# **Different Clinical Manifestations of Dengue Fever**

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# **Abstract**

**Background**: Dengue fever is a widespread mosquito borne infection transmitted by Aedesa egypti arthropod.

**Objectives** to assess the clinical manifestations of gastrointestinal, cochleovestibular, and respiratory systems in patients with Dengue fever and to analyze the variables that affect it.

**Patients and methods:** a prospective cohort study, 100 dengue fever patients were assessed for different clinical presentations of dengue fever. Laboratory and imaging investigations were repeated after one and three months.

**Results:** The mean age was 37.97±16.1 years. Apart from watery diarrhea, there was clinical improvement in GIT symptoms as abdominal pain, anorexia, nausea, vomiting, splenomegaly and ascites after three months during follow up (P 0.003). Four (4%) patients presented with hearing loss and tinnitus after the onset of fever. Two of them (2%) had bilateral mild sensorineural hearing loss, and two (2%) had unilateral sudden profound sensorineural hearing loss. Four patients (4%) complained of tinnitus only pure tone audiometry revealed mild to moderate high frequency sensorineural hearing loss during examination. On one and three month follow-ups, most of those patients show no improvement. As regards respiratory manifestations, twenty-eight (28%) patients presented with respiratory symptoms. The most common symptom was dyspnea seen in 26 (26%) patients, cough in 22 (22%) patients, and hemoptysis in 1 (1%) patient.

**Conclusion:** Patients with serologic dengue infection may present typical GI manifestations such as nausea, diarrhea, and abdominal pain. While atypical GI manifestations were splenomegaly and ascites. Also, concomitant cochleovestibular and respiratory symptoms that were reported for the first time. Their outcome was heterogeneous.

**Keywords:** Dengue fever; Gastrointestinal manifestations; Cochleovestibular manifestations; Respiratory manifestations.

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#### Introduction

Dengue fever (DF) is a widespread mosquito borne infection transmitted by *Aedesa egypti* arthropod. It is caused by the Dengue virus (DENV) which belongs to *genus flavi* virus of *Flavi viridae* family. The disease is concentrated in tropical and sub tropical regions, most prevalent in Southeast Asia, the America, and Western Pacific regions (WHO, 2009).

In Egypt, 2015, the World Health Organization confirmed a dengue fever outbreak in Assiut and in 2017, there was circulation of DENV on the Red Sea Coast affecting travellers. Entomological studies confirmed the apparent re-emergence of Ae. aegypti in Hurghada and El Quseir in 2017. The European Centre for Disease Prevention and Control map on Ae. aegypti distribution in October 2023 shows presence of the mosquito in Red Sea governorate and parts of the upper Nile valley (Frank et al. 2023)

The clinical manifestations of dengue infection range from mild febrile illness known as DF to severe hemorrhagic disease known as Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which is characterized by capillary leakage, organ involvement, and bleeding complications (Pervin et al., 2003; Yacoub and Farrar, 2014; Azad et al., 2018).

Symptoms of DF start after incubation period of 3-7 days. It has three stages: an initial febrile stage, a critical stage, and a spontaneous recovery stage. Patients usually recover after the febrile stage with no complications (Kabir et al., 2008; WHO, 2009; Bhatt et al., 2013). Classical dengue patients usually present with fever, headache, myalgia, arthralgia, rash, retro-orbital pain, lymphadenopathy, and dry cough. Dengue cases also present hemorrhagic manifestation subconjunctival hemorrhage, epistaxis, petechiae, etc.) with or without shock (Pervin et al., 2003), Gastrointestinal (GI) symptoms, reduced platelet count, and abnormal liver function tests were also

evident as presenting features of dengue nowadays (Brady et al., 2012).

