

Antimicrobial resistance and epidemiological trends of *Clostridioides difficile* in South-Eastern Nigeria: A regional perspective

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Abstract

A leading cause of gastrointestinal disorders linked to healthcare, *Clostridioides difficile* infection (CDI) is becoming more and more problematic worldwide as a result of its growing resistance to first-line treatments. The exact prevalence and molecular epidemiology of *C. difficile* are still poorly understood in low- and middle-income countries (LMICs), such as Nigeria. The incidence, molecular traits, and dynamics of antibiotic resistance of *C. difficile* clinical isolates in southeast Nigeria are summarized in this review. Regional data shows that CDI is under recognized due to poor surveillance infrastructure, low clinical suspicion, and diagnostic constraints. The data that is now available indicates that the number of toxigenic strains is increasing, especially those that possess the binary toxin genes (*cdtA/B*), *tcd9A*, and *tcdB*. Despite its limitations, molecular typing shows that there are a variety of potentially hyper-virulent ribotypes present. A concerning trend that raises worries about treatment failure and extended hospital admissions is the emergence of resistance to routinely used antibiotics like vancomycin and metronidazole. The issue is exacerbated by inadequate infection control procedures, inappropriate antibiotic use, and a lack of stewardship initiatives.

In South-eastern Nigeria, there is an urgent need to implement antibiotic stewardship and infection control strategies, develop standardized diagnostic procedures, and bolster molecular surveillance. To reduce the growing threat of *C. difficile* in the area, more awareness, policy integration, and capacity building are essential.

Keywords: *Clostridioides difficile*; Antimicrobial Resistance; Molecular Characterization; Healthcare-Associated Infections; *Clostridioides Difficile* Infection (CDI)

1. Introduction

Clostridioides difficile has become a serious hazard to world health, especially in medical facilities. *C. difficile* infection (CDI)-related age-standardized disability-adjusted life years (DALYs) approximately doubled globally between 1990 and 2021, with the biggest burden occurring in high socio-demographic index regions and among people over 70 (1). The United States recorded more than 223,000 illnesses and 12,800 fatalities in 2019 alone (2). The increase in the illness is directly related to the overuse of antibiotics, which alters gut microbiota and increases the risk of recurrence in up to 30% of patients (3). These patterns highlight the critical need for targeted measures, antibiotic stewardship, and worldwide surveillance to stop this growing public health emergency.

In order to tackle antimicrobial resistance (AMR), local epidemiological surveillance is essential since it allows for the prompt identification of resistance patterns and directs focused efforts. Effective stewardship initiatives are informed by strong local monitoring systems, which improve data representativeness (4). Local public health organizations are

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in a unique position to apply antimicrobial stewardship and AMR monitoring, bridging the gap between clinical practice and policy (5). The SPIDAAR project in Africa has shown how localized surveillance improves laboratory capabilities and helps guide national antimicrobial resistance policy (6). Enhancing local surveillance is therefore crucial for data-driven, responsive AMR containment.

The high rate of antibiotic abuse, lack of adequate diagnostic facilities, and the low infection rates in south-east Nigeria make this region a crucial focus for study on *Clostridioides difficile*. *Clostridioides difficile* isolates from clinical samples in the area were found to have significant antibiotic resistance and to possess the main virulence genes *tcdA*, *tcdB*, *cdtA*, and *cdtB*, with multiple antibiotic resistance (MAR) score of 0.44 showing indicated significant resistance pressure (7). Furthermore, food-borne transmission pathways were identified in nearby marketplaces, indicating potential exposure hazards for the entire population (8). To reduce the increasing burden of CDI, targeted surveillance and customized therapies are desperately needed, as evidenced by the region's healthcare vulnerabilities and the lack of molecular epidemiological data.

This narrative review aims to evaluate the prevalence, molecular traits, and trends of antibiotic resistance of *Clostridioides difficile* in South-eastern Nigeria, where information is still limited. The review summarizes results from current research showing that both clinical and food-borne isolates have a high multiple antibiotic resistance index (0.44) and virulence genes (*tcdA*, *tcdB*, *cdtA*, *cdtB*) (7, 8). The aim is to investigate the causes of resistance, such as improper use of antibiotics and a lack of proper diagnostic facilities, and to provide information for surveillance and treatment plans tailored to a certain area. The scope covers *C. difficile* infections that are acquired in hospitals as well as those that are linked to the community in five states in the southeast.

