## INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION



## FREQUENCY OF MATERNAL SEPSIS AMONG GRAVID FEMALES WHO HAD VAGINAL DELIVERY TREATED WITH PROPHYLACTIC AZITHROMYCIN

Original Research

Khadija Naseer Khan<sup>1</sup>\*, Noor Ul Huda<sup>2</sup>, Alveena Khan<sup>3</sup>, Aqsa Tassadduq<sup>4</sup>, Maria Ahmed<sup>4</sup>, Nimra Sajid<sup>2</sup> <sup>1</sup>PGR Gynae & OBS, Jinnah Hospital Lahore, Pakistan. <sup>2</sup>House Officer, Benazir Bhutto Hospital, Pakistan. <sup>3</sup>Medical Officer, UHS, Pakistan. <sup>4</sup>Medical Officer, DHQ Mirpur, Pakistan. **Corresponding Author:** Khadija Naseer Khan, PGR Gynae & OBS, Jinnah Hospital Lahore, Pakistan. <u>Khadija-naseer@yahoo.com</u>

Conflict of Interest: None

Grant Support & Financial Support: None

## ABSTRACT

**Background:** Maternal sepsis is a significant contributor to maternal morbidity and mortality globally, accounting for nearly 10% of maternal deaths. The use of prophylactic antibiotics during childbirth has shown promise in reducing infection-related complications. Azithromycin, a broad-spectrum macrolide, has demonstrated efficacy in reducing maternal infections in previous studies. This study evaluates the frequency of maternal sepsis among gravid females who underwent vaginal delivery and were treated with a prophylactic dose of azithromycin.

**Objective**: To determine the frequency of maternal sepsis among gravid females who had vaginal delivery and were treated with a single prophylactic dose of oral azithromycin.

**Methods**: This descriptive case series was conducted over six months in the Department of Obstetrics and Gynecology at Jinnah Hospital, Lahore. A total of 140 gravid females, aged 18–40 years, were enrolled using non-probability consecutive sampling. Patients received a single oral dose of 2g azithromycin within six hours of vaginal delivery. They were observed for 24 hours post-delivery, discharged if asymptomatic, and monitored via phone for six days. Maternal sepsis was defined based on clinical symptoms, vital signs, and blood culture results. Data were analyzed using SPSS version 25.

**Results**: Among 140 participants, 27 women (19.2%) developed maternal sepsis. Of these, 22 (15.7%) had a low-grade fever (99°F), while 5 (3.6%) experienced high-grade fever ( $\geq 101^{\circ}$ F). The highest recorded temperature was 103°F. The remaining 113 patients (80.7%) remained asymptomatic, reporting no fever or other signs of infection. All patients tolerated azithromycin without adverse effects.

**Conclusion**: Prophylactic administration of oral azithromycin within six hours of vaginal delivery significantly reduces the risk of maternal sepsis. This intervention is well-tolerated and holds promise for improving maternal outcomes, particularly in settings with limited resources.

Keywords: Azithromycin, bacterial infections, gravid females, maternal morbidity, maternal sepsis, prophylactic antibiotics, vaginal delivery.

# INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION



## INTRODUCTION

Vaginal delivery is widely recognized as the safest mode of childbirth for both the mother and the fetus, particularly when the pregnancy reaches full-term, defined as a gestational age of 37 to 42 weeks. It is generally preferred due to its lower morbidity and mortality rates compared to cesarean delivery. Cesarean births, although sometimes necessary, have been associated with a significant rise in maternal and neonatal complications over time, including uterine rupture, abnormal placentation in subsequent pregnancies, ectopic pregnancies, preterm births, and stillbirths. Additionally, cesarean delivery alters neonatal physiology, potentially affecting short- and long-term outcomes due to differing hormonal, microbiological, and medical exposures during birth (1, 4-6). In contrast, vaginal delivery confers several maternal benefits, including shorter hospital stays, quicker physical and psychological recovery, and an enhanced maternal-infant bond. For neonates, the advantages of vaginal delivery include improved respiratory function, temperature regulation, and hormonal adjustments that support early behavioral development (2, 3).