The prevalence of respiratory symptoms in dengue patients varies; these symptoms are typically minor and mostly impact the upper airway (Marchiori et al., 2009; Simmons et al.,2012; von Ranke et al., 2013; Rodrigues et al., Common ENT manifestations in DF include rhinitis. sore throat. nasal obstruction, bleeding, nasal gingival bleeding, otalgia, tinnitus, and hearing loss (Bhatt et al., 2013). Hearing loss that occurs as a result of a viral infection is typically sensorineural. As the immune system of the patient may have triggered damage to the peripheral auditory system, which may be the result of direct viral destruction (Simmons et al., 2012).

Acute respiratory distress syndrome (ARDS), pleural effusion, pneumonitis, non-cardiogenic pulmonary edema, and pulmonary hemorrhage are less frequent manifestations of pulmonary complications. These complications occur together with thrombocytopenia syndrome. capillary leak The most common causes of dyspnea are pleural effusion, ARDS, pulmonary hemorrhage, pneumonia, and shock. Although it is uncommon, diffuse alveolar hemorrhage is usually associated with severe frequently fatal forms of the disease. According to reports, 1.4% of Dengue infections result in hemoptysis (Marchiori Marchiori 2009; et 2012; Rodrigues et al., 2014).

From a clinical standpoint, tracking changes in the clinical pattern can enhance case-finding and clinical treatment. One of the most common reemerging mosquitoborne illnesses in the world now is dengue. The past 50 years have seen a 30-fold increase in dengue incidence (WHO, **2009**). Dengue is currently endemic in 128 primarily countries, in developing countries, and it threatens over 3.97 billion people per year. Approximately 390 million dengue infections occur annually

according to the current dengue distribution model, with 96 million cases reportedly occurring (Guzman and Kourí, 2002; Cohen et al., 2014).

The aim of this study is to assess the prevalence of GI symptoms and cochleovestibular and respiratory manifestation in patients with post-Dengue fever and to analyze the variables that affect it.

### Patients and methods

**Type of the study:** a prospective study including 100 patients with dengue fever. We assessed all patients for different clinical presentations of dengue fever

**Study Populations:** The study was carried out in out-patient Tropical medicine and Gastroenterology clinic, Chest clinic, and ENT clinic, Qena University Hospital, who had been diagnosed to have Dengue fever from March 2023 to April 2024.

# Study subjects:

### **A-Inclusion criteria:**

- a. Patients with fever, headache, nausea, vomiting, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, positive tourniquet test, leukopenia coupled with exposure to a dengue-endemic country or region
- b. Patients with dengue fever (IgM positive).
- c. Adult patients aged > 18 years old.

### **B-** Exclusion criteria:

- a. Patients with chronic liver disease, pancreatitis.
- b. Patients with Malaria and Enteric fever and other causes of fever.
- c. Patients with a history of chronic suppurative otitis media, hearing loss, or ear surgery.
- d. Patients who have previously been exposed to ototoxic medicines or noise.
- e. Patients with chronic respiratory disease.
- f. Patients who had a previous history of pleural effusion, pneumonia and alveolar hemorrhage.
- g. Patients with history of hypothyroidism, diabetes mellitus,

neurological disease, or autoimmune disease.

# Study tools

- 1- History and physical examination were done for all patients and recorded if were any manifestation gastrointestinal, cochleovestibular and respiratory symptoms, fever, headache, nausea, vomiting, retro-orbital myalgia, arthralgia, rash, hemorrhagic manifestations, positive tourniquet test, leukopenia coupled with exposure to a dengue-endemic country or region and any drug taken.
- **2-Complete blood count (CBC)**: Every patient underwent a complete CBC examination on a regular basis using an automated hematology analyzer called Mindray BC-5150. A WBC count of less than 4000/mm<sup>3</sup> was used to identify leucopenia. A platelet count of less than  $100,000/\text{mm}^3$ was used identify Using a thrombocytopenia. widely available kit from DRG International (USA) to test for the IgM antibody of DF in all the samples.
- **3-Liver function test**: Serum bilirubin, ALT, and AST levels were estimated with a Selecta PRO-M auto analyzer.
- 4- Assessment of pancreatic lipase: Lipase Assay Kit assesses pancreatic lipase improved using an Dimercaptopropanoltributyrate (BALB) method. The reagent kit for the evaluated lipase assay (Lipase Color Liquid, product no.17401) was from Sentinel Diagnostics. In this method, thiol (SH) groups are formed when lipase cleavage of BALB, and they interact with 5,5'-dithiobis (2nitrobenzoic acid) (DTNB) to make a coloured product. proportional Α relationship exists between the enzyme activity in the sample and the colour intensity, which is measured at 412 nm. (Furukawa et al., 1982).

