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# CLINICAL SPECTRUM OF ENTERIC FEVER IN CHILDREN FROM 2 TO 12 YEARS AGE IN RELATION TO TYPHOID VACCINATION STATUS

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**Abstract**

**Objective:** *This study aimed to determine the frequency of clinical manifestations of typhoid fever in children aged 2 to 12 years and compare the clinical spectrum between vaccinated and non-vaccinated children.*

**Methodology:** *The study was a cross-sectional study done in Pediatric Medicine Department, Liaquat University Hospital, Hyderabad/Jamshoro on October 21, 2023, to April 20, 2024. One hundred and thirteen (113) children aged between 2 years and 12 years who had proven blood culture-confirmed typhoid fever were recruited. Vaccination was evaluated by use of recall phenomenon or immunizations cards. A structured proforma was used to collect data on demographic characteristics as well as clinical symptoms.*

**Results:** *The age of participants varied and was median as 5 (IQR: 38) with only a slight majority of males (54.0). The most frequent was the symptom of fever (99.1%), then diarrhea (35.4%), abdominal pain (32.7%), headache (26.5%), and constipation (13.3%). There were no substantial differences between vaccinated and non-vaccinated children on clinical spectrum of any symptom ($p > 0.05$).*

**Conclusion:** *The clinical profile of typhoid fever in children with the age 2-12 years is also reliable irrespective of the use of Typbar-TCV vaccine. At the same time, vaccination can help prevent the disease but does not have a huge impact on the breakthrough cases symptomatology. Such results underline an increased need to enhance diagnostics, further healthcare immunization, and enhance the mitigation of the public health activities. Future research aimed at investigating the effect of vaccines on severity upon acquiring the disease and long-term results should be conducted.*

## INTRODUCTION

Typhoid fever is a systemic infection which is essentially set by Salmonella enterica serotype Typhi, as well as the less frequent Salmonella Paratyphi A, B, and C-gram-negative bacilli which is transmitted mainly by ingestion of infected food or water [1, 2]. The symptoms of typhoid fever are usually nonspecific

and therefore may be complicated in the diagnosis of this disease especially among the children.

Common manifestations are high grade fever which lasts long, abdominal pain, nausea, lethargy, anorexia, diarrhea, and, relatively rarely, even constipation [2]. At the initial stage, the patient might develop abdominal distension, splenomegaly, relative bradycardia, dicrotic pulse, a meningismus. In further progressions, other dangerous conditions like intestinal perforation, gastrointestinal hemorrhage, and myocarditis can occur accompanied by continuous anorexia and weight loss [3]. The presence of relative bradycardia, particularly in relation to prolonged elevated fever, may be rightly regarded as a clinical characteristic of typhoid fever [4].

The disease occurs due to poor sanitation and lack of access to clean drinking water, which is endemic in areas that are inadequately sanitized, and transmission is through faecal-oral contact [5, 6]. About 14.3 million cases of typhoid and paratyphoid fever diseases with 135,900 deaths occur globally per year [7]. The children in the age range 2 to 15 years, are especially at risk in Pakistan with reports showing that incidence in this age category surpasses the 451.7 per 100,000 population [7].

The non-availability of sensitive means of diagnosis does not help to accurate diagnosis. Although the traditional serological testing procedures such as the Widal test are commonly employed, they are not adequately reliable diagnosically [8]. The study previously conducted in Pakistan by Iqbal et al. has shown that fever occurred in 100 percent of the cases, where the intermittent and continuous fever was identified in 72 percent and 28 percent of the cases, respectively. In 75 percent of the children abdominal pain occurred, 50 percent vomited, 50 percent reported diarrhea, and 12 percent reported constipation [9].

In 2019, accompanied by the increasing antimicrobial resistance and sustained endemicity, the introduction of typhoid conjugate vaccine (Typbar-TCV) to the Expanded Program on Immunization (EPI) in Pakistan had been implemented with its vast distribution in the Sindh region [10]. Nonetheless, the available evidence about how the vaccine can affect the presentation of breakthrough cases is scarce.

## METHODOLOGY

This descriptive cross-sectional study was conducted from October 2023 to April 2024 in the Pediatric Medicine Department of Liaquat University Hospital, Hyderabad/Jamshoro, following approval by the institutional ethics committee.