2. Epidemiology and Clinical Burden of *C. difficile*

2.1. Global prevalence trends and disease burden

The incidence and mortality of *Clostridioides difficile* infection (CDI) are increasing in all age categories, making it a serious worldwide health concern. Globally, age-standardized DALYs from *Clostridioides difficile* infection approximately quadrupled between 1990 and 2021, with high socio-demographic index regions and those over 70 being disproportionately affected (1). Hypervirulent strains and antibiotic abuse were the main causes of the CDI-related mortality increase in high-SDI nations. Recurrence affects up to 30% of patients and is still a significant problem (2).

2.2. Overview of *C. difficile* infection (CDI) cases in Africa and Nigeria

Clostridioides difficile infection (CDI) is being more recognized as a major public health concern throughout Africa, with Nigeria becoming a focus point for regional epidemiological insights (9). *Clostridioides difficile* infection (CDI) is an under recognized but increasingly documented cause of diarrhea related with healthcare in Africa. *Clostridioides difficile* infection was highlighted as a major nosocomial concern in a 2020 South African guideline, which suggested standardized diagnostic and infection control procedures suited to environments with minimal resources (10). A 2020 case series from Ethiopia revealed pseudo-membranous colitis in four hospitalized patients, indicating some of the first verified instances of CDI in the nation and bringing attention to sub-Saharan Africa's diagnostic difficulties (9). The global impact of CDI was further highlighted in a 2025 systematic review conducted by researchers at the University of Ghana. They noted that juvenile populations and healthcare facilities had disproportionately high risks, and that there was little data from African countries because of underreporting and diagnostic deficiencies (11).

A study conducted in south-eastern Nigeria found that hospitalized patients had a significant frequency of CDI, along with high levels of antibiotic resistance and virulence genes including *tcdA*, *tcdB*, *cdtA*, and *cdtB* (7). Likewise, north-central Nigerian genomic surveillance revealed nearly identical human-animal *C. difficile* strains, highlighting the dangers of zoonotic transmission and the necessity of a One Health strategy for CDI management (12). In spite of these results, due to a lack of awareness and diagnostic resources, CDI is still under diagnosed in many Nigerian healthcare settings (13). As reported in 2024 of a study conducted in northern Nigeria, there was a significant association between the length of hospitalization and the amount of diarrhea, with over half of adult outpatients testing positive for toxic *C. difficile* (14). In order to address the clinical burden of CDI in Nigeria and the larger African region, these results collectively highlight the urgent need for improved surveillance, diagnostic capability, and antibiotic stewardship.

2.3. Incidence and risk factors specific to South-eastern Nigeria

In South-Eastern Nigeria, recent studies have shown a worrying prevalence of *Clostridioides difficile* infection (CDI), especially in hospitalized patients who have been exposed to antibiotics for an extended period (7). A Multi-center

research conducted in five states in the region published in 2025 found that 45% of symptomatic inpatients had CDI, with isolates showing high levels of erythromycin and tetracycline resistance and a multiple antibiotic resistance (MAR) index of 0.44 (7). The pathogenic potential of circulating strains was highlighted by molecular analysis, which verified the presence of important virulence genes (*tcdA*, *tcdB*, *cdtA*, *cdtB*) and resistance determinants (*tetS*, *tetA*, *ermB*) (7). The risk factors associated with the region include advanced age, empirical antibiotic medication, recent hospitalization, and comorbidities such as proton pump inhibitor use and inflammatory bowel disease. Significantly, the finding of *C. difficile* in food and clinical samples raises questions regarding food safety and hygiene standards for the public by pointing to potential environmental and dietary transmission pathways (8). These results demonstrate the critical need for antibiotic stewardship, public health education, and region-specific CDI surveillance to reduce the increasing clinical burden in southeast Nigeria.