### 5- Dengue fever diagnostic tests

We used IgM antibody test; Dengue IgM Capture ELISA (InBios kit, InBios International, Inc., Seattle, WA, USA) kits

following respective manufacturer's instructions. We used 1:100 diluted sera on a microplate coated with anti-human IgM antibodies, then adding dengue antigen and DENV-specific monoclonal antibody labeled horseradish with enzyme peroxidase (Mab/HRP), in a succession of incubations and washings. the Dengue IgM appeared between the 4th and 5th day of fever. Immune status ratio (ISR) was determined by calculating the ratio of the absorbance over DENRA the NCA absorbance of the tested serum. An ISR < 1.65 is interpreted as negative, ISR between 1.65 and 2.84 as equivocal, and ISR > 2.84 as positive.

**6-Imaging:** every patient had a chest radiograph and imaging ultrasonography for abdomen and chest. The same serum laboratory tests were performed, along with an ultrasound follow-up after one and three months.

7-**Audiological** examinations including pure tone audiometry (PTA) with average of 500 Hz, 1000 Hz, 2000 Hz calculated and tympanometry. Patients were re-evaluated after 1 and 3 months to confirm hearing loss and to assess reversibility. In patients with unilateral hearing loss, MRI petrous bone with gadolinium was prescribed to exclude retrolabrynthine lesions. Patients with sudden hearing loss were treated by steroids as a line of management of sudden sensorineural hearing loss (Salmon et al., 2025)

**8- Follow up of the patients:** it was done one and three months from the diagnosis, every patient had a chest radiograph and abdominal ultrasonography. The same serum laboratory tests were performed, along with an ultrasound

follow-up after one and three months.

# Ethical considerations

The ethical approval was granted by the Ethics Committees of the Faculty of Medicine at South Valley University, under approval number SVU, MED, GIT023, 4,23,8,705. in compliance with the criteria put by the Declaration of Helsinki. It was evident that participants were fully informed about the goals, advantages, and dangers of the study, as well as their unrestricted right to accept or reject, and that informed consent had been obtained.

# Statistical analysis

Version 27.0 of the Statistics Package for Social Science (SPSS Inc., Chicago, IL, USA) was used to analyze the data. The McNemar's test was used to compare categorical data from the start, after one month, and three months. A P value of < considered 0.05 was statistically significant, and a P value of < 0.01 was considered highly statistically significant. P1: Comparison between baseline and 1month. P2: Comparison between baseline and three months. P3: Comparison between one month and three months. Wilcoxon Signed Ranks test was used for constant data (lab data). On the other hand, the facts about the duration of the disease did not follow the normal distribution. To express continuous data, mean and standard deviation (Mean ± SD) were used. The Independent Samples T test was used for parametric data and the Mann-Whitney U test was used for non-parametric data to see if there were any differences between the two groups.

# Results

# Demographic data and investigation

Baseline characteristics data for all patients were described in **(Table.1).** 

Table 1. Baseline characteristics data.

| Variables     | No. (100)   | % |
|---------------|-------------|---|
| Age           |             |   |
| MinMax.       | 7 – 76      |   |
| $Mean \pm SD$ | 37.97±16.11 |   |
| Sex           |             |   |

| Male            | 54 | 54.0% |
|-----------------|----|-------|
| Female          | 46 | 46.0% |
| Residence       |    |       |
| Urban           | 29 | 29.0% |
| Rural           | 71 | 71.0% |
| Footnote Habits |    |       |
| No              | 90 | 90.0% |
| Smoker          | 10 | 10.0% |

**(Table.2)** shows the observed GI manifestations at the time of diagnosis. There was a significant improvement in GI

symptoms in the three-months follow-up except in watery diarrhea.

