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Review article

Vertical transmission of multidrug-resistant pathogens: Challenges and strategies in maternal and neonatal care

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ABSTRACT

Background: The increasing prevalence of multidrug-resistant (MDR) pathogens presents a critical threat to maternal and neonatal health worldwide. Vertical transmission of these pathogens from mother to child can occur at various stages, including in utero, during delivery, and postnatally through breastfeeding or close contact. Such transmission pathways significantly contribute to neonatal morbidity and mortality, often leading to severe infections that are challenging to treat due to limited therapeutic options. This review delves into the mechanisms underlying vertical transmission, providing insights into the epidemiology, risk factors, and clinical impact of MDR pathogens on neonatal health outcomes. Furthermore, it highlights the current challenges associated with early detection, accurate diagnosis, and effective prevention of these infections within healthcare settings. Addressing this complex issue requires a multifaceted strategy that incorporate enhanced surveillance, antimicrobial stewardship, and infection control measures. Emphasizing the importance of a One Health approach, this review underscores the need for interdisciplinary collaboration across human, animal, and environmental health sectors to mitigate the spread of MDR pathogens and safeguard maternal and neonatal well-being.

Introduction

Antimicrobial resistance (AMR) is increasingly recognized as one of the most pressing global public health threats of the 21st century. The widespread misuse and overuse of antibiotics in human medicine, veterinary practice, and agriculture have accelerated the emergence and dissemination of multidrug-resistant (MDR) pathogens, rendering many conventional treatments ineffective. This growing crisis not only threatens individual patient outcomes but also undermines broader public health efforts to control infectious

diseases, leading to longer hospital stays, increased medical costs, and higher mortality rates.

Among the populations most vulnerable to AMR, pregnant women and neonates face particularly grave risks. Neonates, in particular, are at heightened susceptibility to MDR infections due to their immature immune systems, limited exposure to diverse microbial environments, and reliance on maternal microbial transfer for early immune development. Infections caused by MDR pathogens in this group are associated with severe complications, including neonatal sepsis, pneumonia, and meningitis, which contribute

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significantly to neonatal morbidity and mortality worldwide. The burden of MDR infections is especially pronounced in low- and middle-income countries (LMICs), where limited access to appropriate antimicrobial therapy, inadequate infection control measures, and a high prevalence of hospital-acquired infections exacerbate the problem.

One of the key pathways for the persistence and spread of MDR pathogens in neonatal populations is vertical transmission, the transfer of pathogens from mother to child during pregnancy, childbirth, or postpartum interactions. This transmission route is complex and influenced by multiple factors, including the maternal microbiome composition, the presence of MDR bacteria in the maternal genital or gastrointestinal tract, the mode of delivery (vaginal birth versus cesarean section), and the neonatal gut colonization patterns postnatally. Additionally, maternal antibiotic exposure during pregnancy or labor significantly alter both the maternal and neonatal microbiota, potentially promoting the selection and persistence of resistant strains.

Given the critical role of vertical transmission in the perpetuation of MDR infections across generations, a deeper understanding of its mechanisms is essential for developing targeted interventions. Strategies to mitigate the impact of vertical transmission include improved maternal screening protocols, judicious use of antibiotics during pregnancy and labor, promotion of breastfeeding to support neonatal immune development, and enhanced infection prevention and control practices in healthcare settings.

This review aims to provide comprehensive analysis of the mechanisms underlying vertical transmission of **MDR** pathogens, evaluate the current burden of MDR infections in maternal and neonatal populations, and explore potential strategies to curb this escalating public health challenge. By synthesizing current evidence, this review seeks to inform clinical practices and public health policies aimed at reducing the impact of AMR in vulnerable populations.