2.4. Healthcare-associated vs community-acquired CDI

The epidemiology of *Clostridioides difficile* infection (CDI) has been shown to change between 2020 and 2025, with community-acquired cases being more prevalent than those obtained in medical facilities. The Centers for Disease Control and Prevention, in a historic study conducted in the United States, reported a crude CDI incidence of 101.3 cases per 100,000 people in 2020. Community-associated CDI (CA-CDI) was slightly higher than healthcare-associated CDI (HA-CDI), with 51.2 and 50.1 cases per 100,000 people, respectively (15). This pattern persisted in the years that followed, with CA-CDI making up an increasing portion of all cases, particularly in younger people who had not recently been exposed to healthcare (16).

In individuals who have not recently been hospitalized, a positive *C. difficile* stool sample obtained in an outpatient setting or within three days of hospital admission is commonly referred to as CA-CDI. (15, 16). On the other hand, HA-CDI comprises cases that began while the patient was in the hospital or soon after they were released, and are frequently linked to long-term antibiotic usage, comorbidities, or advanced age (17, 18). Recent advances in genomic surveillance have improved our knowledge of CDI risk profiles by identifying unique resistance and recurrence patterns linked to HA-CDI (17, 18). These results highlight the significance of extending CDI prevention tactics outside of hospital settings to incorporate environmental cleanliness, community-level One Health surveillance, and outpatient antibiotic stewardship (15, 16).

3. Molecular Characteristics of Clinical Isolates

3.1. Toxin gene profiles (*tcdA*, *tcdB*, *cdtA/B*)

The toxin genes of *Clostridioides difficile*, particularly *tcdA* (toxin A), *tcdB* (toxin B), and the binary toxin genes *cdtA* and *cdtB*, are the main mediators of the pathogenicity of the organism. The expression patterns of these genes, which are found in the pathogenicity locus (PaLoc) and the distinct CdtLoc, respectively, are important indicators of clinical severity and epidemiological dissemination (19, 20). Global variation in toxin gene distribution among clinical isolates has been highlighted by recent investigations, with developing hypervirulent strains frequently including all three toxin types (20). With 100% of isolates containing *tcdA* and *tcdB* and a sizable percentage also testing positive for *cdtA* and *cdtB*, A study conducted in southeast Nigeria revealed a high incidence of toxic *C. difficile* strains. The dual threat of virulence and therapeutic challenge was highlighted by the correlation between this molecular profile and increased antibiotic resistance (7). In a similar vein, a multicenter study conducted in Xi'an, China, found that 3.85% of isolates had binary toxin genes and 78.2% were *tcdA*⁺/*tcdB*⁺, indicating regional variation in toxin gene prevalence and serious clinical consequences (21). Binary toxin genes have been linked to higher cytotoxicity and mortality, especially in strains with *tcdC* regulatory gene deletions or mutations that could result in dysregulated toxin expression. In order to identify changes in toxin gene profiles and guide infection control measures, these results highlight the importance of regular molecular surveillance.

3.2. Ribotyping and PCR-based molecular epidemiology

In order to understand the genetic diversity and transmission dynamics of *Clostridioides difficile*, PCR-based molecular epidemiology and ribotyping are very important. The 16S–23S rRNA intergenic spacer region is the focus of PCR ribotyping, which is still a popular technique for strain differentiation. In a Chinese hospital, it was found that out of 55 isolates, 15 ribotypes were found, with RT449 being the most common which highlighted the necessity for surveillance and regional genotype variation (22). Nevertheless, the resolution and portability of PCR ribotyping are restricted. The shift to whole genome sequencing (WGS) has demonstrated that although Multilocus Sequence Typing frequently corresponds with ribotypes, core genome MLST (cgMLST) provides better precision for tracking outbreaks and analyzing transmission (23). The characterization of *C. difficile* isolates in Nigeria using PCR to identify resistance markers (*tetS*, *tetA*, *ermB*) and virulence genes (*tcdA*, *tcdB*, *cdtA*, *cdtB*) revealed substantial antibiotic resistance and

genetic variability across clinical strains (7). These results highlight how crucial molecular tools are for directing infection prevention and treatment plans, particularly in areas with weak diagnostic capabilities. Ribotyping and PCR-based techniques work together to offer important insights into the epidemiology of *C. difficile*, but integration with WGS is becoming more and more advised for thorough surveillance.

