapeutic drug monitoring is not readily available.

This study also has limitations. First, β-lactam antibiotics present in blood samples may interfere with chemiluminescent microparticle immunoassay measurements of gentamicin, potentially affecting measured concentrations when analysis is delayed. In this study, samples were analyzed promptly when feasible, and when delayed analysis was anticipated, samples were stored frozen to minimize the potential for assay interference. Second, the study was conducted at a single regional referral hospital, which may limit the generalizability of the findings to other neonatal populations and healthcare settings. Third, because this was an observational study, the identified associations should not be interpreted as causal relationships. Finally, although the study identified clinical and dosing-related factors associated with elevated trough concentrations, therapeutic drug monitoring was not used to guide individualized dose adjustment during routine treatment.

Conclusions

In this cohort of term neonates receiving once-daily intravenous gentamicin, more than one-quarter had elevated trough concentrations, with substantially higher concentrations observed among those receiving 5 mg/kg compared with 4 mg/kg. Younger age, low body weight, non-weight-based dosing, vomiting, diarrhea, inability to suck, and high-normal baseline serum creatinine within the laboratory reference range were independently associated with elevated gentamicin trough concentrations. These readily available clinical and dosing-related factors may help identify neonates at increased risk of gentamicin accumulation and support safer, more individualized antibiotic dosing, particularly in resource-limited settings where routine therapeutic drug monitoring is not readily available.

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Competing interests
The authors declare that they have no competing interests.

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Author contributions
MEJ, PS, AL, and DB contributed to the conception and design of the study. MEJ was responsible for data collection, data analysis, and drafting of the manuscript. PS, AL, and DB supervised the study and critically reviewed the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

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