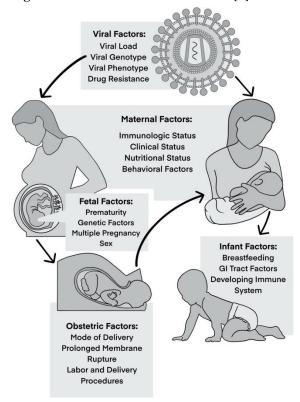
Mechanisms of vertical transmission

The mechanisms through which MDR pathogens are transmitted from mother to child can be broadly categorized into three stages: placental transfer, perinatal exposure during delivery, and postnatal transmission. Each of these pathways

presents unique challenges and opportunities for intervention [1,2].

The placenta, typically seen as a protective barrier for the growing foetus against dangerous pathogens, can paradoxically function as a conduit for microbial transmission. Research has shown the existence of multidrug-resistant bacteria, including Escherichia coli and Klebsiella pneumoniae, in placental tissues, indicating that these pathogens can penetrate the placental barrier [7]. Their techniques involve the exploitation of trophoblast invasion pathways, wherein bacteria usurp the normal cellular processes that enable placental growth and nutrient exchange. Furthermore, bacterial infection can provoke localised inflammation in the placenta, resulting in compromised barrier integrity and facilitating the translocation of pathogens into foetal circulation [8]. This form of transmission is particularly concerning in cases where maternal infections go undiagnosed or are inadequately treated, allowing MDR pathogens to establish a foothold within the intrauterine environment [3].

Figure 1. Mechanism of vertical transfer [4].



The perinatal period represents another critical window for the transmission of MDR pathogens. The mode of delivery plays a significant role in determining the extent of neonatal exposure to maternal microbiota, which may harbor resistant

organisms. Vaginal delivery, for instance, exposes neonates to maternal vaginal and fecal microbiota, which can include MDR strains such as vancomycin-resistant Enterococcus (VRE) and extended-spectrum beta-lactamase (ESBL)producing Enterobacteriaceae. These bacteria can colonize the neonate's skin and gastrointestinal tract, potentially leading to early-onset infections and long-term colonization. On the other hand, cesarean section deliveries, while circumventing direct exposure to vaginal microbiota, introduce their own risks [5]. The routine administration of prophylactic antibiotics during cesarean procedures contribute to the selection and proliferation of organisms, altering resistant the neonatal microbiome in ways that may predispose the infant to opportunistic infections and antibiotic-resistant colonization.

Postnatal transmission of MDR pathogens is a multifaceted issue that encompasses several potential routes, including breastfeeding, close maternal contact, and exposure to the healthcare environment. Breastfeeding, while offering numerous immunological and nutritional benefits, can also serve as a vehicle for pathogen transmission [6]. Methicillin-resistant Staphylococcus aureus (MRSA) has been detected in both breast milk and on maternal skin, posing a risk of neonatal colonization and infection. The intimate contact involved in breastfeeding and routine caregiving practices facilitates the transfer of MDR organisms from mother to child, underscoring the need for stringent hygiene measures and targeted interventions to minimize transmission risks [7].

Healthcare-associated infections (HAIs) further complicate the postnatal period, particularly in neonatal intensive care units (NICUs), where vulnerable infants are exposed to a wide array of potential pathogens. NICUs provide an environment where MDR bacteria can thrive due to high antibiotic usage, invasive procedures, and prolonged hospital stays [8]. Environmental contamination from surfaces, medical equipment, and healthcare personnel can contribute to the spread of MDR pathogens, with outbreaks of organisms such as carbapenem-resistant Acinetobacter baumannii and ESBL-producing *Klebsiella pneumoniae* frequently reported in these settings. Strict infection control protocols, including hand hygiene, environmental decontamination, and antimicrobial stewardship programs, are crucial to minimizing the burden of MDR infections in hospital settings [9].

The burden of MDR pathogens in maternal and neonatal health

The burden of multidrug-resistant infections in maternal and neonatal health is significant and complex, and it affects both groups. There is a tremendous pressure placed on healthcare systems all over the world as a result of infections caused by MDR bacteria, which are associated with increased morbidity, mortality, and monetary expenditures for medical care [15]. Women who are pregnant and have MDR infections are at an increased risk of complications such as preterm chorioamnionitis, and postpartum endometritis. Each of these complications has the potential to have a domino impact on the outcomes for the newborn being considered. There is a higher likelihood that neonates who are born to mothers who have been colonized with multidrug-resistant organisms will suffer severe illnesses such as sepsis, pneumonia, and other infections that require urgent medical care [16].