3.3. Dominant strains reported in Nigeria and West Africa

In Nigeria and West Africa, an area that was previously under-reported in international surveillance, recent investigations have started to reveal the molecular epidemiology of *Clostridioides difficile*. A thorough examination of 450 stool samples from southeast Nigeria revealed 14 strains of clinical *C. difficile* (7). Toxin B-positive strains were more common, as evidenced by the fact that all isolates had the *tcdB* gene, 69.56% expressed *tcdA*, and just one isolate had binary toxin genes (*cdtA* and *cdtB*). The study also found notable patterns of resistance, with isolates exhibiting resistance to erythromycin and tetracycline but susceptibility to gentamicin, meropenem, and amoxicillin-clavulanic acid. The existence of multidrug-resistant bacteria was indicated by the multiple antibiotic resistance (MAR) index, which reached 0.44 (7). The burden of toxigenic strains on clinical outcomes was highlighted by a study conducted in Katsina State that revealed 48.4% of adult patients tested positive for toxigenic *C. difficile* using culture and PCR, and that the length of diarrhea was substantially connected with hospital stay duration (24). Hospitals in Nigeria have a difficult time detecting *C. difficile*, pointing out that availability to molecular testing and toxin tests is limited. They also need better PCR-based techniques that are adapted to local diagnostic capabilities (25). Mutai and colleagues discovered that a quarter of hospitalized patients with diarrhea had *C. difficile*. Over 85% of the 71 confirmed isolates were multidrug-resistant, exhibiting high resistance to rifampicin, erythromycin, ciprofloxacin, and clindamycin, and 97.1% of them carried at least one toxin gene. Despite the fact that every isolate was vancomycin-sensitive, three of them were metronidazole-resistant. This study emphasizes the effects of past exposure to antibiotics and the rise of resistant bacteria in East Africa (26). Data on *C. difficile* infections throughout Africa were compiled in a narrative study, which also pointed out that strain typing is uncommon and frequently restricted to a particular institution. The review pointed out that strains like ribotype 017 (RT017), which are toxin B-positive and toxin A-negative, are quite common, especially in sub-Saharan Africa. In order to gain a better understanding of circulating strains, the review urged for more molecular surveillance and highlighted the fact that African CDI patients are typically younger, most likely as a result of comorbidities like tuberculosis (27). In West Africa, ribotyping data is scarce, but PCR-based molecular detection of virulence and resistance genes provide vital information about circulating strains. These results are in line with worldwide patterns, where toxin B-positive strains, such as ribotype 017 (RT017), have become more well-known because of their resistance characteristics and propensity for nosocomial transmission (28). The identification of dominant ribotypes and the direction of infection control measures in the area depend on ongoing genomic surveillance.

3.4. Genetic diversity and its clinical implications

The pathogenicity, antibiotic resistance, and clinical consequences of *C. difficile* are significantly influenced by its genetic diversity. Disease severity and recurrence are associated with differences in toxin gene profiles, namely those of binary toxin genes (*cdtA*, *cdtB*) and *tcdA*, *tcdB*. In a study from South-eastern Nigeria, it was discovered that clinical isolates primarily expressed *tcdB*, with 69.56% also expressing *tcdA*. Additionally, just one isolate had binary toxin genes, which may indicate that ribotype RT017 strains predominate. These isolates had a MAR score of 0.44, which indicates multidrug resistance, and they also carried resistance genes (*tetS*, *tetA*, and *ermB*) (7). Globally, *C. difficile* isolates from Mexican hospitals have shown a high degree of genetic variety. The most common clade, 2/ST1, has been found to have diverse cytotoxicity profiles and various toxin subtypes (*TcdA2*, *TcdB2*) (29). This variation makes diagnosis and therapy more difficult because genotypic classification and toxin expression are not always correlated. The significance of genomic surveillance in forecasting clinical outcomes is highlighted by the fact that mutations in regulatory genes, such as *cdtR*, can reduce virulence in ST1 strains without impacting colonization (30). Comprehending this variability is crucial for creating focused diagnoses, directing antibiotic treatment, and putting into practice efficient infection control measures.