Despite these benefits, vaginal delivery remains a complex process associated with inherent risks, particularly infections. Maternal infections during pregnancy are relatively common and are usually managed effectively in clinical practice; however, in some cases, they can escalate to life-threatening conditions like sepsis. Maternal sepsis, defined as organ dysfunction due to infection during pregnancy, childbirth, or the postpartum period, poses a significant risk to maternal health and is a leading cause of maternal morbidity and mortality in resource-limited settings. Globally, between 2003 and 2009, maternal sepsis accounted for 10.7% of all maternal deaths, with a disproportionate burden observed in low- and middle-income countries due to limited access to timely and appropriate care (7-10).

To mitigate the risks associated with maternal infections, particularly postpartum infections such as puerperal sepsis, antimicrobial prophylaxis has been explored as a preventative measure. Azithromycin, a macrolide antibiotic with broad-spectrum activity against both gram-positive and gram-negative bacteria, has demonstrated efficacy in reducing maternal infections, including endometritis and wound infections. Its bacteriostatic mechanism, through inhibition of bacterial protein synthesis, and bactericidal effects at higher doses make it a valuable intervention. Studies have shown that azithromycin not only decreases the incidence of maternal infections but also reduces hospital readmissions and unscheduled care visits, thereby offering substantial benefits in obstetric care without compromising neonatal outcomes (11-13).

Given the critical importance of reducing maternal morbidity and mortality, particularly in settings with high prevalence rates of postpartum sepsis, the objective of this study is to determine the frequency of maternal sepsis among gravid females undergoing vaginal delivery and treated prophylactically with azithromycin. This research aims to provide evidence-based insights into the efficacy of azithromycin in minimizing infection-related complications, contributing to improved maternal health outcomes.

## **METHODS**

The study was conducted after obtaining approval from the ethical review committee of the hospital. A total of 140 gravid females presenting to the labor room in the Obstetrics Department of Jinnah Hospital, Lahore, were included based on predefined inclusion and exclusion criteria. All participants were thoroughly counseled, and the details of the study were explained. Written informed consent was obtained from each participant before enrollment. The study included gravid females aged 18 to 40 years with a gestational age greater than 37 weeks, confirmed via obstetric ultrasound, who had undergone normal vaginal delivery. Maternal sepsis was defined as a body temperature exceeding  $38^{\circ}$ C ( $100.4^{\circ}$ F) or below  $36^{\circ}$ C ( $96.8^{\circ}$ F) on more than one occasion during the first six days postpartum, accompanied by tachycardia, elevated white blood cell counts, and a respiratory rate exceeding 20 breaths per minute. Additionally, sepsis was confirmed by blood culture findings indicating significant bacterial growth of gram-positive or gram-negative organisms (>5 colonies on gram-staining) (14).

Eligible participants received a single oral dose of 2g azithromycin within six hours of vaginal delivery. Following administration, patients were observed in the hospital for 24 hours, during which they were monitored for any significant clinical events. Those who remained clinically stable were discharged and followed up via phone calls for six days. In cases where fever recurred (defined as fever occurring more than once during the follow-up period), participants were recalled for clinical evaluation, admitted, and investigated



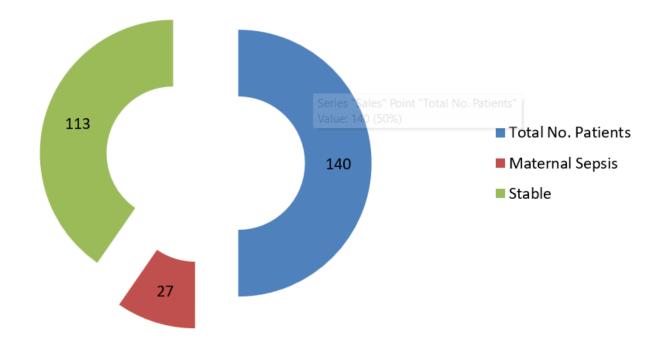
further. Blood samples (5 ml) were collected and sent to the hospital laboratory for culture and sensitivity testing to identify the causative organism. Maternal sepsis was labeled based on the operational definition, and further antibiotic therapy was administered according to the culture and sensitivity results. To ensure uniformity, all cultures were conducted in the hospital laboratory to minimize bias and maintain consistency.

Confounding variables were controlled by exclusion criteria. Patients with documented sensitivity to azithromycin, a history of recent steroid use (more than two doses in the past two weeks), or a diagnosis of poorly controlled diabetes (HbA1c >6.9%) were excluded. Additionally, participants with urinary tract infections, evidenced by 2-5 pus cells on a complete urine examination before labor, were not included in the study.