Table 2. GIT symptoms follow-up distribution in dengue fever patients

| Variables    | At baseline |             | At 1 mor                | ıth               | At 3 months |         |  |
|--------------|-------------|-------------|-------------------------|-------------------|-------------|---------|--|
| variables    | %           | Yes         | %                       | Yes               | %           | Yes     |  |
| Fever -      | 35(35%)     | 65(65%)     | 59(59%)                 | 41(41%)           | 78(78%)     | 22(22%) |  |
| rever        |             | F           | P1 < 0.001** P2 < 0.0   | 001** P3 < 0.001* | *           |         |  |
| Pain         | 22(22%)     | 78(78%)     | 10(10%)                 | 10(10%) 90(90%)   |             | 48(48%) |  |
|              |             | P1 0.001**  | P2 <0.001**             | P3 <0.001**       |             |         |  |
| Anorexia     | 28(28%)     | 72(72%)     | 38(38%)                 | 62(62%)           | 83(83%)     | 17(17%) |  |
|              |             | P1 0.004**  | P2 <0.001**             | P3 <0.001**       |             |         |  |
| Nausea       | 7(7%)       | 93(93%)     | 83(83%)                 | 17(17%)           | 77(77%)     | 23(23%) |  |
|              |             | P1 <0.001** | P2 <0.001**             | P3 0.041*         |             |         |  |
| Vomiting     | 41(41%)     | 59(59%)     | 29(29%)                 | 71(71%)           | 69(69%)     | 31(31%) |  |
|              |             | P1 0.001**  | P2 <0.001** P3 <0.001** |                   |             |         |  |
| Diarrhea     | 16(16%)     | 84(84%)     | 25(25%)                 | 75(75%)           | 14(14%)     | 86(86%) |  |
|              |             | P1 0.008**  | P2 0.480                | P3 0.003**        |             |         |  |
| Splenomegaly | 87(87%)     | 13(13%)     | 95(95%)                 | 5(5%)             | 97(97%)     | 3(3%)   |  |
|              |             | P1 0.013*   | P2 0.004**              | P3 0.480          |             |         |  |
| Ascites      | 95(95%)     | 5(5%)       | 98(98%)                 | 2(2%)             | 99(99%)     | 1(1%)   |  |
|              |             | P1 0.248    | P2 0.134                | P3 1.000          |             |         |  |

McNemar's test was used to compare categorical. 0.05 considered statistically significant; \*\* P < 0.01 considered highly statistically significant; P1: Comparison between at baseline and one month; P2: Comparison between at baseline and 3month; P3: Comparison between at one month and three months.

(Table.3) shows the investigation findings of cases confirmed for Dengue that was positive for Dengue IgM antibody. As regards platelets and WBCs there was significant increase (improvement) in follow-up duration. In other hand, there was significant decrease (improvement) in follow-up duration as regards ALT, AST,

ALP, amylase and lipase enzyme. (**Table.4**) shows the general ENT symptoms. (**Table.5**) shows the audiological findings at the first visit and after 1- and 3-months follow-up.

