

**Case Series**

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## A Retrospective Study of the Relationship Between Typhoid and Vestibular Disorders- A Case Series

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**Background:** Typhoid fever is caused by *Salmonella enterica* serovar Typhi (*Salmonella* Typhi). faecal-oral is the main route of transmission by contaminated water or food. Over the last few years, the classic presentation of typhoid fever has varied, and the cases with atypical presentation are increasing. In this study we are presenting a retrospective evaluation of patients presenting with giddiness post history of typhoid, to correlate a link between vestibular disorders and typhoid. **Aims and Objectives:** To retrospectively study the relationship between typhoid and vestibular disorders. **Materials and Methods:** This is a retrospective hospital-based case series conducted in vertigo clinic in The Department of ENT at SGT Medical College Hospital and Research Institute, Budhera, Gurugram. Five patients who gave positive history of typhoid, their case files were retrospectively evaluated. All the patients were made to undergo routine ENT, vertigo, and audiological evaluation. **Results:** Total of 5 patients presented to vertigo clinic at SGT hospital with complains of giddiness, all of them gave a history of typhoid in the past few weeks. Majority of patients presented with giddiness within four weeks after history of typhoid infection. Patients developed symptoms of giddiness, nausea, and vomiting. Out of 5 patients, 4 were females and one male. Two patients were in the age group of 30-40 years. Two patients were in paediatric age group. On examination, Dix Hallpike test was positive in 3 patients. Patients were treated with vestibular sedatives and corrective manoeuvre like Epley's. Pure tone audiometry, MRI brain and lab parameters were all normal in all the five patients. **Conclusion:** Endotoxins of the typhoid bacillus are capable of producing cochleovestibular lesions but only a few isolated reports suggest the same. Since very few literatures has been discussed on the possible correlation between vestibular disorders and typhoid, clinicians should be aware of atypical presentations of typhoid is to avoid any delay in diagnosis and prompt treatment. Therefore, there is a strong need to analyse and study the correlation between typhoid fever and vestibular disorders.

**Keywords:** Typhoid, Vertigo, Cochleovestibular Lesions, Giddiness.**INTRODUCTION**

Typhoid fever causative organism is either *Salmonella* serovar typhi or Para typhi. Estimate of enteric fever globally is twenty-seven million cases every year with about 200 000 deaths. There's a high annual incidence of 100–1600 cases per 100 000 population in South Asian countries [1,2,3] proper antibiotic therapy can be used to treat Uncomplicated typhoid fever but sometimes even that does not help prevent complications.[1]

It is a huge burden in low- and middle-income countries caused by the bacteria *S. typhi*. Contact with food or water contaminated by faecal matter or sewage is the most common mode of contact; typhoid fever diagnosis is based on symptoms, Widal test, and blood culture. [4]

High-grade fever, bacteraemia, and constipation during the first week, then followed by abdominal pain, diarrhoea, and sometimes hepatosplenomegaly and intestinal bleeding are the most common clinical presentations.

Over the last few years, the classic presentation of typhoid fever has varied, and the cases with atypical presentation, like sensorineural hearing loss has been increasing.[5] Lot of factors are implicated in the above scenario. According to one study from India, MDR (multidrug resistant) and XDR strains and inappropriate use of antibiotics in terms of type and duration, play a significant role.[6]

Acute sensorineural hearing loss cases are mostly idiopathic. Viral infections are most common, but

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bacterial causes like Salmonella Typhi are rare.<sup>[7]</sup> In a literature review, six cases of pathologically confirmed cochleovestibular lesions due to typhoid fever, symptoms appeared during the second week, females were in majority, and the more affected ear was left.<sup>[6,8]</sup>

All six patients had normal otoscopic profiles and presented with following symptoms hearing loss, feeling of fullness in the ear, tinnitus, and dizziness. In 5 of the 6 patients, cochleovestibular symptoms occurred between the second and third weeks of disease. Very less studies are conducted on typhoid-related lesions in the inner ear. Endotoxins of the typhoid bacillus are capable of producing cochlear lesions but only a few isolated reports suggest the same, further such lesions can be reversible was suggested by Hirasugi.<sup>[8,9]</sup>

Studies describe that arteritis caused by focal lesions with necrosis and an exaggerated response to pressor substances suggest that ischemia plays an important pathophysiological role in the presentation of cochleovestibular lesions caused by typhoid fever.<sup>[8]</sup> Since very few literature has been discussed on the possible correlation between vestibular disorders and typhoid, here we have done a retrospective hospital based case series of 5 patients who presented with giddiness to our vertigo clinic and presented with a significant history of typhoid.