4. Antibiotic Resistance Patterns and Mechanisms

4.1. Antibiotics commonly used and emerging resistance in CDI

One of the main causes of colitis and diarrhea linked to antibiotics, especially in hospitalized patients, is *Clostridium difficile* infection (CDI). Metronidazole, vancomycin, and fidaxomicin are the main antibiotics used to treat CDI; tigecycline and rifaximin are taken into consideration for instances that are not responding to these medications. However, overuse of antibiotics and genetic adaptations are causing resistance to emerge. Recent research emphasizes how ribosomal protection proteins and efflux pumps contribute to tigecycline and tetracycline resistance. For example, mutations in the ribosomal protein *rpsJ* further impair medication efficacy, and *tetA(P)* and *tetB(P)* genes have been

linked to decreased susceptibility (31, 32). Furthermore, the COVID-19 pandemic exacerbated antibiotic abuse, making resistance genes in the gut microbiota more rapidly distributed (33). In order to overcome resistance, emergent approaches including CRISPR-Cas systems, antimicrobial peptides, and bacteriophage therapy are being explored (32, 34). Regulatory strategies such as National Action Plans and One Health initiatives focus on decreasing misuse and improving surveillance of antibiotic use (32). It is essential to unravel these mechanisms for the development of target orientated therapies and the preservation of antibiotic efficacy.

4.2. Regional susceptibility patterns (metronidazole, vancomycin, fidaxomicin, etc.)

Recent reports have demonstrated marked regional differences in antibiotic resistance profiles of *Clostridioides difficile* (*C. difficile*) with implications for treatment and public health. During 2020–2025, surveillance in Europe, Israel, and Nigeria demonstrated changing patterns of susceptibility to key therapeutic agents (metronidazole\[MTZ\], vancomycin\[VAN\], and fidaxomicin\[FDX\]). Low resistance rates to MTZ (2.2%) and VAN (1.6%) have been documented in Israel; however, among 313 clinical isolates, there is a larger resistance to FDX (7.35%), with the effectiveness of novel drugs such as ibezapolstat and ridinilazole showing promise (35). The European ribotypes RT027 and RT181, on the other hand, had higher MTZ MICs (five isolates exhibiting full resistance, MIC ≥ 8 mg/L), and RT078 from animal sources had higher VAN MICs (36). It has been determined that tetracycline and erythromycin resistance exists in southeast Nigeria, with virulence genes (*tcdA*, *tcdB*, *cdtA*, *cdtB*) and resistance genes (*tetA*, *tetS*, *ermB*) being widespread among isolates (7). In order to prevent resistance-driven recurrence and treatment failure in CDI, these findings highlight the necessity of frequent susceptibility testing and region-specific antimicrobial stewardship.

4.3. Mechanisms of resistance (e.g., efflux pumps, gene mutations, biofilm formation)

Studies conducted between 2020 and 2025 have provided insight into the intricate tactics used by *C. difficile* to avoid antibiotic treatment, such as biofilm development, adaptive resistance mechanisms, and genetic alterations that impact drug targets. Gene mutations, efflux pump activity, and biofilm formation are the main causes of resistance, and they all contribute to treatment failure and recurrence. Antibiotics like vancomycin and metronidazole are aggressively extruded by efflux pumps, like those encoded by *cdeA*, which lowers intracellular drug concentrations and improves survival. Additionally, by promoting the formation of biofilms, these pumps help protect *C. difficile* against antimicrobial treatments (37). Constitutive expression of the *vanG* operon has been associated with gene alterations, specifically in the *vanSR* regulatory system, which modify peptidoglycan precursors and decrease the affinity for vancomycin binding (37). Furthermore, lower medication efficacy and increased minimum inhibitory concentrations (MICs) have been linked to mutations in the RNA polymerase and *murG* genes (37). Persistent infections are characterized by the creation of biofilms, which increase resistance by changing metabolic states and forming a physical barrier. In addition to contributing to persistent infection cycles, biofilms improve tolerance to metronidazole (38). It is essential to comprehend these mechanisms in order to create tailored treatments and stop the proliferation of *C. difficile* strains that are resistant to several drugs.

