

# Typhoid in Pakistan: Challenges, Efforts, and Recommendations

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**Abstract:** Typhoid, and its extra drug resistant form which is highly prevalent in Pakistan, is increasing the burden on healthcare through multiple factors. These range from lack of sanitation, the collapsing economy, and poor access to clean drinking water which have made it arduous for the government and various other organizations in containing it. With the COVID-19 pandemic, treatment of typhoid became a challenge as focus was driven towards limiting the COVID-19 spread, and hence preferential use of antibiotics such as azithromycin may limit future empirical antibiotic therapy for typhoid. Socioeconomic disparities and geographical as well as demographic barriers further limit access to appropriate typhoid management. Lastly, illiteracy and self-medication with antibiotics may predispose Pakistan to another outbreak of typhoid. These concerns, although largely unaddressed effectively, need immediate action. Previously, the government and international organizations have made efforts to control the spread through the introduction of TCV as a part of EPI and awareness, additional improvements are needed. These include: improving access to telemedicine in rural areas, extensive vaccination programs, and routine awareness programs especially in schools.

**Keywords:** typhoid, COVID-19, water sanitation, healthcare, vaccine, Pakistan

## Introduction

Typhoid fever is caused by a bacterium *Salmonella enterica* serotype Typhi and to a lesser extent, serotypes *Paratyphi* A, B, and C. It is a life-threatening disease which spreads through human contact via the fecal-oral route.<sup>1,2</sup> Undercooked or raw food and contaminated water contain *Salmonella* Typhi and can be a significant cause of spread.<sup>1</sup> The most common symptom of Typhoid is sustained fever which can reach up to 103–104°F (39–40°C).<sup>1</sup> Other symptoms may include headache, lethargy, cough, stomach ache, altered bowel habits, loss of appetite, and some may also develop rose-colored spots.<sup>1</sup> Population at risk include poor communities who have lack of access to clean water, and vulnerable groups including children and immunocompromised.<sup>3</sup> Vaccines to develop immunity have been available which include; Typhoid Conjugate Vaccines (TCVs) for children under the age of two, purified antigen for children over 2 years of age, and live attenuated oral vaccine for those aged 5 and above.<sup>3,4</sup>

Typhoid is most common in South Asian countries like India, Bangladesh, and Pakistan.<sup>1</sup> Pakistan has been estimated to have the highest rate of Typhoid among the South Asian countries with 493.5 per 100,000 cases in 2018.<sup>5</sup> Cases in Pakistan drastically increased after a new extensive drug resistant (XDR) typhi outbreak began in Hyderabad in 2016, affecting the province of Sindh the most.<sup>5</sup> This new strain rendered the treatment with Chloramphenicol, Ampicillin, Cotrimoxazole, Fluoroquinolones, and Third-generation Cephalosporins ineffective, and ultimately requiring treatment with stronger antimicrobials including; Carbapenems, Tigecycline, and Azithromycin.<sup>3,6</sup>

After the emergence of COVID-19 in Pakistan, the primary goal of healthcare workers (HCW) shifted towards controlling the spread of COVID-19.<sup>7</sup> This affected the spread of Typhoid drastically, as evident by the increase in number of XDR cases as in Karachi between January 2017 and June 2021 there were a reported 14,360 cases, compared to 864 new cases just within the months of June 2021 to August 14, 2021 alone. This is emphasized with the number of

new XDR cases reaching 52 in the week just before August 14.<sup>6</sup> On the contrary, some sources have reported a fall in Typhoid cases after the emergence of COVID-19, which can be explained by possibly decreased surveillance in different states secondary to the lack of resources amidst the pandemic.<sup>8</sup> Moreover, the mutual symptoms and differential diagnoses of COVID-19 and Typhoid also made it difficult for physicians to differentiate between them,<sup>7</sup> which can potentially mask the true number of Typhoid cases. Furthermore, during the initial phase of the pandemic, treatment with Azithromycin was gaining importance.<sup>7</sup> This meant that one of the few treatment options left for Typhoid, ie, Azithromycin, could also become ineffective due to resistance and make the current situation worse.

In addition to the aforementioned challenges, insufficient availability of clean water, poor sanitation and hygiene (WASH) practices, low vaccination coverage, and limited surveillance for Typhoid also contribute to the prevalence of Typhoid in Pakistan.<sup>9</sup>

This article aims to comment on the current situation of Typhoid in Pakistan amidst COVID-19 and provide possible recommendations on how to prevent further spread.

## Challenges and Implications

Various factors ranging from financial instability, lack of hygiene, self-treatment and COVID-19, and suffering healthcare system contribute to the prevalent spread of Typhoid in Pakistan.