Table 3. Laboratory investigation follow-up distribution of dengue fever

| Variables           | At baseline                           | At 1- month  | At 3-months |  |  |  |
|---------------------|---------------------------------------|--------------|-------------|--|--|--|
| Plt/mm <sup>3</sup> | 127.15±91.64                          | 178.36±99.09 | 195.26±85.9 |  |  |  |
|                     | P1 <0.001**; P2 <0.001**; P3 <0.001** |              |             |  |  |  |
| Hb g/dL             | 13.08±2.35                            | 13.21±2.24   | 13.28±2.17  |  |  |  |
|                     | P1 0.068                              | P2 0.026*    | P3 0.102    |  |  |  |

| WBC/ mm <sup>3</sup> | 3.81±2.56                 | 4.54±2.51                  | 5.09±2.56                  |  |  |
|----------------------|---------------------------|----------------------------|----------------------------|--|--|
|                      | P1 <0.001**               | P2 <0.001**                | P3 <0.001**                |  |  |
| Bili<br>mg/dL        | 1.7±0.49                  | 1.67±0.5                   | 1.51±0.45                  |  |  |
|                      | P1 0.007**                | P2 <0.001**                | P3 0.001**                 |  |  |
| Alb<br>g/L           | 3.96±0.65                 | 3.96±0.65                  | 3.99±0.63                  |  |  |
| 8-                   | P1 1.000                  | P2 0.068                   | P3 0.068                   |  |  |
| ALT (U/L)            | 41.09±23.17               | 37.08±16.51                | 28.64±11.68                |  |  |
|                      | P1 0.018*                 | P2 <0.001**                | P3 <0.001**                |  |  |
| AST (U/L)            | 33.92±16.34<br>P1 0.001** | 29.98±13.11<br>P2 <0.001** | 26.52±11.73<br>P3 <0.001** |  |  |
| ALP<br>(IU/L)        | 122±17.72                 | 115.3±22.88                | 105.23±25.67               |  |  |
|                      | P1 <0.001**               | P2 <0.001**                | P3 <0.001**                |  |  |
| Amylase<br>(U/L)     | 43.25±6.5                 | 39.79±9.07                 | 32.83±11.76                |  |  |
|                      | P1 <0.001**               | P2<0.001**                 | P3 <0.001**                |  |  |
| Lipase<br>(U/L)      | 109.6±115.79              | 80.7±100.64                | 91.77±105.16               |  |  |
|                      | P1 <0.001**               | P2 0.080                   | P3 0.033*                  |  |  |

McNemar's test was used to compare categorical. The data were presented as the mean  $\pm$  SD, Abbreviations: P. value: Comparison between at baseline, at 1month and at 3 months follow-up for continuous data (Binary paired continuous data) were used Wilcoxon Signed Ranks test; P < 0.01 considered highly statistically significant; P1: Comparison between baseline and 1 month; P2: Comparison between baseline and 3 months; P3: Comparison between 1-month and 3-months.

Table 4. General ENT symptoms noticed 2-10 days after Dengue fever

| Table 4. General Ervi symptoms noticed 2-10 days after Dengue level |        |             |  |  |  |  |
|---|--------|-------------|--|--|--|--|
| Complaint   | Number | Percent (%) |  |  |  |  |
| Sore throat   | 75     | 75%         |  |  |  |  |
| Rhinitis and nasal obstruction                                      | 62     | 62%         |  |  |  |  |
| Otalgia   | 24     | 24%         |  |  |  |  |
| Epistaxis   | 11     | 11%         |  |  |  |  |
| Tinnitus  | 9      | 9%          |  |  |  |  |
| Hearing loss  | 4      | 4%          |  |  |  |  |
| Vertigo Vertigo   | 0      | 0%          |  |  |  |  |

Table 5. Audiological findings at first visit and after 1- and 3-months follow-up

| Variables        | Number of patients | Finding   |
|------------------|--------------------|---|
| PTA at the first | 2(2%)              | Profound sensorineural hearing in left ear with very poor speech discrimination |