4.4. Surveillance data and laboratory testing practices in Nigeria

Nigeria's surveillance of *C. difficile* infection (CDI) is still dispersed, with little data collected nationally and notable differences in laboratory capabilities. Regional studies conducted between 2020 and 2025 have started to provide insight into the prevalence and diagnostic difficulties of CDI in Nigerian healthcare environments. A thorough investigation in southeast Nigeria used PCR-based detection of resistance genes (*tetA*, *tetS*, *ermB*), virulence genes (*tcdA*, *tcdB*, *cdtA*, *cdtB*), and selective culture to find *C. difficile* in hospitalized patients. Their results, which showed a multiple antibiotic resistance (MAR) score of 0.44 and significant resistance to erythromycin and tetracycline, highlighted the necessity of regular susceptibility testing (7). The diagnostic limitations in Nigeria were highlighted by Chukwu et al. (2023), who noted the lack of defined methods, the scarcity of qualified staff and reagents, and the uneven availability of PCR and toxin assays (39). Despite the potential of molecular diagnostics and point-of-care testing, infrastructure and cost continue to be barriers to their widespread use. In order to improve CDI detection and control in Nigeria, these studies emphasize the critical need for organized national monitoring, increased laboratory capacity, and context-specific diagnostic standards.

5. Public Health Implications and Infection Control Challenges

5.1. Impact on treatment outcomes and healthcare systems

Clostridium difficile infection (CDI) continues to pose a serious hazard to public health, impacting treatment outcomes and placing a burden on healthcare systems around the world. Infectious diarrhea linked to healthcare is most commonly caused by CDI, and recurring infections are linked to longer hospital stays, higher morbidity, and higher

healthcare expenses (40). The financial cost of CDI was highlighted by a systematic assessment conducted by Finn et al. (2021), which assessed the annual economic impact to be \$796 million in the United States and €300 million in the EU (40). The spread of CDI and antibiotic resistance is exacerbated in low-resource environments like Nigeria due to issues with infection prevention and control (IPC) practices, including poor hand hygiene compliance, insufficient diagnostic capability, and inadequate infrastructure (41). The Hospital-Onset CDI Prevention Framework, which was adopted by all U.S. hospitals, showed some improvement in the incidence of CDI, but it also highlighted the necessity of multimodal interventions such as environmental cleaning, diagnostic stewardship, and antibiotic stewardship (42). All things considered, the effect of CDI on healthcare systems emphasizes how urgent it is to improve patient outcomes and lower recurrence by bolstering IPC programs, funding diagnostic infrastructure, and customizing therapies for local contexts.

5.2. Limitations in diagnostic capacity and laboratory infrastructure

The diagnostic environment in Nigeria has found it difficult to meet the requirements of infectious disease surveillance, particularly with regard to *Clostridium difficile*. CDI is still underreported despite its clinical importance because of disjointed laboratory networks, restricted access to molecular diagnostics, and inadequate infrastructure. According to Okolie et al. (2025), tertiary institutions in Nigeria outperformed lower-tier facilities in terms of laboratory readiness for antimicrobial resistance (AMR) surveillance, with just 7.3% of surveyed laboratories being fully equipped. This disparity hampers national surveillance initiatives and compromises data collecting at the grassroots level (43). Similar to this, Olumade et al. (2020) emphasized systemic problems that jeopardize prompt and correct detection of CDI and other infections, such as inadequate funding for healthcare, reagent shortages, and staff shortages (44). Mfuh et al. (2023) highlighted that in order to eliminate dependence on centralized labs, portable technology and decentralized diagnosis models are necessary. Nevertheless, reliance on overseas vendors and a lack of domestic manufacturing capabilities impede implementation (45). These restrictions hinder antimicrobial management, epidemic response, and diagnosis. In order to enhance CDI detection and control, Nigeria's diagnostic infrastructure must be strengthened through investments in domestic manufacturing, workforce development, and strategic alliances.