As a result of geographical disparities in healthcare infrastructure, antibiotic usage habits, and infection control methods, the global distribution of multidrug-resistant infections in maternal and newborn populations differs. For a variety of reasons, including restricted access to healthcare resources, insufficient surveillance systems, and suboptimal antimicrobial stewardship, low- and middle-income countries (LMICs) endure a disproportionate burden of these illnesses. Overuse and improper use of antibiotics in human and veterinary medicine both contribute to the development and spread of antibiotic resistance, which in turn makes the task of managing multidrug-resistant diseases much more difficult to manage [16].

The prevalence of multidrug-resistant (MDR) pathogens among neonates is a growing global concern, with significant variations across different regions [13,14]. The highest burden of these infections is observed in LMICs, where healthcare infrastructure and resources are often insufficient to combat such threats effectively. Neonatal sepsis caused by MDR *Klebsiella pneumoniae* has been reported at alarming rates, particularly in South Asia and sub-Saharan Africa [14]. These regions face unique challenges related to infection control, antimicrobial stewardship, and the availability of appropriate treatment options. Additionally, carbapenem-resistant *Acinetobacter baumannii* has emerged as a significant pathogen in

neonatal intensive care units (NICUs) worldwide, further complicating the management of infections in this vulnerable population [15].

The impact of MDR infections on neonatal outcomes is profound and multifaceted. Neonates infected with MDR pathogens face an increased risk of severe sepsis and septic shock, conditions that significantly contribute to morbidity and mortality in this age group. Such infections often lead to prolonged hospital stays, which not only increase healthcare costs but also expose neonates to additional nosocomial infections and complications [16]. Furthermore, the long-term consequences of MDR infections extend beyond hospitalization, as they are associated with neurodevelopmental impairments that can affect cognitive and physical development. These impairments may result from direct bacterial invasion of the central nervous system, systemic inflammatory responses, or the toxic effects of prolonged antibiotic use [17]. Mortality rates for neonatal sepsis caused by MDR pathogens are particularly concerning, with estimates suggesting that over 40% of affected neonates succumb to the infection, highlighting the urgent need for improved prevention and treatment strategies.

Strategies to combat vertical transmission of MDR pathogens

Addressing the challenge of vertical transmission of MDR pathogens requires a multifaceted approach that combines surveillance, prevention, and treatment strategies. Strengthening surveillance systems to monitor the prevalence and distribution of MDR pathogens in maternal and neonatal populations is essential for guiding evidence-based interventions [10]. Routine screening of pregnant women for colonization with high-risk MDR bacteria, such as ESBL-producing Escherichia coli and carbapenem-resistant Klebsiella pneumoniae, can facilitate early identification and targeted management to reduce transmission risks [11].

Infection prevention measures ought to be given top priority throughout the entirety of the continuum between the mother and the newborn. It is important for antenatal care programs to incorporate instruction on infection prevention measures. These activities include proper hand cleanliness, safe food handling, and the appropriate use of medications under appropriate circumstances. The practices of delivery should be optimized in

order to minimize the exposure of neonates to multidrug-resistant bacteria. This should be done with careful assessment of the risks and benefits associated with the various modes of delivery offered. In order to reduce the risk of healthcare-associated infections, postnatal care should place an emphasis on the significance of adhering to stringent cleanliness procedures, particularly in neonatal intensive care unit (NICU) environments [17].

Antimicrobial stewardship programs play a critical role in curbing the emergence and spread of resistance by promoting the rational use of antibiotics. Implementing guidelines for the appropriate use of prophylactic antibiotics during pregnancy and delivery can help reduce selective pressure on bacterial populations and prevent the proliferation of resistant strains. Research into alternative therapies, such as probiotics and bacteriophage therapy, also holds promise for managing MDR infections without contributing to further resistance [12].