| visit                | 2(2%) | Mild sensorineural hearing in both ears with very good speech discrimination  |
|----------------------|-------|---|
|                      | 4(4%) | Mild to moderate high-frequency sensorineural hearing loss in both ears with excellent speech discrimination                          |
|                      | 1(1%) | Persistent profound sensorineural hearing loss in left ear with very poor speech discrimination                                       |
| PTA at 1-            | 1(1%) | Improved from profound sensorineural hearing loss to moderate sensorineural hearing loss in left ear with fair speech discrimination. |
| month<br>follow-up   | 2(2%) | Persistent mild sensorineural hearing loss in both ears with very good speech discrimination.   |
|                      | 4(4%) | Persistent as mild to moderate high-frequency sensorineural hearing loss in both ears with excellent speech discrimination.           |
|                      | 1(1%) | Persistent profound sensorineural hearing loss in left ear with very poor speech discrimination                                       |
| PTA at 3-            | 1(1%) | Improved from profound sensorineural hearing loss to moderate sensorineural hearing loss in left ear with fair speech discrimination. |
| months<br>Follow-up  | 2(2%) | Persistent mild sensorineural hearing loss in both ears with very good speech discrimination.   |
| PTA: pure tope audio | 4(4%) | Persistent as mild to moderate high-frequency sensorineural hearing loss in both ears with excellent speech discrimination.           |

PTA: pure tone audiometry.

**(Table.6)** shows the observed respiratory manifestations in 28 patients.

The most common symptom was dyspnea.

Table 6. Respiratory symptoms follow-up distribution of dengue fever

| Table 6. Respiratory symptoms follow-up distribution of deligible level |         |               |       |            |        |             |             |          |         |
|---|---------|---------------|-------|------------|--------|-------------|-------------|----------|---------|
| Variables   | At base | At baseline A |       | At 1 month |        | At 3 months |             | P2       | Р3      |
|   | No      | Yes           | No    | Yes        | No     | Yes         | P1          | P2       | rs      |
| Cough   | 78      | 22(22         | 90    | 10         | 99(9   | 1(1%)       | 0.001**     | <0.001** | 0.008** |
|   | (78%)   | %)            | (90%) | (10%)      | 9%)    | 1(170)      |             |          |         |
| Dyspnea   | 74      | 26            | 87    | 13         | 95     | 5           | <0.001**    | <0.001** | 0.013*  |
|   | (74%)   | (26%)         | (87%) | (13%)      | (95%)  | (5%)        | <0.001      | <0.001   | 0.013   |
| Chast nain  | 95      | 5             | 98    | 2          | 100    | 0           | 0.248 0     | 0.074    | 0.480   |
| Chest pain  | (95%)   | (5%)          | (98%) | (2%)       | (100%) | (0%)        |             | 0.074    |         |
| Hemoptysis  | 99      | 1             | 99    | 1          | 100    | 0           | 1 000       | 0.490    | 1 000   |
|   | (99%)   | (1%)          | (99%) | (1%)       | (100%) | (0%)        | 1.000 0.480 | 1.000    |         |

\*P < 0.05 significant, \*\* P < 0.01 highly significant; P1: Comparison between baseline versus at 1 month; P2: Comparison between baseline and 3 months; P3: Comparison between 1 month and 3 months.

# **Discussion**

DF is a viral disease spread by arthropods that affects more than 100 million people globally (Islam et al., 2006;

Biswas et al., 2014). An estimated 390 million cases occur worldwide each year, with 96 million of those cases exhibiting symptoms (Bhatt et al., 2013). In 2000,

there was the first documented dengue outbreak, with 5551 cases and 93 reported deaths (Sharmin et al., 2015).

According to our research, the majority of the affected individuals were male adolescents. One of the most remarkable observations made regarding this outbreak was the existence of gastrointestinal signs, in addition to the typical general characteristics. Symptoms of dengue usually include fever, pain, and rash. On the other hand, bleeding and GI symptoms may appear in different proportions, as reported previously (Hasan et al, 2016).

In this study, nausea, diarrhea, and abdominal pain are the most common GI symptoms watery diarrhea occurred in eighty percent of patients. manifestations reported in the study were splenomegaly (13%) of patients with clinical improvement during follow-up of patients. There was significant improvement in GI symptoms in three months follow-up except in watery diarrhea there was significant worsening after three months follow up (P = 0.003). As regards splenomegaly and ascites there was clinical improvement during 3 months follow-up, but this improvement was statistically insignificant. There was significant improvement in platelets and WBCs in the follow-up duration. In other hand, there significant was statistical decrease (improvement) in follow-up duration as regards ALT, AST, ALP, amylase, and lipase enzyme.