A major contributing factor to Typhoid spread in Pakistan is financial instability and external debts, leaving only 151 million USD for its entire health-care system.<sup>10</sup> This is a drastically insufficient amount especially for accommodating the 40% of the population living below the poverty line who reside in overcrowded areas and slums.<sup>10</sup> The lack of proper sewage systems, clean food and water result in air-borne diseases.<sup>6,10</sup> Moreover, despite the establishment of health units set up by the government in local districts, adequate residential infrastructure and standard sanitation routines are not provided due to a lack of funding.<sup>11</sup> Hence, many doctors refuse to work in rural areas. Consequently, many villagers are unable to seek medical attention or advice which leads to an increasing number of Typhoid cases and mortality.<sup>11</sup>

Potential carriers from underdeveloped areas migrate to cities in search of stable jobs or to seek refuge, ultimately increasing Typhoid cases among urban dwellers.<sup>6</sup> Street foods are a popular option among many, however, high levels of Typhoid cases are caused by 70% to 90% reports of animals, insects and liquid waste found in food preparation areas.<sup>12,13</sup> Carts are often placed next to roads or above drains, contaminating food items with feces and dust.<sup>12</sup> It is a common practice for vendors to handle food without proper sanitation, for example, not washing their hands after handling raw materials, money, or food packages.<sup>12</sup> Cross contamination is exceedingly common as surfaces are not disinfected appropriately and may contain remains from food prepared earlier.<sup>13</sup> All these factors significantly increase the risk of getting Typhoid, as supplemented by a study conducted in Lyari Town, Karachi, which shows that those who consumed street food had a higher risk of getting Typhoid than those who consumed home-cooked food.<sup>14</sup>

In majority of rural areas, primary sources of water include rivers and wells as they lack access to facilities such as taps, toilets, and personal hygiene utilities.<sup>15</sup> To add, many of their sources of water are not qualified for safe drinking as they have not been subjected to quality assessment and can contain heavy bacterial load.<sup>15</sup> Furthermore, their sources of water are defiled by industries using their land as dumping grounds.<sup>10</sup> All these factors combined lead to extreme environmental pollution and contamination of their only sources of water thus increasing the risk of contracting *Salmonella* infections.

Rural areas are vulnerable targets to Typhoid as preventative methods like personal and sanitation hygiene are not well practiced. This is evident as around 25 million<sup>16</sup> people practice open defecation in bushes, rivers and roads throughout Pakistan, making them more susceptible to microbial attacks.<sup>10</sup> As indicated by a study in Kenya, those who use pit latrines and/or practice open defecation are at a significant risk of contracting Typhoid (1.6%;  $p=0.048$ ), therefore, raising a concern for risk of Typhoid in the rural population of Pakistan.<sup>17</sup>

The ongoing global pandemic has further burdened the already struggling healthcare system, as many of the resources are re-directed to combat the spread of COVID-19.<sup>7</sup> Blood cultures, which are the most reliable test for Typhoid, are being sparingly used as many laboratories have been turned into COVID-19 testing centers. Moreover, many symptoms like fever and headache are common between COVID-19 and Typhoid, along with a few other diseases including dengue<sup>18</sup> and measles,<sup>19</sup> making definitive diagnosis a significant challenge.<sup>7</sup>

Lastly, vaccines are an effective method to limit the dissemination of the disease; however, many children, mainly in rural areas, are not immunized against the Typhoid infection. This is partly due to cultural and religious stigmas surrounding vaccines which limit widespread vaccination.<sup>6,20</sup> Apart from this, poor infrastructure, low-income rates and few healthcare facilities present in the rural areas add up to the low vaccination rates.<sup>21</sup> Moreover, many locals tend to self-medicate due to lack of awareness causing excess use of antibiotics increasing the chances of resistance. This further increases the probability of new multidrug-resistant strains of Typhoid.<sup>7,22</sup>

In the long term, use of Azithromycin for COVID and Typhoid, as discussed previously, would increase the chance of resistance.<sup>7</sup> This would mean decreased availability of empiric antibiotic choices for future, as for the XDR strain the spectrum of anti-microbials is already limited, which could potentially lead to future outbreaks of Typhoid. Moreover, the inability to contain the number of XDR Typhoid cases could lead to the spread of this strain to different parts of the world. As indicated by a study, which presents the first Canadian pediatric case of XDR which was found out to be originated from and outbreak in Pakistan.<sup>23</sup> In addition to the long-term implications, difficulty in establishing a good differential diagnosis, increased variants, and poor surveillance may all add up to impact the current vaccination efforts amidst COVID-19 in the short term, which can prove to be detrimental for the current situation of Typhoid in Pakistan.