Children aged 2 to 12 years presenting with blood culture–confirmed Salmonella enterica serovar Typhi were eligible for inclusion. Typhoid fever was operationally defined as sustained fever >38°C for more than three days, accompanied by at least one of the following: headache or abdominal pain rated >4 on a 10-point visual analog scale (VAS), diarrhea (≥3 loose stools per day), or constipation (no stool passage for ≥4 days).

A non-probability consecutive sampling technique was employed to enroll 113 children of either gender, whose caregivers provided written informed consent. Children were excluded if they had a confirmed alternative febrile illness (e.g., malaria, dengue, meningitis, tuberculosis), were on immunosuppressive therapy, or had significant comorbid conditions.

Vaccination status was determined through caregiver interviews and review of immunization cards, classifying children into vaccinated and non-vaccinated groups.

After consent, trained research assistants administered a structured proforma to collect demographic data (age, gender, socioeconomic status), clinical history (duration of symptoms, prior antibiotic use), and physical examination findings. VAS scores for headache and abdominal pain were recorded at presentation. Blood samples were drawn under aseptic conditions for culture and antibiotic sensitivity testing. The data analyzed using the SPSS software system (Ver. 26). Descriptive statistics are shown as means ± standard deviations, and frequencies with percentages. The Chi-square test was employed to ascertain the statistical test of significance, with a significance level established at 5% to evaluate statistical relevance.

## RESULTS

The research study has included a total of 113 subjects. A greater proportion of the participants had a median age of 5 years with an interquartile of between 3 to 8 years. It was established that the

median length of the illness was 12 days (IQR: 8 days 15 days). Sixty-one percent (54.0) of them were found to be male, with 46.0 percent (52) of them being female. As far as the vaccine status is concerned, 51 children (45.1%) were classified as being vaccinated and 62 children (54.9%) were not vaccinated (Table I). Relating the study of the anti-vaccination attitudes to the clinical manifestation of the disease among the 113 participants, no significant correlations were found. Almost all patients possess the symptom of fever; 50 (44.6%) of the group of vaccinated patients with 62 (55.4%) of the non-vaccinated patients being affected by it (p=0.451). As far as abdominal pain is concerned 12 (32.4%) patients in the vaccinated group and 25 (67.6%) patients in the unvaccinated group showed it (p=0.541), and constipation was also noticed among 5 (33.3%) of the vaccinated and 10 (66.7%) of the non-vaccinated patients (p=0.491). The prevalence of diarrhea was found in 18 (45 percent) of the immunized children and 22 (55 percent) of non-vaccinated children (p=0.999). The frequency of headaches was also equal between both groups with 15 (50%) headaches among the non-vaccinated and the vaccinated groups (p=0.669). Not one of the associations made between the vaccine status and the clinical symptoms were significant (Table II).

| Table I: Baseline Characteristics of Study Participants (n=113) | |
|---|---|
| **Characteristics** | **Median (IQR)** |
| **Age (years)** | 5 (3-8) |
| **Duration of Illness (days)** | 12 (8-15) |
| **Gender, n** (%) | |
| Male | 61 (54.0%) |
| Female | 52 (46.0%) |
| **Vaccination Status, n** (%) | |
| Vaccinated | 51 (45.1%) |
| Non-Vaccinated | 62 (54.9%) |

| Table II: Comparison of Vaccination Status with Clinical Spectrum (n=113) | | | | |
|---|---|---|---|---|
| **Clinical Spectrum** | | **Vaccinated** | **Non-vaccinated** | **P-value** |
| **Fever** | Yes | 50 (44.6) | 62 (55.4) | 0.451 |
| | No | 1 (100) | 0 (0.0) | |
| **Abdominal pain** | Yes | 12 (32.4) | 25 (67.6) | 0.541 |
| | No | 39 (51.3) | 37 (48.7) | |
| **Constipation** | Yes | 5 (33.3) | 10 (66.7) | 0.491 |
| | No | 46 (46.9) | 52 (53.1) | |
| **Diarrhea** | Yes | 18 (45) | 22 (55) | 0.999 |
| | No | 33 (45.2) | 40 (54.8) | |
| **Headache** | Yes | 15 (50) | 15 (50) | 0.669 |
| | No | 36 (43.4) | 47 (56.6) | |

## DISCUSSION

Typhoid fever continues to pose a significant public health challenge in developing countries, particularly in regions where access to clean water and sanitation remains inadequate [11,12]. In children, the disease presents with nonspecific clinical features, complicating early diagnosis and timely treatment. The present study confirms that fever is the most

consistent symptom of typhoid fever, observed in 99.1% of participants. This finding aligns with previous literature identifying persistent high-grade fever as a hallmark of the disease [1, 9, 14, 16].

