

# Monitoring Aminoglycoside Therapy in Neonates: Gaps and Opportunities in a Resource-Limited Setting



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## INTRODUCTION

A significant portion of mortality observed in newborns, especially in low- to middle-income countries, such as the Philippines, may be attributed to neonatal infections. In the clinical setting, the combination of ampicillin and gentamicin is routinely ordered for neonatal patients who are either suspected to be septic due to maternal factors or have a confirmed diagnosis of sepsis<sup>1</sup>. The antibiotic regimen selection, dosing, and duration of therapy for this patient are consistent with recommended treatment guidelines for neonatal sepsis<sup>2,3</sup>. Close monitoring of aminoglycoside levels is recommended as this class of drugs may cause nephrotoxicity and ototoxicity. In resource-limited settings in some parts of the world, access to laboratory evaluations may be intermittent or not available. In the absence of clinical pharmacokinetic monitoring of peak and trough concentrations in a neonatal intensive care unit (NICU), a potential compromise in safely administering aminoglycosides<sup>4</sup> may be encountered. This study aimed to evaluate the practice of aminoglycoside use and monitoring in an urban, public, resource-limited hospital in Manila, Philippines, and identify gaps in the clinical use of aminoglycosides and opportunities for improvement of therapeutic drug monitoring in pediatrics.



Figure 1. Pediatric aminoglycoside (gentamicin) vial.

## RESULTS AND DISCUSSIONS

### PHASE I

Table 1. Summary of patient admissions at the study site from January to March 2021

ADMISSIONS	JANUARY 2021	FEBRUARY 2021	MARCH 2021
Total Ward Admissions	34	76	102
Neonatal Admissions	3 (8.8%)	6 (7.8%)	22 (22%)

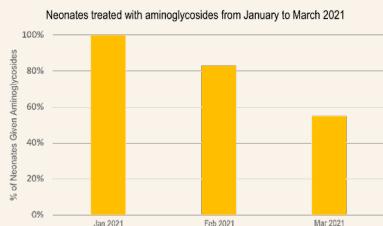


Figure 3. Percentage of neonates that were given aminoglycosides, either alone or in combination with ampicillin, for prophylaxis or treatment of suspected or confirmed bacterial infections.

Retrospective analysis of patient censuses and charts revealed that the combination of ampicillin and gentamicin is routinely given to neonates. This approach, encompassing the drugs involved, the dosages given, and the duration of therapy are all consistent with standard recommendations<sup>2,5</sup>.

### PHASE II

Based on the interview with practicing pediatricians, the following responses were noted:

- The participants have never been involved in therapeutic drug monitoring (TDM);
- The participants have not requested for TDM;
- The participants acknowledged the importance of TDM for drugs with narrow therapeutic index (including aminoglycosides);
- The participants affirmed the need for TDM training;
- The participants mentioned that the pediatricians' primary reference material for the identification of dosages of antimicrobial agents is Nelson's Antimicrobial Therapy<sup>6</sup>;
- The participants affirmed that there is no aminoglycoside TDM currently being performed in their hospital;
- The participants reported lack of a double-checking system before administration of an aminoglycoside; and
- The participants affirmed the need to establish a protocol for aminoglycoside use and monitoring.

These findings demonstrated several issues and concerns, regarding the effectiveness and safety monitoring of aminoglycosides.

### PHASE III

Table 2. Gaps and opportunities in improving aminoglycoside use and monitoring

GAPS	OPPORTUNITIES
Absence of clinical pharmacists	<ul style="list-style-type: none"> <li>▪ Establishment of a clinical pharmacy service;</li> <li>▪ Interprofessional collaboration to improve patient outcomes; and</li> <li>▪ Empower pharmacists to conduct therapeutic drug monitoring (TDM).</li> </ul>
Lack of healthcare TDM knowledge and absence of TDM protocols	<ul style="list-style-type: none"> <li>▪ TDM training of drugs with narrow therapeutic indices such as aminoglycosides;</li> <li>▪ Modernization of the hospital and patient medical records which are currently on paper; and</li> <li>▪ Use of medical calculators to compute the correct aminoglycoside dose.</li> </ul>
Insufficient diagnostic protocol for sepsis	<ul style="list-style-type: none"> <li>▪ Development of a sepsis workup protocol including antibiotic therapy selection, assessment methods to monitor for efficacy and safety; and</li> <li>▪ Documentation of incidence of early onset sepsis in the medical record.</li> </ul>

These findings could serve as the bases in formulating strategic directions to improve the practices of aminoglycoside use and monitoring to ensure patient safety and quality of care.

## CONCLUSIONS AND RECOMMENDATIONS

The present study revealed that aminoglycoside use appeared to be common among neonates admitted in the study site. However, compliance to treatment guidelines was suboptimal, which raises concerns around potential, avoidable harm to patients. A hallmark challenge in treating neonatal patients in an adult institution is the lack of a dedicated neonatal service line and healthcare workers who specialize in the care of this special patient population. Inadequate monitoring of neonates on aminoglycosides is another matter of concern that requires urgent attention. The identified gaps highlight the need for potential strategies to improve the practice of aminoglycoside use including the development of TDM protocols.

It is recommended that further studies be performed on much longer time frame to improve data analytics. Increasing the number of participants by involving other healthcare professionals (e.g. nurses, pharmacists, and medical technologists) as respondents is also suggested. Lastly, a comparative analysis of practices in aminoglycoside use and monitoring between public and private hospitals shall also be carried out to improve the study outcome.

## REFERENCES

- Onyango, E.J., Okalebo, F., Oluka, M., Kinuthia, R., Achieng, L., Godman, B., Kurdi, A. (2020). Evaluation of the clinical practice of aminoglycoside use in paediatric patients in Kenya: findings and implications for lower-middle income countries. *JAC-Antimicrobial Resistance*, Volume 2, Issue 1, dz087, <https://doi.org/10.1093/jacamr/dz087>
- Bradley JS, Nelson JD, Barnett ED et al. (2021). *Nelson's Pediatric Antimicrobial Therapy* (American Academy of Pediatrics 27th Edition).
- Fuchs A, Bielicki J, Mathur S, Sharland M, Van Den Anker J. (2016). Antibiotic use for sepsis in neonates and children: 2016 Evidence Update. WHO Reviews. Available from: [http://www.who.int/selection\\_medicines/committees/expert/21/applications/s6\\_paed](http://www.who.int/selection_medicines/committees/expert/21/applications/s6_paed)
- duToit M, Burger JR, Rakumakoe DM, Rheebers M. (2019). Standards of aminoglycoside therapeutic drug monitoring in a South African private hospital: perspectives and implications. *Ghana Med J*; 53(1):8-12. doi: 10.4314/gmj.v53i1.2. PMID: 31138938; PMCID: PMC6527830.
- Lexicomp Drug Information. (2021). Gentamicin (Systemic).