## CASE SERIES

**Study Setting**—This is a retrospective hospital-based case series conducted in vertigo clinic in The Department of ENT at SGT Medical College Hospital and Research Institute, Budhera, Gurugram.

Five patients who gave positive history of typhoid, their case files were retrospectively evaluated. All the patients were made to undergo routine ENT, vertigo, and audiological evaluation. The case studies are discussed as follows.

### Case 1

A 33-year female patient presented with complaints of giddiness with swaying to left on and off associated with nausea and vomiting for 6 weeks. Vertigo was non rotatory type; lasting for 1-2 sec; intermittent; episodic type; it's triggered by head movements; and it's got relieved by drugs.

No history of hearing loss or ear discharge or ear pain.

She gives a history of episodes of migraines.

She was diagnosed with typhoid fever 7-8 weeks back with widal titer of 1/160 for both O and H antigen. For which she was treated with oral antibiotic Ciprofloxacin and cefixime from local hospital for 7-14 days. Following which blood culture negative for salmonella.

On examination vitals were stable; bilateral tympanic membranes were normal limits; gaze evoked nystagmus was positive on left side with left beating; Dix Hallpike was positive on left; Head impulse, bilateral fistula test and supine roll test were negative.

Saccades and pursuit were normal. Cerebellar signs also within normal limits.

Patient evaluated with pure tone audiometry, that showed hearing with normal limits followed by MRI Brain, which was showed no significant abnormality.

Patient advised to do Epley's maneuver on alternate day basis along with vestibular sedatives.

### Case 2

A 30-year female patient presented with complaints of giddiness associated with nausea and vomiting for 15 days. Vertigo was sudden in onset, continuous, rotatory type; lasting for 24 hrs; it's triggered when head turned to left side.

No history of hearing loss or ear discharge or ear pain.

She is a known case of hypothyroidism and on tab. Thyronorm 50 mcg, and she gives a history of episodes of migraines.

She was diagnosed with typhoid fever 1 month back with widal test and blood culture. For which she was treated with oral antibiotic Ciprofloxacin from local hospital for 7 days. Following which blood culture negative for salmonella.

On examination vitals were stable; bilateral tympanic membranes were normal limits; gaze evoked nystagmus present on left side with left beating; Dix Hallpike was positive on both sides but left side was more positive than right side; Supine roll test was showing increased giddiness on left side. Head impulse and bilateral fistula test were negative.

Saccades and pursuit were normal. Cerebellar signs also within normal limits.

Patient was admitted and evaluated with pure tone audiometry, that showed hearing with normal limits followed by MRI Brain, which was showed no significant abnormality.

Patient managed by Epley's maneuver on alternate days along with intravascular vestibular sedatives.

### Case 3

A 50-year female patient presented with complaints of giddiness associated with nausea and vomiting for 4-5 days. Vertigo was sudden in onset, continuous, rotatory type, lasting for 24 hrs.; it's associated with swaying and imbalance, and it's triggered when looking up.

No history of hearing loss or ear discharge or ear pain.

She was diagnosed with typhoid fever 15 days back with widal test and blood culture. For which she was treated with oral antibiotic Ciprofloxacin from local hospital for 7 days. Following which blood culture negative for salmonella.

On examination vitals were stable; bilateral tympanic membranes were normal limits; gaze evoked nystagmus present on right side with right beating; Head impulse was impaired on right side; Bilaterally Pursuit was nystagmic type with full range. Dix Hallpike was positive on both sides but right side was more positive than left side; Supine roll test and bilateral fistula test were negative. Saccades were within normal limits. Cerebellar signs were also within normal limits.