Dengue virus attacks host cells and causes the release of many cytokines and stimulates the immune system, vascular endothelial changes, infiltration of mononuclear cells, and perivascular edema. Amin et al. (2025).

As regards ENT manifestations in our study, 75 patients (75%) sore throat, 62 patients (62%) had rhinitis and nasal obstruction, 24 patients (24%) had otalgia, 11 (11%) had epistaxis, 10 patients (10%) had a history of tinnitus in both ears. 4

patients (4%) had a history of hearing loss (2 unilateral and 2 bilateral). No history noticed regard vertigo in all patients. All symptoms are noticed about 2-10 days after dengue fever onset.

In our study, four (4%) patients complained of hearing loss and tinnitus the PTA at first visit of two patients (2%) revealed profound sudden sensorineural hearing loss (SSNHL) in left ear with very poor speech discrimination. One of them moderate improved to sensorineural with hearing loss fair speech discrimination; other patient persisted with profound sensorineural hearing loss with very poor speech discrimination in one and three months follow-up. The other two patients (2%), the PTA revealed mild sensorineural hearing loss with very good speech discrimination in both ears with no improvement in one and three months follow-up. From the 96 patients who were not complaining of hearing loss, about 4 patients (4%) had mild to moderate highfrequency sensorineural hearing loss at 4 KHz and 8 KHz with excellent speech discrimination in both ears discovered during examination with no improvement in one and three months follow-up, these 4 patients (4%) complained of tinnitus only in both ears, and one patient complained of tinnitus only in both ears with normal hearing during examination. As regards the tinnitus complaints in nine patients, there was no improvement in follow-up visits.

Patients with DF typically come with ambiguous symptoms; like fever, fatigue malaise and rarely have positive diagnostic results. A few patients may also experience frontal headaches or retro-orbital pain along with nasal discharge, while others may have hyperaemia of the nose, nasopharynx, and oropharynx (Greco et al., 2011). Symptoms that involve the ears include vertigo, tinnitus, and SSNHL (Schreiber et al., 2010 and Soni et al. 2021) discovered that patients may come symptoms such bleeding as manifestation, frontal headache, retroorbital discomfort, or upper respiratory infection. These symptoms may be accompanied low platelet count, ear pain, vertigo, tinnitus, and hearing loss.

Rahme et al. (2020) discovered that patients with a serologically proven dengue infection had varying combinations of cochleovestibular symptoms, such vertigo, tinnitus, sudden hearing loss, and sound intolerance. They also discovered heterogeneous outcomes, improved following treatment, tinnitus and sound intolerance spontaneously dissipated after dengue was resolved, and sudden hearing loss accompanied by tinnitus experienced partial recovery in some patients after treatment, while no recovery was observed in others, despite partial improvement of tinnitus and vertigo.

The SSNHL may be due to viral infection or vascular or immunologic factors. It can be associated with tinnitus and vertigo (Schreiber et al., 2010). Three mechanisms can explain the SSNHL: a) viral invasion of the cochlear cavity or nearby soft tissues by cerebrospinal fluid causing inflammation (cochlitis/neuronitis); b) neurotropic virus reactivation which is dormant in the cochlear nerve; c) triggering immune-mediated response in the inner ear by systemic viral infection. All these mechanisms cause damage to the inner ear structures (Schreiber et al., 2010; Ribeiro et al, 2015).

