NIJBAS
Publications 2025

OPEN ACCESS
ONLINE ISSN: 2992-5797
PRINT ISSN: 2992-6122

NEWPORT INTERNATIONAL JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES (NIJBAS)

Volume 7 Issue 1 Page 49-52, 2026

https://doi.org/10.59298/NIJBAS/2026/7.1.4952

Long-term Health Complications Associated with Untreated or Late-Treated Typhoid Fever

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ABSTRACT

Typhoid fever, caused by *Salmonella enterica* serovar Typhi, remains a significant public health issue, particularly in low-resource settings. Despite the availability of antibiotics, delayed or inadequate treatment continues to lead to serious long-term health complications. This review explores the range of long-term health effects resulting from untreated or late-treated typhoid fever, emphasizing the role of delayed diagnosis, incomplete treatment, and antimicrobial resistance (AMR). Long-term complications include chronic gastrointestinal issues, intestinal perforation, neurological disturbances, cardiovascular conditions, and renal failure. Additionally, individuals who survive the acute phase may experience psychological effects such as depression and anxiety, as well as a risk of becoming chronic carriers of the bacteria, continuing to spread the infection. The review also discusses the growing challenge posed by AMR, particularly the emergence of multidrug-resistant strains, which complicate treatment and increase the risk of prolonged illness and complications. By addressing these long-term outcomes, this review underscores the importance of early and effective intervention, as well as the need for public health strategies aimed at improving healthcare access, timely diagnosis, and treatment, alongside enhanced efforts to combat AMR.

Keywords: Typhoid fever, long-term complications, untreated typhoid, late-treated typhoid, antimicrobial resistance.

INTRODUCTION

Typhoid fever is a serious and systemic infectious disease caused by *Salmonella enterica* serovar Typhi, a bacterium that primarily affects the gastrointestinal system but can also spread throughout the body. It is typically transmitted through contaminated food or water and remains a significant public health issue, especially in developing countries and regions with inadequate sanitation and healthcare infrastructure [1]. Despite the availability of effective antibiotics, typhoid fever continues to pose a major health challenge globally due to delayed treatment, misdiagnosis, and a rising threat of antimicrobial resistance. The World Health Organization (WHO) estimates that there are between 11 and 20 million cases of typhoid fever each year, leading to approximately 128,000 to 161,000 deaths annually. While typhoid fever is often classified as an acute illness, the consequences of untreated or late-treated cases can extend far beyond the initial infection [2]. The clinical course of the disease can be complicated by the development of chronic sequelae, some of which are severe, debilitating, and even life-threatening. In this article, we explore the long-term health complications associated with untreated or late-treated typhoid fever, including the physiological, psychological, and socio-economic impact. We discuss the role of delayed diagnosis, inadequate or incomplete antimicrobial treatment, and the increasing prevalence of antimicrobial resistance (AMR) in exacerbating the long-term outcomes of typhoid fever [3]. By doing so, this review underscores the importance of timely and effective treatment in preventing these complications and minimizing the burden of the disease.

Typhoid fever is primarily endemic in countries with poor sanitation, overcrowding, and limited access to healthcare. Despite improvements in global public health, the disease remains prevalent in many low- and middle-income countries, where access to medical care can be delayed or inadequate. In such settings, a significant number of

individuals suffer from complications resulting from untre ated or improperly treated typhoid fever [4]. Historically, the advent of antibiotics revolutionized the treatment of typhoid fever. However, the development of *Salmonella Typhi* strains resistant to commonly used antibiotics has made the disease harder to treat in some regions. Additionally, a lack of awareness and timely diagnosis, combined with limited healthcare resources, leads to delayed treatment, which can result in prolonged illness and severe complications. The long-term complications of untreated or late-treated typhoid fever are wide-ranging [5]. They include chronic gastrointestinal issues, prolonged fever, bacteremia, and complications like septic shock, multi-organ failure, and even death. Some survivors may experience long-term consequences such as intestinal perforations, chronic fatigue, and psychological impacts, including depression and anxiety. Understanding the full extent of these complications is essential to improving prevention and treatment strategies for typhoid fever [6].

Although typhoid fever is treatable with appropriate antibiotic therapy, many individuals in low-resource settings either receive delayed treatment or are misdiagnosed, leading to significant morbidity and mortality. The rise in antimicrobial resistance is further complicating treatment options, making it more difficult to control the disease in certain populations [7]. This study aims to address the knowledge gap in understanding the long-term health complications of untreated or late-treated typhoid fever. While immediate clinical outcomes such as fever and gastrointestinal distress are well documented, the lasting impact of typhoid fever on long-term health has received less attention. By examining the complications that can arise from untreated or improperly treated typhoid fever, we aim to provide a clearer understanding of the disease's full impact on affected individuals and communities [8]. This research also seeks to identify gaps in healthcare systems that contribute to delayed treatment and to highlight the importance of improving early detection and treatment protocols. This study aims to investigate the long-term health complications associated with untreated or late-treated typhoid fever. The specific objectives include identifying and categorizing these complications, exploring how delayed diagnosis and treatment exacerbate health outcomes, and assessing the impact of antimicrobial resistance on treatment efficacy. Additionally, the research will examine the psychosocial and socio-economic consequences of surviving typhoid fever with long-term effects. By proposing strategies for improving early diagnosis, treatment, and prevention, the study seeks to reduce the incidence of long-term complications. Research questions will focus on understanding the primary long-term health complications, the role of delayed diagnosis in severity, and how antimicrobial resistance impacts outcomes. It will also explore the socio-economic conditions of survivors in resource-poor settings and recommend strategies for improving health outcomes. This study is significant as it fills an important gap in existing literature, shedding light on the often-overlooked long-term consequences of typhoid fever. The findings could inform better management strategies, advocate for early detection, and highlight the need for effective antibiotics in endemic regions. Moreover, by addressing the issue of antimicrobial resistance, the study will contribute to discussions on the development of new treatments and enhanced surveillance. It will also help policymakers understand the broader socio-economic implications, encouraging improvements in healthcare access and prevention in low-resource areas.