Patient was admitted and evaluated with pure tone audiometry, that showed hearing with normal limits.

Patient managed by Epley's maneuver on alternate days to right side along with vestibular sedatives.

### Case 4

A 13-year girl child referred to ENT OPD with complaints of giddiness associated with nausea and vomiting for 1 month. Vertigo was sudden in onset, intermittent, rotatory type, lasting for seconds, aggravated by head movements. There is a history of black outs during the episodes.

No history of hearing loss or ear discharge or ear pain or tinnitus. No history of abnormal movements, migraine.

She was diagnosed with typhoid fever 1 month back with widal test. For which she was treated with oral antibiotic from local hospital for 7 days.

She was also giving history of varicella zoster infection 2 weeks back.

On examination vitals were stable; bilateral tympanic membranes were normal limits; gaze evoked nystagmus present on right side with gaze

evoked; Head impulse was impaired on right side; Dix Hallpike was negative on both sides; Supine roll test and bilateral fistula test were negative. Pursuit and Saccades were within normal limits. Cerebellar signs were also within normal limits.

Patient was admitted and evaluated with pure tone audiometry, that showed hearing with normal limits. MRI brain was done and that showed normal brain parenchyma. EEG also showed normal study. Lab parameters were also normal.

**Case 5**

A 10-year male child referred to ENT OPD with complaints of giddiness associated with nausea and vomiting for 4-5 days. Vertigo was sudden in onset, intermittent, rotatory type, lasting for 10-15 seconds, not aggravated by head movements. history of fever was present.

No history of hearing loss or ear discharge or ear pain or tinnitus. No history of abnormal movements, migraine.

He was diagnosed with typhoid fever 6 months back with widal test. For which she was treated with oral antibiotic from local hospital for 14 days.

On examination vitals were stable; bilateral tympanic membranes were normal limits; gaze evoked nystagmus present on right side with gaze evoked; Dix Hallpike was negative on both sides; Head impulse was negative on both sides; Supine roll test and bilateral fistula test were negative. Pursuit and Saccades were within normal limits. Cerebellar signs were also within normal limits.

Patient was admitted and evaluated with pure tone audiometry, that showed hearing with normal limits. MRI brain was done and that showed normal brain parenchyma. EEG also showed normal study. Lab parameters were also normal.

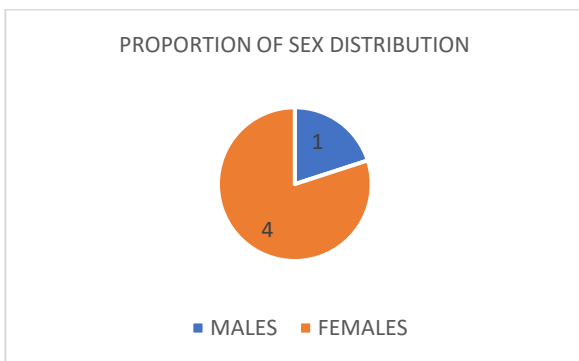
Patient managed symptomatically and advised for follow up.

**RESULTS**

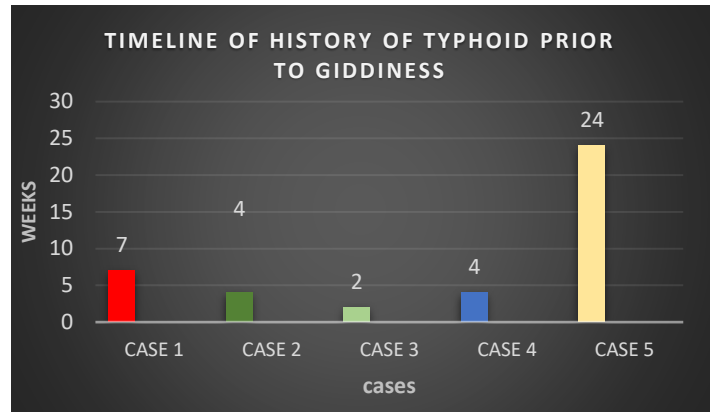
Total of 5 patients presented to vertigo clinic at SGT hospital with complains of giddiness, all of them gave a significant history of typhoid in the past few weeks. Most of the patients developed immediate symptoms of giddiness, nausea, and vomiting. One patient gave history of blackouts. All the patients were treated with oral antibiotics at home, hence none of the infection proved to be severe.