This methodology ensured a robust framework for accurately assessing the frequency and management of maternal sepsis in the study population while minimizing confounding factors and maintaining ethical and scientific rigor.

### RESULTS

A total of 140 gravid females were included in the study, all of whom received a single prophylactic dose of 2g oral azithromycin within six hours of vaginal delivery. Participants were initially observed for 24 hours post-delivery. Among them, 6 patients (4.3%) developed fever spikes within the first 24 hours. Of these, 4 patients experienced low-grade fever (99°F), while 2 patients had high-grade fever (101°F). These individuals were admitted for further evaluation and treatment. Patients who remained asymptomatic and fever-free after 24 hours were discharged and monitored via telephone for the subsequent six days.



#### Figure 1 Total Number of Patients



## Distribution of Fever Reports Over 6 Days

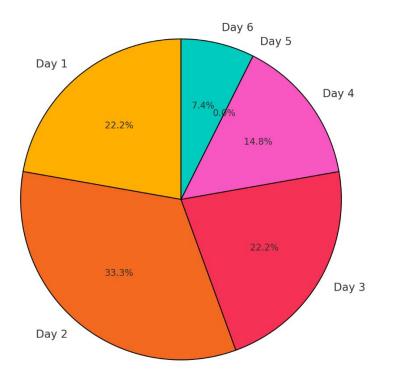


Figure 2 distribution of Fever Reports over 6 Days

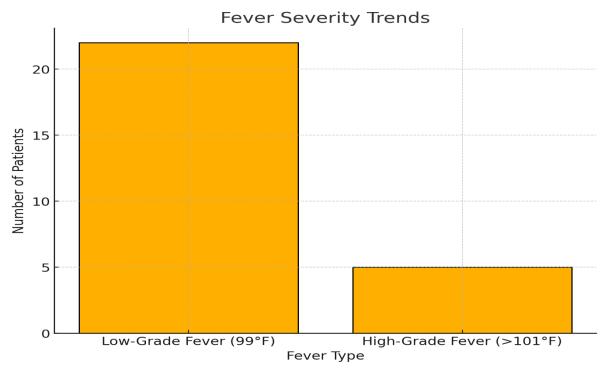
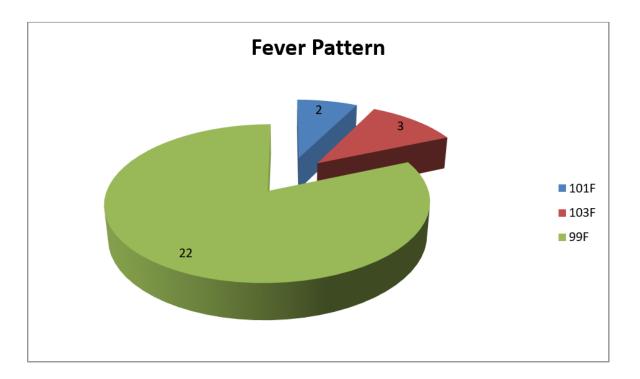


Figure 3 Fever Severity Trends





#### Figure 4 Temperatur Trend

During the phone follow-ups, 9 patients (6.4%) reported a single low-grade fever spike (99°F) on the second day postpartum and were subsequently recalled for evaluation. On the third day, 6 patients (4.3%) reported fever spikes, followed by 4 patients (2.9%) on the fourth day. No symptoms, including fever, were reported by any patient on the fifth day. On the sixth day, 2 patients (1.4%) again reported symptoms, primarily low-grade fever. In total, 27 patients (19.3%) reported at least one fever spike during the study period, with the majority (81.4%, n=22) experiencing low-grade fever (99°F), and 5 patients (3.6%) presenting with high-grade fever spikes of 101°F or higher. Notably, 3 patients reported a fever as high as 103°F.

Day	Number of Patients with Fever	Fever Percentage (%)	
Day 1	6	4.3	
Day 2	9	6.4	
Day 3	6	4.3	
Day 4	4	2.9	
Day 5	0	0.0	
Day 6	2	1.4	

All 27 patients who reported fever spikes were readmitted and thoroughly evaluated for other potential causes of fever. Investigations included laboratory tests and clinical assessments, ensuring no missed diagnoses. No significant findings related to other systemic complications, such as tachycardia, increased sweating, or palpitations, were identified in these patients. The remaining 113 participants (80.7%) remained completely asymptomatic throughout the observation period, reporting no fever, symptoms of sepsis, or other complications.