Detection and surveillance strategies

Accurate and timely diagnosis of MDR infections is critical for effective management and improved neonatal outcomes [13]. Advances in diagnostic technologies have the potential to revolutionize the detection of MDR pathogens, enabling rapid and precise identification of resistance genes and infectious agents directly from clinical specimens. Multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) are among the most promising tools in this regard, offering high sensitivity and specificity in detecting a wide range of pathogens [14]. These technologies allow clinicians to initiate targeted antibiotic therapy more quickly, thereby improving patient outcomes and reducing the unnecessary use of broad-spectrum antibiotics. However, despite their potential, the widespread implementation of these diagnostic tools remains a challenge in many LMICs due to high costs, infrastructure limitations, and the need for specialized training of healthcare personnel [15].

In addition to improving diagnostic capabilities, maternal screening represents an essential strategy for the early detection and prevention of neonatal MDR infections. Routine screening of pregnant women for MDR pathogens can help identify colonized mothers and facilitate timely interventions to prevent vertical transmission [16]. Screening for Group B *Streptococcus* (GBS)

during pregnancy has been widely adopted in many countries and serves as a valuable model for expanding pathogen screening protocols to include MDR organisms. By identifying colonized mothers before delivery, healthcare providers can implement targeted interventions such as prophylactic antibiotics or enhanced infection control measures to reduce the risk of neonatal infection [17]. However, the success of maternal screening programs depends on several factors, including the availability of reliable diagnostic tests, the implementation of standardized screening protocols, and the willingness of healthcare systems to invest in preventive care.

Surveillance programs are essential for monitoring the frequency of multidrug-resistant organisms and informing public health measures. Global initiatives, such the World Health Organization's (WHO) Global Antimicrobial Resistance and Use Surveillance System (GLASS), furnish critical data on the epidemiology of multidrug-resistant illnesses and assist in shaping policy decisions at national and international tiers. Surveillance initiatives facilitate the detection of growing resistance patterns, enabling healthcare professionals and governments to respond preemptively with specific treatments [26].

Additionally, robust surveillance systems can facilitate the evaluation of antimicrobial stewardship programs and infection control measures, ensuring that resources are allocated effectively to combat the spread of MDR pathogens. However, the success of surveillance initiatives requires strong collaboration between healthcare institutions, regulatory agencies, and research organizations to ensure the collection and analysis of high-quality data [18].

Strategies for prevention and management

Preventing MDR infections in neonates requires a comprehensive approach that includes infection control measures, antimicrobial stewardship, and the promotion of maternal and neonatal health [14]. Rigorous compliance with infection prevention and control (IPC) policies in healthcare settings is crucial for mitigating the spread of multidrug-resistant bacteria. This encompasses hand hygiene, ambient sanitation, and the utilisation of personal protective equipment (PPE) to reduce the danger of cross-contamination. The adoption of antimicrobial stewardship programs in newborn units can optimise antibiotic use, ensuring prescriptions are made only when necessary and in alignment with evidence-based standards. These activities are essential for averting the emergence and dissemination of antibiotic resistance, especially in environments characterised by the misuse and overuse of antibiotics [25].

Education and awareness campaigns workers. healthcare targeting parents, communities are also important components of prevention strategies. Training programs that emphasize the importance of hand hygiene, proper antibiotic use, and early recognition of infection signs can empower caregivers to take proactive measures in protecting neonates from MDR infections. Public health initiatives aimed at promoting maternal health and prenatal care can further contribute to reducing the risk of neonatal infections by addressing underlying risk factors such as preterm birth, low birth weight, and maternal infections [13].