## Efforts and Recommendations

Multiple government agencies, alliances, and NGOs are working tirelessly to reduce the spread of Typhoid in Pakistan. In 2019, Pakistan, with financial assistance from Global Alliance for Vaccines and Immunization (GAVI), became the first country to implement TCV in its routine immunization program.<sup>24</sup> Reports from 2017 show that 63% of Typhoid cases and 70% of Typhoid deaths in Pakistan were among children younger than 15 years of age.<sup>24</sup> These high infection and death rates among children made the introduction of TCV crucial as this is the first vaccine that can be given to children as young as 6 months of age and confers long-term protection.<sup>24</sup> Fears that XDR Typhoid might spread to other parts of the world along with the fact that majority of the affected population comprised of children, made it essential to make TCV a part of Expanded Program on Immunization (EPI).<sup>25</sup>

A cohort study from Pakistan demonstrates the effectiveness of TCV as Typhoid fever was seen in 20,886 per 100,000 unvaccinated children but only in 9490 per 100 000 vaccinated children.<sup>26</sup> Additionally, data from Pakistan also show that TCV has an efficacy of 95% against culture-confirmed *Salmonella* Typhi and 97% against XDR *Salmonella* Typhi strains.<sup>26</sup> These high efficacy rates further highlight the vaccine's effectiveness and could help reduce the over reliance on antibiotics which led to the emergence of different strains of Typhoid. A two-week vaccination campaign was launched in the province of Sindh in 2019, where XDR was first reported, with the aim of vaccinating 10 million children between 9 months and 15 years of age.<sup>24</sup> After Sindh, the second phase of the vaccination campaign was launched in Punjab in 2021, with aims to vaccinate more than 6.6 million children between the same age group.<sup>27</sup> These joint efforts by World Health Organization (WHO) and local government have had great success, as XDR Typhoid cases have reduced by two-thirds in Sindh since the introduction of TCV,<sup>28</sup> while 100% of the target population has been vaccinated in Punjab.

High open defecation numbers along with poor sanitation infrastructure, leads to contamination of water sources and contributes to Typhoid's rampant spread. To tackle this issue, United Nations Children's Fund (UNICEF) along with the local government's help has built 40,000 new toilets in Punjab in an effort to end open defecation by 2025.<sup>29</sup> Approximately, \$442 million worth of funds were also approved by the World Bank in 2021 to enhance the sanitation services. Rural areas lack accessibility to clean water and the Punjab Rural Sustainable Water Supply and Sanitation Project (PRSWSSP) aims to correct this by increasing accessibility to water for more than six million rural residents, especially in drought struck areas.<sup>30</sup>

Although vaccination seems to be the most potent short-term measure, various long-term measures must also be implemented alongside it to efficiently combat the spread of Typhoid. Firstly, basic hygiene practices such as regular hand washing, drinking only purified water and avoiding undercooked food are all essential.<sup>31</sup> Secondly, schools could be more pro-active and have students research and make presentations about Typhoid fever and its preventive measures. This would spread awareness among students and their families and reduce the number of Typhoid cases among children younger than 15 years old, which reports in 2017 suggested were as high as 63%.<sup>32</sup> Furthermore, HCWs should work

with local clerics, who have significant influence, to warn the population about the dangers of Typhoid and persuade more people to get vaccinated.

To prevent the emergence of new drug-resistant strains, strict laws must be implemented to reduce non-essential antibiotic prescriptions.<sup>6</sup> Physicians must be cautious and limit Azithromycin prescription in COVID-19 patients while simultaneously not hand out antibiotics without a verified prescription to prevent self-medication. This is necessary to prevent further antibiotic resistance, as Azithromycin is among the few drugs still effective against XDR Typhoid. Additionally, providing clean water and food, and an efficient waste management system could help reduce the spread of Typhoid and consequently would decrease the excessive reliance on antibiotics.<sup>6</sup>

The government should also invest in telehealth as this would make healthcare more accessible to people in remote areas and cut down transportation costs. The lack of trained physicians in rural areas could be addressed using telehealth to provide virtual medical assistance, while local authorities could incentivize more physicians to work in rural areas by paying them higher salaries.<sup>33</sup> Lastly, investments should be made to improve the surveillance capacity and buy more diagnostic tools to help better differentiate Typhoid from similar diseases which will make it easier to devise an appropriate plan to combat its spread.

## Conclusion

To sum up, various factors have impacted the spread of Typhoid in Pakistan. This includes the presence of XDR strains of Typhoid, COVID-19 outbreak and simultaneous antibiotic therapy, socioeconomic disparities, and illiteracy. These concerns have been addressed to an extent with the EPI program, and introduction of TCV. However, to improve the situation further, awareness programs, telehealth, and more vaccinations programs are warranted.

## Consent for Publication

All authors agreed to the publication of this manuscript.

## Disclosure

The authors declare that they have no competing interests.

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