Two patients presented with history of migraine and one patient had a concomitant history of hypothyroidism. 1 patient presented with history of varicella infection post typhoid infection.

Out of 5 patients, 4 were females and one male. (Figure 1). Two patients were in the age group of 30-40 years. Two patients were in pediatric age group. Majority of patients presented with giddiness within four weeks after history of typhoid infection. (Figure 2). The type of giddiness, duration of episode is discussed in (Table 1).



**Figure 1:** Proportion of Sex Distribution



**Figure 2:** Timeline of history of typhoid prior to giddiness

On examination, Dix Hallpike test was positive on the left in two patients and one patient it was positive on the right. Other two patients Dix Hallpike was negative. (Table 2) Patients were treated with vestibular sedatives and corrective maneuver like Epley’s. Gaze evoked nystagmus was positive in all cases. Case 2 discussed has concomitant supine roll test and dix hallpike test was positive on the left showing involvement of both left horizontal and posterior semicircular canal. Pure tone audiometry, MRI brain and lab parameters were all normal in all the five patients.

**Table 1:** Description of vertigo episodes of all the cases

	Type of giddiness	Duration of episode	Triggers
<b>CASE 1</b>	SWAYING, NON-ROTATORY	1-2 SECS	HEAD MOVEMENTS
<b>CASE 2</b>	CONTINUOUS, ROTATORY	24HRS	HEAD MOVEMENTS
<b>CASE 3</b>	CONTINUOUS, ROTATORY	24HRS	LOOKING UP
<b>CASE 4</b>	ROTATORY, BLACKOUTS	SECONDS	HEAD MOVEMENTS
<b>CASE 5</b>	ROTATORY	10-15 SECS	NO TRIGGER

**Table 2:** Number of cases indicating vestibular disorders (Note: Case 2 showed concurrent dix hall pike and supine roll positive on left)

<i>Dix Hallpike positive</i>	3
<i>Dix Hallpike negative</i>	2
<i>Supine role test positive</i>	1

**DISCUSSION**

Typhoid fever is caused by salmonella enterica serovar typhi (salmonella typhi, S. typhi). Faecal-oral is the main route of transmission, generally by contaminated water or food. It clinically presents as an acute febrile illness and most common signs and symptoms are headache, abdominal pain, diarrhoea or constipation, and malaise. [3] Severe complications of typhoid fever include intestinal perforation, hepatitis, pneumonia, and tissue abscesses. Acute encephalopathy or meningitis has also been described, most frequently as neurologic illness. Neurologic signs have been documented, include acute neuropsychiatric illness, spasticity and clonus, ataxia, aphasia,

and cerebritis. They are mostly reported as case reports or small case series.<sup>[10]</sup>

A rare complication which presents is cranial mononeuropathy.<sup>[2]</sup> Few cases of diplopia and 4 to 5 isolated cases of sixth nerve palsy have been reported. Awareness about the rare complications of common diseases like enteric fever is very essential. Proper antibiotic therapy can be used to treat uncomplicated typhoid fever, but in some cases even the right therapy might not help to prevent complications.<sup>[1]</sup>

The clinical symptoms of typhoid appear during the second septicaemia phase during which endotoxins are released. Endotoxins are pyrogen, a significant vessel response to catecholamines with pressor and vasomotor changes in the microcirculation, and increased serotonin resulting in arteritis, which accompanies typhoid fever explain the main clinical factors.<sup>[11-15]</sup>