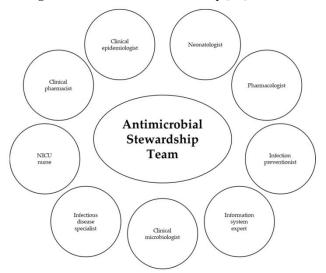
Antimicrobial Stewardship during pregnancy

Antimicrobial stewardship pregnancy is a crucial component in the fight against MDR bacterial infections. The judicious use of antibiotics in pregnant women is essential to mitigate the selection pressure that drives the emergence and spread of MDR strains [19]. Pregnancy presents unique challenges, as both maternal and fetal health must be considered when prescribing antimicrobial agents. Tailored antibiotic regimens, guided by susceptibility testing, offer a targeted approach that minimizes unnecessary antibiotic exposure while ensuring effective treatment of infections [20]. This approach helps to reduce the risk of complications arising from both untreated infections and the adverse effects of inappropriate antibiotic use. Furthermore, healthcare providers must be well-versed in current guidelines and resistance patterns to optimize treatment strategies. Patient education regarding the responsible use of antibiotics and adherence to prescribed regimens is equally important in minimizing resistance [21].

Infection control measures in labor and delivery settings play a pivotal role in preventing the transmission of MDR pathogens. One of the most fundamental aspects of infection control is the enforcement of strict hygiene practices. Proper hand hygiene protocols, including the use of alcoholbased hand sanitizers and thorough handwashing techniques, are essential to reducing the risk of nosocomial infections [22]. Additionally, sterilization of delivery equipment and adherence to

aseptic techniques during childbirth are critical to preventing contamination and subsequent infections. Healthcare facilities must implement standardized protocols for cleaning and disinfecting labor and delivery rooms to minimize environmental reservoirs of MDR organisms [22].

Figure 2. Antimicrobial stewardship [24].



The use of prophylactic antibiotics is often necessary, particularly in cases of cesarean deliveries, to prevent post-operative infections. However, the indiscriminate or inappropriate use of these antibiotics can contribute to the development of resistance. It is essential to carefully select antibiotics based on established guidelines, considering local resistance patterns and the individual patient's risk factors. Adherence to evidence-based protocols for prophylactic antibiotic administration can help strike a balance between preventing infections and minimizing the risk of resistance development. In addition, continuous surveillance and periodic audits of antibiotic use in obstetric settings can identify areas for improvement and ensure compliance with best practices [25].

Neonatal intensive care units (NICUs) represent a high-risk environment for the transmission of MDR pathogens, necessitating stringent infection prevention and control measures. One of the most effective strategies to prevent the spread of MDR organisms in NICUs is the implementation of contact precautions. Neonates colonized with MDR bacteria should be isolated in designated areas to prevent cross-transmission to other vulnerable infants. Healthcare workers must adhere to strict personal protective equipment (PPE)

protocols when handling colonized neonates to minimize the risk of spreading pathogens [16].

Environmental cleaning and disinfection in NICUs are critical to reducing the microbial load of MDR organisms. Routine cleaning of surfaces, medical equipment, and high-touch areas using hospital-grade disinfectants can help eliminate potential reservoirs of infection. Regular surveillance microbiological of the **NICU** environment can aid in identifying potential sources of contamination and inform targeted cleaning interventions [26]. Furthermore, adopting antimicrobial stewardship principles in NICUs by limiting the use of broad-spectrum antibiotics to cases where they are absolutely necessary can help preserve the efficacy of existing antimicrobial agents.

Another promising strategy in neonatal care is the use of probiotics to support the development of a healthy gut microbiome. Beneficial bacteria such as *Lactobacillus* and *Bifidobacterium* have been shown to promote gut health and may help outcompete MDR pathogens, reducing their colonization and potential for infection [27]. Probiotic supplementation in neonates, particularly those born prematurely or with compromised immune systems, can offer a non-antibiotic approach to infection prevention. Ongoing research is needed to determine the optimal strains, dosages, and duration of probiotic therapy in neonates to maximize their benefits while ensuring safety.

Vaccination is a cornerstone of infectious disease prevention and plays a significant role in reducing the burden of MDR bacterial infections. Maternal vaccination against common pathogens such as *Streptococcus pneumoniae* and influenza has been shown to provide passive immunity to neonates, reducing their exposure to these infections during the critical early months of life. Ensuring high vaccination coverage among pregnant women through targeted public health campaigns and education can significantly reduce neonatal morbidity and mortality associated with preventable infections [21].