#### **Table 2: Fever Severity Trends**

Fever Type	Number of Patients	Percentage (%)	
Low-Grade Fever (99°F)	22	81.4	
High-Grade Fever (>101°F)	5	18.6	

The results demonstrated that prophylactic administration of azithromycin effectively prevented significant maternal infections in the majority of patients, with only a small proportion experiencing mild fever spikes. No severe complications, maternal sepsis, or adverse events related to azithromycin were observed in this cohort. These findings support the potential role of azithromycin in reducing infection-related postpartum complications following vaginal delivery.

## DISCUSSION

Maternal infections, including sepsis, remain a significant cause of maternal mortality worldwide, accounting for approximately 10% of maternal deaths and ranking among the top three causes of maternal mortality globally. Over time, the proportion of deaths caused by maternal infections has increased, while deaths from other causes such as hemorrhage and preeclampsia have shown stability or decline. Recognizing this trend, global health organizations, including the World Health Organization (WHO), have prioritized reducing maternal sepsis as a critical strategy to lower maternal mortality rates. Prophylactic antibiotic interventions, such as the administration of azithromycin, have emerged as a promising approach in this context, particularly for women during the peripartum period (15, 16).

Evidence from randomized controlled trials has demonstrated the efficacy of azithromycin in reducing maternal infections. A large multicenter, double-blind, placebo-controlled study conducted across low- and middle-income countries reported a significantly lower incidence of maternal sepsis or death in women who received 2g of oral azithromycin compared to those given a placebo. Similar findings were observed in a trial conducted in the United States, where azithromycin use led to a 50% reduction in maternal infections, including endometritis and wound infections, with fewer readmissions and unscheduled care visits. These results align with the findings of the current study, where 19.2% of patients developed fever or signs of maternal sepsis after receiving prophylactic azithromycin, while the majority remained asymptomatic. This consistency supports the potential role of azithromycin as a protective agent against maternal infections in diverse settings (17-19).

Smaller trials conducted in Cameroon and The Gambia further highlighted the potential benefits of azithromycin, particularly in reducing neonatal infections and maternal sepsis rates. Similarly, the A-PLUS trial, conducted in seven countries including Pakistan, demonstrated a significant reduction in maternal sepsis and endometritis among participants who received azithromycin. The cumulative evidence underscores the role of azithromycin in improving maternal outcomes, particularly in resource-constrained settings where maternal infections contribute disproportionately to morbidity and mortality (20-22).

In the present study, 140 women who underwent vaginal delivery were administered a single 2g dose of azithromycin and monitored for six days postpartum. Of these, 27 patients (19.2%) exhibited signs of maternal sepsis, with the highest recorded temperature being 103°F, while the average temperature among the septic group remained 99°F. The majority of these patients presented with low-grade fever, which resolved following evaluation and appropriate management. Importantly, no adverse effects related to azithromycin, such as nausea, vomiting, or abdominal pain, were reported, suggesting good tolerability. These findings reinforce the potential utility of azithromycin in preventing maternal infections and improving postpartum outcomes.

The study is not without limitations. Being a single-center study, the generalizability of the results to a broader population is constrained. Additionally, the lack of a placebo group limits the ability to compare outcomes with a control population. The relatively short follow-up period and reliance on phone-based monitoring may have resulted in underreporting of symptoms or other clinical events. These factors highlight the need for larger, multicenter studies with extended follow-up and more rigorous monitoring protocols to validate the findings and extend their applicability to diverse populations.

Despite these limitations, the study provides valuable insights into the potential of azithromycin as a prophylactic agent in reducing maternal infections. Its findings are consistent with existing literature and add to the growing body of evidence supporting the role of



azithromycin in improving maternal health outcomes. However, further research is warranted to address the limitations and to explore its applicability in larger and more heterogeneous populations.

## CONCLUSION

The findings of this study demonstrate that the administration of a single oral dose of azithromycin within six hours of vaginal delivery effectively reduces the risk of maternal sepsis and related infections. This underscores the protective role of azithromycin in preventing postpartum complications, aligning with the objective of improving maternal outcomes. These results highlight its potential as a simple and effective prophylactic measure to enhance maternal health during the critical postpartum period.