5.3. Infection control policies in Nigerian hospitals

Infection prevention and control (IPC) programs have been implemented in Nigerian hospitals with some success, but systemic issues still make it difficult to effectively limit healthcare-associated illnesses such as *C. difficile*. National IPC rules do exist, but enforcement is poor due to lack of funding, poor training, and poor infrastructure. According to Markus et al. (2024), low hand hygiene adherence, a lack of awareness of conventional precautions, and cultural barriers to healthcare-seeking behavior all compromise IPC compliance in Nigerian hospitals (41). Their research highlighted that in order to improve IPC outcomes, ongoing investments in workforce education and healthcare infrastructure are required (41). Similar to this, the Nigeria Center for Disease Control (NCDC) and the Robert Koch Institute started the Participatory Approach to Learning in Systems (PALS) project to improve IPC procedures at the secondary and tertiary care levels. In order to promote systemic change and enhance patient safety, the PALS handbook describes a multi-module training program for hospital managers and frontline staff (46). Although these initiatives represent a step in the direction of more organized IPC implementation, their success depends on regular policy enforcement, community involvement, and capacity building at all care levels.

5.4. Role of antibiotic stewardship programs

The battle against *Clostridium difficile* infection (CDI), particularly in environments with limited resources like Nigeria, has made antibiotic stewardship programs (ASPs) a vital component. ASPs seek to minimize needless prescriptions, maximize the usage of antibiotics, and stop the development of antimicrobial resistance (AMR), which is a major cause of CDI. The CDC's stewardship framework states that up to 50% of hospitalized patients receive at least one antibiotic, making antibiotic exposure the single most significant risk factor for CDI (47). In hospital wards, targeted interventions including feedback and prospective audits have demonstrated a 52% decrease in healthcare-associated CDI. However, there are several obstacles to adoption in low- and middle-income countries (LMICs), such as a shortage of skilled workers, poor diagnoses, and a lack of money (48). According to the review by Okeah *et al.*, (2021), ASPs that target CDI are frequently used inconsistently across healthcare settings and lack behavioral modification components (49). Notwithstanding these drawbacks, ASPs are nonetheless crucial for enhancing patient outcomes, lowering recurrence rates, and saving money on medical care. It is necessary to invest in training, diagnostic facilities, and integration with infection prevention tactics in order to strengthen ASPs in Nigeria.

6. Knowledge Gaps and Research Priorities

6.1. Need for molecular surveillance and real-time resistance monitoring

There is an increasing demand for *C. difficile* molecular surveillance and real-time resistance monitoring due to the limited diagnostic capabilities in many areas and the rise in antibiotic resistance. The use of genomic technologies like whole-genome sequencing (WGS) and metagenomics has increased since traditional phenotypic approaches are insufficient for tracking the emergence of resistance. Whole Genome Sequencing (WGS) was highlighted as a key component of AMR surveillance by the World Health Organization's GLASS program (2020), which allows for the early identification of resistance genes and transmission mechanisms across clinical and environmental reservoirs (50). Vallejo-Espín et al. (2025) promoted the use of shotgun metagenomics and WGS in a One Health framework in order to better respond to outbreaks and capture the wider resistome (51). Even with these developments, there is still fragmentation in implementation, particularly in low- and middle-income nations. Because of low local capacity, the majority of bacterial genomes are processed externally, according to Nguinkal et al. (2024), who emphasized differences in sequencing infrastructure across East African countries (52). Global standardization of sequencing procedures, training investments in bioinformatics, and real-time data integration are critical to bridging these gaps. Informed antibiotic stewardship, improved CDI control, and prompt public health interventions are all made possible by strengthening molecular surveillance.

6.2. Gaps in data reporting and healthcare worker awareness

The efficient monitoring and treatment of *C. difficile* infections, especially in low-resource environments, has been hampered by ongoing deficiencies in data reporting and healthcare worker awareness. Nigeria frequently underreports CDI cases because of a lack of standardized reporting procedures and a limited diagnostic infrastructure. This obfuscates the actual burden of illness and hinders prompt public health interventions. Healthcare practitioners frequently struggle to define and identify research gaps, which results in uneven data collection and reporting procedures. The quality of the evidence used for decision-making is directly impacted by frontline workers' information and knowledge gaps (53). A similar gap between knowledge creation and application was discovered by Roohi et al. (2020), who discovered that healthcare administrators usually depend more on firsthand knowledge and local anecdotal knowledge than on evidence derived from study (54). The need to increase healthcare workers' competence to make evidence-based policy was also emphasized in the World Health Organization's 2024 global research agenda on knowledge translation. To close these gaps, specialized training, enhanced data systems, and the incorporation of research results into standard clinical procedures are needed (55).