In addition to existing maternal vaccines, ongoing research into vaccines targeting MDR bacteria holds promise for enhancing preventive strategies. The development of vaccines against MDR pathogens such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and carbapenem-resistant

Enterobacterales could provide an additional layer of protection in high-risk populations, including pregnant women and neonates. Encouraging investment in vaccine research and development, as well as ensuring equitable access to new vaccines, will be essential in combating the growing threat of antimicrobial resistance [28].

Comprehensive education and training of healthcare professionals are fundamental to the successful implementation of intervention and prevention strategies. Healthcare providers should receive regular training on the latest guidelines and best practices in antimicrobial stewardship, infection control, and neonatal care. This training should emphasize the importance of a multidisciplinary approach, where obstetricians, neonatologists, microbiologists, and infection control specialists collaborate to optimize patient care and minimize the risk of MDR infections [29].

Public health initiatives aimed at raising awareness about antimicrobial resistance and infection prevention among pregnant women and their families are equally important. Educating expectant mothers about the dangers of self-medication, the importance of completing prescribed antibiotic courses, and the benefits of vaccination can empower them to make informed decisions about their health and that of their newborns. Community-based interventions, such as antenatal classes and outreach programs, can serve as valuable platforms for disseminating this information and promoting healthy behaviors [30].

Future perspectives and one health approaches integrating human, animal, and environmental health

The One Health framework underscores the intricate connections between human, animal, and environmental health, emphasizing that these domains are not isolated but rather interdependent [31]. The rise of MDR pathogens necessitates a comprehensive approach that transcends traditional boundaries of healthcare. Addressing antibiotic misuse in agriculture is a critical component of this strategy. The widespread use of antibiotics in livestock for growth promotion and disease prevention has led to the emergence of resistant bacterial strains, which can be transmitted to humans through the food chain, direct contact, or environmental pathways [32]. Moreover, resistant bacteria and antibiotic residues often enter natural ecosystems through agricultural runoff and wastewater discharge, contaminating soil and water

sources. This environmental contamination creates a reservoir of resistance that can persist and spread, complicating efforts to control MDR infections [33].

To mitigate these challenges, stringent regulations and policies must be implemented to curb the overuse and misuse of antibiotics in agriculture. Educational initiatives targeting farmers and veterinarians can promote responsible antibiotic Additionally, stewardship. environmental monitoring programs are essential to track the presence and spread of resistant bacteria in soil, water, and wildlife [34]. Efforts should also focus on developing sustainable agricultural practices that reduce reliance on antibiotics, such as improved hygiene, vaccination programs for animals, and the use of probiotics to enhance livestock health. Collaboration between public health authorities, veterinarians, and environmental scientists is crucial to create integrated strategies that address the root causes of antibiotic resistance and protect the interconnected health of humans, animals, and ecosystems [35].

Conclusion

Vertical transmission of MDR pathogens poses a significant challenge to maternal and neonatal healthcare, with potentially devastating consequences for both mothers and newborns. Addressing this issue requires a multifaceted approach that encompasses enhanced surveillance, rational antibiotic use, robust infection control practices, and a commitment to global collaboration under the One Health framework. Enhanced surveillance systems can provide critical insights into resistance trends and inform targeted interventions. Rational antibiotic use, supported by evidence-based guidelines and antimicrobial stewardship programs, can help preserve the efficacy of existing drugs and prevent the emergence of resistance. Robust infection control practices, including stringent hygiene protocols and the implementation of advanced sterilization techniques, are essential to minimizing the spread of MDR pathogens in healthcare settings.

Competing interests

None.

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None.

Data availability

All data generated or analyzed during this study are included in this puplished article.

Authors' contribution

All authors made significant contributions to the work presented, including study design, data collection, analysis, and interpretation. They also contributed to the article's writing, revising, or critical evaluation, gave final approval for the version to be published.

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