Pathophysiology of Typhoid Fever

Typhoid fever, caused by *Salmonella enterica* serotype Typhi (S. Typhi), begins when a person ingests contaminated food or water, leading to infection. After entering the gastrointestinal tract, the bacteria penetrate the intestinal epithelium, a crucial defense barrier, and invade the underlying mucosal tissues. This process marks the start of the infection, as the bacteria cross into the bloodstream, initiating bacteremia [9]. This phase enables the bacteria to disseminate widely, infecting various organs such as the liver, spleen, bone marrow, and gallbladder. This systemic spread is characteristic of typhoid fever and accounts for the multi-organ involvement seen in severe cases. If the infection is not promptly treated, persistent bacteremia can escalate into life-threatening complications like septicemia, where the bloodstream becomes overwhelmed with pathogens, and intestinal perforation, which can cause peritonitis. Such complications arise due to the body's inability to control the bacterial load, allowing the infection to progress unchecked [10]. The immune response to S. Typhi exacerbates the situation, as it leads to chronic inflammation within the infected tissues. This ongoing inflammatory process contributes to tissue damage, fibrosis, and dysfunction in affected organs. The immune response not only promotes tissue destruction but also increases the risk of long-term sequelae such as gallbladder disease and the development of intestinal strictures, which may require surgical intervention [11]. In summary, while the primary effect of *S. Typhi* is its direct invasion of tissues and systemic spread, the long-term effects of immune-mediated damage, including chronic inflammation and organ dysfunction, significantly influence the severity and outcomes of the disease. Therefore, the pathophysiology of typhoid fever involves a complex interplay of bacterial dissemination, immune responses, and subsequent tissue damage [12].

Long-term Health Complications of Untreated or Late-Treated Typhoid Fever

Untreated or late-treated typhoid fever can result in a range of severe, long-term health complications that not only affect the immediate recovery of an individual but also pose ongoing risks to their long-term well-being. One of the

most life-threatening consequences is intestinal perforation, which occurs when the Salmonella Typhi bacteria invade the intestinal wall, causing it to rupture. This leads to the leakage of intestinal contents into the peritoneal cavity, causing peritonitis, a potentially fatal condition [13]. Even if the rupture is managed promptly, the long-term damage to the intestines can result in chronic gastrointestinal issues such as malabsorption, bowel obstructions, and the need for repeated surgeries. Another major complication of untreated typhoid fever is the chronic carrier state, which affects around 1-5% of people who have recovered from the illness. These individuals harbor the bacteria in their gallbladders, often without showing symptoms, but remain infectious and can pass the bacteria onto others [14]. Chronic carriers are at higher risk for recurrent infections, liver dysfunction, and gallbladder complications, including the potential development of gallbladder cancer. Neurological complications, although rare, are more common in untreated cases and can manifest as encephalopathy, delirium, and seizures. Additionally, some patients may face long-term cognitive and psychiatric disorders such as depression, anxiety, and memory loss [15]. Cardiovascular complications, while infrequent, can include myocarditis, endocarditis, and arrhythmias. In severe cases, untreated or improperly treated typhoid fever can lead to chronic heart failure, as the infection causes widespread systemic inflammation. Renal complications are another concern, particularly in more severe or delayed cases [16]. Acute kidney injury (AKI) is a common outcome, and if left untreated, it can progress to chronic kidney disease (CKD), especially in individuals who already have pre-existing kidney issues. Typhoid fever can also lead to endocrine disorders, particularly thyroid dysfunction, due to the systemic inflammation that affects the hypothalamic-pituitary-thyroid axis [17]. Additionally, the growing threat of antimicrobial resistance (AMR) complicates the treatment of typhoid fever, making infections harder to manage and significantly increasing the likelihood of these long-term complications. The rise of multidrug-resistant strains, such as XDR-Typhi, has made it increasingly difficult to treat the disease effectively, further heightening the risk of chronic health issues. As such, timely diagnosis and appropriate treatment are critical to preventing the long-term consequences of this potentially deadly infection [18].

CONCLUSION

Typhoid fever remains a serious public health challenge, especially in areas with limited healthcare infrastructure. Despite being preventable and treatable through early diagnosis and intervention, the disease continues to have devastating effects, particularly when treatment is delayed or incomplete. Without timely care, typhoid fever can result in severe complications, such as intestinal perforation, chronic carrier states, and organ damage, including neurological, cardiovascular, and kidney issues. Additionally, the emergence of antimicrobial resistance poses a growing threat, making treatment more difficult and undermining public health efforts. These complications extend beyond the individual, placing a significant strain on healthcare systems and contributing to a broader societal burden. Therefore, it is essential to focus on early detection, effective treatment protocols, and preventive measures, such as vaccination and improved sanitation practices, to reduce both the incidence and the long-term consequences of the disease. The increasing challenge of antimicrobial resistance calls for cautious use of antibiotics and the development of new therapeutic options. Public health initiatives aimed at ensuring timely diagnosis and appropriate management are critical to mitigating the long-term effects of typhoid fever and improving overall health outcomes.

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CITE AS: Katu Amina H. (2026). Long-term Health Complications Associated with Untreated or Late-Treated Typhoid Fever. NEWPORT INTERNATIONAL JOURNAL OF BIOLOGICAL AND APPLIED SCIENCES, 7(1):49-52. https://doi.org/10.59298/NIJBAS/2026/7.1.4952