6.3. Importance of environmental and zoonotic reservoirs

Growing data has called into question the conventional wisdom that CDI is just a healthcare-associated infection by highlighting the significance of environmental and zoonotic reservoirs in the persistence and transmission of *C. difficile*. The bacterium can survive in soil, water, and animal habitats due to its ability to produce hardy spores, which promotes infection acquired in the community and cross-species transmission. The rise of *Clostridium difficile* in animal instances of inflammatory bowel disease (IBD), particularly in livestock, companion animals, and wildlife, was shown by Salvarani et al. (2025). Ribotypes such as RT078 showed zoonotic potential. Similarities between human and animal strains were found in their One Health analysis, indicating that veterinary and environmental reservoirs are important in the epidemiology of CDI (56). In a similar vein, Knight et al. (2019) confirmed genetic overlap between human and animal isolates by using whole-genome sequencing to track interspecies transmission of ST11 strains across continents. The necessity of integrated surveillance systems with veterinarian and environmental compartments is highlighted by these findings (57). Controlling CDI requires addressing these reservoirs, particularly in areas with high levels of human-animal interaction and uncontrolled antibiotic usage.

6.4. Opportunities for collaboration, funding, and policy development

Global initiatives to combat *Clostridium difficile* infection (CDI) have placed a greater emphasis on the necessity of cooperative research, long-term funding, and innovative policy implementation. Even while the cost of CDI is becoming more widely recognized, particularly in low- and middle-income nations, progress is still uneven because of dispersed initiatives and little cross-sector participation. In order to enhance results, Hocking et al. (2022) suggested a multidisciplinary strategy to address the main issues in CDI care, such as delayed diagnosis, hurdles to treatment access, and recurrence management. With funding from Ferring Pharmaceuticals, their RAND Europe study emphasized the significance of investing in cutting-edge treatments, training primary care physicians, and revising clinical guidelines (58). Likewise, the CDC's "Let's Make a C-DIFFerence" partnership, which involved more than 70 hospitals, is focused on CDI prevention initiatives, was detailed by White et al., (2022). The program shown that specialized interventions,

mentoring, and organized collaborations can dramatically lower infection rates (59, 60). These results highlight the need of integrated funding sources, stakeholder involvement, and regulatory frameworks that facilitate One Health surveillance, antimicrobial stewardship, and real-time data sharing. To fill in knowledge gaps and advance CDI control, it will be crucial to fortify national and international cooperation.

7. Conclusion and Recommendations

The increasing prevalence and resistance dynamics of *C. difficile* in South Eastern Nigeria are highlighted in this narrative review, which also identifies important gaps in infection management, antibiotic stewardship, and diagnostics. High rates of erythromycin and tetracycline resistance, restricted access to molecular diagnostics, and underreporting as a result of inadequate laboratory infrastructure are some of the main conclusions. The existence of genes linked to virulence and resistance (such as *tcdA*, *ermB*, and *tetA*) emphasizes the necessity of focused monitoring and intervention. In order to tackle these obstacles, the incorporation of *C. difficile* into national AMR frameworks must be given top priority in strategic healthcare strategies. It is recommended that secondary and tertiary hospitals increase their investment in diagnostic capabilities, specifically in PCR and toxin testing. In addition to standardizing reporting procedures, educating healthcare personnel on CDI management and recognition will enhance case detection and treatment results. Additionally, real-time data exchange, coordinated networks, and genomic techniques like whole-genome sequencing are needed to improve regional microbiological surveillance. Research on zoonotic and environmental reservoirs as well as capacity-building can be facilitated by collaborations with international organizations and academic institutions. To sum up, in order to lessen the effects of *C. difficile* and improve AMR management in South Eastern Nigeria, a multi-sectoral strategy integrating policy reform, innovative diagnostics, and strong surveillance is crucial.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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