Sensorineural hearing loss is a typical manifestation seldom seen in dengue fever of pro-inflammatory to release cytokines which activated endothelium to expresses excess Von Willebrand factor on its surface causing platelets to adhere to it, thus decreasing number of circulating **Platelets** platelets. sticking on endothelium occlude its microvasculature causing reduced organ perfusion, organ failure and death (Eapen and Nair, 2017). The cochlea is supplied by an end artery and a vascular occlusion can be a possible cause of sudden irreversible hearing loss in Dengue (Bruno et al., 2015). Burno et al.(2015) and Soni et al.(2021), have published reports on sensorineural hearing loss in Dengue. In both, the hearing loss varied from mild to severe and was irreversible. The use of steroids in treatment was not documented in either of them. In contrast to (Jacob et al., 2022), they found acute severe bilateral hearing loss, which showed dramatic improvement and reversibility following treatment with oral steroid.

As regards respiratory manifestations, twenty-eight patients presented with respiratory symptoms in our study 26 patients (26%) had dyspnea, 22 patients (22%) had cough, 20 patients (20%) had chest pain, and 2 patients (2%) had clinical hemoptysis. There was improvement in all respiratory symptoms during follow-up with only statistical significant improvement in cough and dyspnea in follow-up duration. Pulmonary manifestations like pneumonia, pleural effusion and ARDS were more common in the severe cases of dengue as compared to mild DF.

It was reported by (Guzman et al., 1999), that lung pathology was present in every fatal case of dengue, and that the virus was found in the lungs of those who had died from the disease. The same thing was found in reports from Venezuela, twothirds of dengue deaths were caused by lung diseases including bronchopneumonia, pneumonitis. thromboembolism, diffuse alveolar damage and non-cardiogenic pulmonary oedema (Guzmán et al., 1999; Sharma et al., **2007)**. It was reported that pleural effusion from plasma leakage was detected in 38.6% of severe dengue cases (Arismendi-Morillo et al., 2011; Zhang et al., 2014).

According to Samarth et al. (2020) the prevalence of pulmonary symptoms in severe dengue cases differed statistically significantly from that in mild dengue cases. In the cases of DHF and DSS, these manifested as unilateral and bilateral pneumonitis, hemoptysis, ARDS, and

pleural effusion. Out of 100 dengue patients in this study, 18 had mild dengue fever, one had dengue hemorrhagic fever, and 28 had pulmonary complications (table 6). The most common pulmonary symptoms were dyspnea and cough, followed by chest pain and hemoptysis. These findings are explained by the fact that the alveolar lining of the lungs contains the dengue viral antigen and that increased alveolar permeability oedema in the lung cavities, which in turn leads to pulmonary dysfunction. have found ARDS in people with DHF (Nagat et al., 2013; Samarth et al., 2020).

This study has a special importance and uniqueness, not only because it is the first in our locality, but also due to the presence of very large cohorts of patients with GIT, cochleovestibular, and respiratory manifestations related to dengue outbreaks who need early diagnosis by the confirmatory tests and early management.

**Study limitation:** The main limitation was the small sample size and short period of follow up.

#### Conclusion

Patients with serologic confirmed dengue infection may present typical GI manifestations such as nausea, diarrhea and abdominal pain. While GI manifestations were splenomegaly, and ascites. Also, concomitant cochleovestibular symptoms that were manifested for the first time. Their outcome was heterogeneous. Larg sample size must be analyzed and had to be followed for a more extended period to establish the association of hearing loss and DF.

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**Data availability:** The datasets used and/or analyzed during the current study available

from the corresponding author on reasonable request.

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<u>5684794/v1</u>. The preprint present in different clinical manifestations of dengue fever/Research Square).

# **Abbreviation:**

Dengue fever (DF)

Dengue virus (DENV)

Dengue hemorrhagic fever (DHF)

Dengue Shock Syndrome (DSS)

gastrointestinal (GI)

Acute respiratory distress syndrome (ARDS)

Complete blood count (CBC)

Alanine aminotransferase (ALT)

Aspartate aminotransferase (AST)

5,5'-dithiobis (2-nitrobenzoic acid) (DTNB)

Pure tone audiometry (PTA)

Sudden sensorineural hearing loss (SSHL)

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