### REFERENCES

1. Lagrew DC, Low LK, Brennan R, Corry MP, Edmonds JK, Gilpin BG, et al. National Partnership for Maternal Safety: Consensus Bundle on Safe Reduction of Primary Cesarean Births-Supporting Intended Vaginal Births. Obstet Gynecol. 2018 Mar;.

2. Iams JD. Prediction and early detection of preterm labor. Obstet Gynecol. 2003 Feb;101(2).

3. Buhimschi CS, Buhimschi IA. Advantages of vaginal delivery. Clin Obstet Gynecol. 2006 Mar;49(1).

4. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final Data for 2017. Natl Vital Stat Rep. 2018 Nov;67(8).

5. Abenhaim HA, Tulandi T, Wilchesky M, Platt R, Spence AR, Czuzoj-Shulman N, et al. Effect of Cesarean Delivery on Long-term Risk of Small Bowel Obstruction. Obstet Gynecol. 2018 Feb;131(2).

6. Danilack VA, Nunes AP, Phipps MG. Unexpected complications of low-risk pregnancies in the United States. Am J Obstet Gynecol. 2015 Jun;212(6).

7. Arulkumaran N, Singer M. Puerperal sepsis. Best Pract Res Clin Obstet Gynaecol. 2013 Dec;27(6):893-902.

8. Bishaw KA, Sharew Y, Beka E, Aynalem BY, Zeleke LB, Desta M, et al. Incidence and predictors of puerperal sepsis among postpaftuut women at Debre Markos comprehensive specialized hospital, northwest Ethiopia: A prospective cohort study. Front Glob Womens Health. 2023;4:966942.

9. Duan R, Xu X, Wang X, Yu H. Perinatal outcome in women with bacterial sepsis. Medicine (Baltimore). 2019;98(44):e17755.

10. Zhong X, Lin R, Zhang W, Huang S, Luo Y, Wang D. Epidemiology and clinical features of maternal sepsis: A retrospective study of the whole pregnancy period. Medicine (Baltimore). 2022;101(40):e30599.

11. Retsema J, Girard A, Schelkly W, Manousos M, Anderson M, Bright G, et al. Spectrum and mode of action of azithromycin (CP-62,993), a new 15-membered-ring macrolide with improved potency against gram-negative organisms. Antimicrob Agents Chemother.

12. Jelić D, Antolović R. From Erythromycin to Azithromycin and New Potential Ribosome-Binding Antimicrobials. Antibiotics (Basel). 2016 Sep 01;5(3).

13. Drew RH, Gallis HA. Azithromycin--spectrum of activity, pharmacokinetics, and clinical applications. Pharmacotherapy.

14. Olutoye AS, Agboola AD, Bello OO. Puerperal Sepsis at University College Hospital, Ibadan: A 10-Year Review. Ann Ib Postgrad Med. 2022 Jun;20(1).

15. World Health Organization. WHO recommendations for the prevention and treatment of maternal peripartum infections. 2015 Sep 28.

16. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385:430-440.



17. Reinhart K, Daniels R, Kissoon N, Machado FR, Schachter RD, Finfer S. Recognizing sepsis as a global health priority — a WHO resolution. N Engl J Med. 2017;377:414-417.

18. Roca A, Oluwalana C, Bojang A, et al. Oral azithromycin given during labour decreases bacterial carriage in the mothers and their offspring: a double-blind randomized trial. Clin Microbiol Infect. 2016.

19. Tita AT, Szychowski JM, Boggess K, et al. Adjunctive azithromycin prophylaxis for cesarean delivery. N Engl J Med. 2016;375:1231-1241.

20. Bojang A, Camara B, Jagne Cox I, et al. Long-term impact of oral azithromycin taken by Gambian women during labor on prevalence and antibiotic susceptibility of Streptococcus pneumoniae and Staphylococcus aureus in their infants: follow-up of a randomized clinical trial. Clin Infect Dis. 2018.

21. Bojang A, Baines SL, Camara B, et al. Impact of intrapartum oral azithromycin on the acquired macrolide resistome of infants' nasopharynx: a randomized controlled trial. Clin Infect Dis. 2020.

22. Tita ATN, Carlo WA, et al. Azithromycin to prevent sepsis or death in women planning a vaginal birth. New England Journal of Medicine. DOI: 10.1056/NEJMoa2212111.