Other clinical features such as diarrhea (35.4%), abdominal pain (32.7%), headache (26.5%), and constipation (13.3%) were reported with variable frequency, reflecting the well-established heterogeneity in symptom presentation [9, 14, 17–19]. These manifestations are characteristic of pediatric typhoid fever and, in severe cases, may progress to life-threatening complications such as intestinal perforation, gastrointestinal hemorrhage, or myocarditis [14, 15]. To address the burden of typhoid fever, Pakistan incorporated the typhoid conjugate vaccine (Typbar-TCV) into its Expanded Program on Immunization (EPI) in 2019, with large-scale rollout particularly in Sindh province [10, 20, 21]. While Typbar-TCV is effective in preventing typhoid infection, its role in modifying the clinical presentation of breakthrough cases is less well understood. In this study, no statistically significant differences were observed in clinical symptoms between vaccinated and non-vaccinated children. This suggests that while the vaccine may reduce infection rates, it does not markedly alter symptomatology in cases where vaccinated individuals contract the disease. These findings are in line with previous studies reporting comparable symptom profiles among vaccinated and non-vaccinated patients with confirmed typhoid fever [22, 23].

Although some reports suggest milder illness in vaccinated individuals, our results did not demonstrate significant attenuation of symptoms.

Several factors may account for this, including host immune variability, the bacterial load at exposure, and the time elapsed since vaccination [24, 25]. Additionally, suboptimal vaccine coverage, incomplete immunization, or waning immunity could contribute to the observed lack of difference in clinical features [22,26]. The recent introduction of Typbar-TCV into the national immunization program also limits long-term data on vaccine impact. Longitudinal studies are needed to determine whether vaccination influences disease severity or reduces complications over time [20,21]. In this context, booster schedules and strategies to maintain high immunity levels may warrant evaluation.

Several limitations should be considered. First, the study focused on symptom frequency but did not assess severity, duration of illness, or hospitalization outcomes, which are critical for understanding vaccine-modified disease. Second, the modest sample size may have limited the statistical power to detect subtle differences between groups. Third, reliance on caregiver recall for vaccination status introduces the potential for recall bias. Lastly, the interval since vaccination was not accounted for, which may influence individual immune responses and clinical outcomes.

Despite these limitations, the findings have important clinical and public health implications. In resource-limited settings, diagnosis of typhoid fever often relies on clinical judgment due to the unavailability or unreliability of confirmatory tests [13]. Improved access to accurate diagnostics is essential to avoid both overdiagnosis and missed cases. Moreover, the strong association between typhoid risk and poor water, sanitation, and hygiene (WASH) conditions—consistently reported in the literature—underscores the need for integrated interventions [5,6,11,12].

The current study demonstrates that the clinical presentation of typhoid fever remains consistent among children aged 2–12 years, irrespective of vaccination status. While Typbar-TCV remains an essential preventive tool, its impact on modifying symptoms in breakthrough infections appears limited. These findings highlight the need for improved diagnostic tools, enhanced vaccine coverage, and long-term studies assessing disease severity and vaccine durability. Strengthening WASH infrastructure and public health education remains critical to reducing the overall burden of typhoid fever in endemic regions.

## CONCLUSION

The clinical profile of typhoid fever in children with the age 2-12 years is also reliable irrespective of the use of Typbar-TCV vaccine. At the same time, vaccination can help prevent the disease but does not have a huge impact on the breakthrough cases symptomatology. Such results underline an increased need to enhance diagnostics, further healthcare immunization, and enhance the mitigation of the public health activities. Future research aimed at investigating the effect of

vaccines on severity upon acquiring the disease and long-term results should be conducted.

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