Degeneration of the organ of Corti can be caused by endotoxins.<sup>[8]</sup> Majlesi et al. discussed a case where *S. typhi* was cultured in a mastoid abscess after an infection of typhoid fever, findings indicate that cochleovestibular lesions can be produced by the bacillus itself.<sup>[16]</sup>

The patients discussed in this study out of which 3 patients presented with Dix-Hallpike positive and one patient presented with concomitant supine roll test positive showing peripheral vestibulopathy in these patients, the patients also had a significant history of typhoid in the past hence predisposing them to cochleovestibular lesions. (table 2)

Ramon et al discussed a case series where five of the six patients in this study were female, there is a possibility that women may be predisposed to cochleovestibular lesions. Vestibular symptoms prevailed over cochlear lesions; the left ear was more affected (71.1 0/0) than the right.<sup>[8]</sup> Our study showed similar findings where females were in majority. (Figure 2)

Neurologic manifestations of typhoid are projected as a late manifestation of illness<sup>[10]</sup> and the interval between symptom onset and documentation of neurologic signs in the patients was 12 days. Delayed presentation to clinical care and ineffective antimicrobial treatment early in the course of disease because of resistance of the causative salmonella typhi strain to multiple drugs<sup>[17]</sup> have led to a prolonged course of illness very early in the outbreak, which results in a greater prevalence of neurologic signs.<sup>[10]</sup>

Our study most patients complained of giddiness after 4 weeks of typhoid infection (Figure 1).

Some of the most common neurologic manifestations discussed in literature were upper motor neuron signs: deep tendon hyperreflexia, spasticity, and sustained ankle clonus. Twenty patients demonstrated truncal or appendicular ataxia or both, which also resulted in gait abnormalities. Ataxia was seen along with nystagmus or intention tremor. Subjective neurologic symptoms including hearing loss and visual problems were described by many patients.<sup>[10]</sup>

According to a randomized controlled trial done in Indonesia, the addition of high-dose dexamethasone to chloramphenicol for 48 h proved a significant reduction in case fatality rate compared to chloramphenicol alone (10% versus 55%). The usage of adjunctive dexamethasone did not increase the risk of side effects in a patient with severe typhoid fever, which is defined as bacteraemia which is associated with reduced level of consciousness, disorientation, obtundation, or coma.<sup>[18]</sup> The benefit of adjunctive dexamethasone in addition to antibiotics is not proven.

Systemic steroids could reduce inflammation and oedema in the hearing organs,

They are usually used in patients with acute sensorineural hearing loss, this helps to heal the possible idiopathic acute inflammation of the labyrinth or cochlear nerve.<sup>[19,20]</sup>

The same principle can be used for sensorineural hearing loss or cochleovestibular lesions presenting after a typhoid fever. The recommended duration of adjunctive steroids is 6 weeks.<sup>[6]</sup>

However, there is a paucity of data on the use of systemic steroids in typhoid fever. It is very essential for physicians to be aware of such presentations, and to consider including typhoid fever as a cause in their differentials. Prompt diagnosis, appropriate antibiotic therapy, and adjunctive steroids with proper follow up can assist in preventing severe complications like cochleovestibular lesions and achieving rapid recovery in typhoid patients.<sup>[6]</sup>

The importance of being aware of atypical presentations of typhoid is to avoid any delay in diagnosis and prompt treatment, this prevents progression of serious complications caused by typhoid fever.

## CONCLUSION

As per the study we evaluated 5 patients post typhoid fever, and all of them complained of dizziness few weeks after the infection. Therefore, there might be a correlation between the endotoxins of typhoid bacillus and vestibular disorders post infection. According to available literature there might be a correlation as, endotoxins of the typhoid bacillus can produce cochleovestibular lesions. Main limitation of our study is that very few numbers of cases were reported. Since very few literatures have been discussed on the possible correlation, clinicians should be aware of these atypical presentations to create awareness among patients and to avoid any delay in diagnosis and prompt treatment. Therefore, there is a strong need to analyse and study the correlation between typhoid fever and vestibular disorders.

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## Conflict of Interest

The authors declare no conflicts of interest.

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