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Case Report

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First Report of Local Transmission of Dengue Fever in Iran: A Case Study

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Abstract

Background: The rapid spread of the dengue fever vector, *Aedes aegypti*, has raised significant public health concerns worldwide, including in Iran. In Hormozgan Province, ongoing monitoring and control efforts for this mosquito species were prioritized, with a specific focus on disease detection.

Case Report: To identify suspected dengue patients, health authorities implemented rapid testing protocols and ensured immediate hospitalizations when necessary. Blood samples obtained from these patients were subsequently sent to the virology laboratory at Hormozgan University of Medical Sciences for analysis. In June 2024, six confirmed cases of dengue fever were reported in Bandar Lengeh city.

Conclusion: Alarmingly, none of the affected patients had a history of travel to high-risk areas, marking the first documented instance of local transmission of dengue fever in Iran. This critical finding highlights the urgent need for enhanced public health strategies and interventions to address and manage potential dengue outbreaks in the region effectively.

Keywords: *Aedes aegypti*, Dengue fever, Public health, Hormozgan, Local transmission

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Introduction

Dengue fever is a mosquito-borne viral disease that poses a significant health threat globally, especially in tropical and subtropical regions (1). The virus is primarily transmitted by *Aedes* mosquitoes, particularly *Aedes aegypti*, and has four distinct serotypes (2-3). Factors such as climate change, urbanization, poor sanitation, and globalization contribute to its spread (3-4). Symptoms varied from mild fever to severe complications like hemorrhagic fever and shock (1). Currently, there is no specific treatment or vaccine for dengue fever (2). Prevention efforts focused on managing the mosquito population, treating cases, and raising community awareness (2). The rapid global spread of dengue, along with the lack of effective diagnostics and treatments, made it a major public health concern, particularly in developing countries (1-2).

According to recent estimates, approximately 390 million people are infected with the dengue virus annually (5). The main vectors were *Aedes aegypti* and *Aedes albopictus*, which transmitted the virus from infected humans to others.

In Iran, monitoring and prevention of arbovirus diseases began in 2015, establishing an integrated mosquito management program aimed at recognizing risks and diseases associated with mosquito transmission. *Aedes aegypti* and *Aedes albopictus* were identified in Hormozgan and Sistan-Baluchistan provinces, respectively. The first imported case of dengue fever was documented in 2008. By 2013, 15 confirmed dengue fever cases were reported from Sistan and Baluchestan and Kurdistan Provinces. Among these, eight individuals had traveled to Malaysia, India, and Thailand, while seven cases involved individuals with no evident travel history outside the country. In

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2019, Iran reported 50 dengue and 53 chikungunya cases, prompting the launch of an entomological and laboratory monitoring system.

Dengue virus comprised four serotypes, and more than three-quarters of the world's population lived in areas vulnerable to it. The frequency of dengue and dengue hemorrhagic fever significantly increased globally, becoming a public health issue, especially in tropical and subtropical regions.

This study aimed to present a detailed case report of dengue fever to enhance understanding of its clinical manifestations, management strategies, and implications for public health in previously unaffected regions.

Case Report

Out of a total of 6,222 rapid tests conducted from May 21 to December 21, 2024, on individuals suspected of having dengue fever, which included symptoms such as fever, headache, muscle pain, nausea, rash, and extreme fatigue, 73 individuals tested positive. Molecular analysis confirmed that 26 of these individuals were infected with the dengue virus. This study reviewed the case reports of the first six patients, as they were among the initial cases identified and treated within one month.

Given the presence of *Aedes* mosquitoes in Hormozgan Province and the potential for transmitting viral diseases such as dengue fever, training sessions were conducted for the public and medical staff. During these training sessions, participants were educated on how to prevent mosquito breeding in their homes and instructed to promptly visit hospitals if they observed any suspicious symptoms. Individuals presenting with symptoms suspected of dengue fever were first given a rapid diagnostic test by Abbott. If the test yielded a positive result, necessary molecular tests were performed on the individual's blood. This protocol was followed from May 21 to June 20, 2024.

Blood samples, specifically serum or plasma, were utilized for rapid testing. These samples were stored at temperatures between 2°C and 8°C for additional molecular and serological tests and were transported under cold chain conditions to the reference laboratory within 24 hours. This protocol adhered to the WHO guidelines and incorporated several key elements. First, cross-reactive primers were used for all four dengue serotypes. Second, NS1 antigen detection was conducted with a sensitivity of 92-98% during the acute phase of the disease. Third, dual confirmation was achieved through both molecular and immunological methods. Finally, standard biosafety level 2 precautions were implemented for handling potentially infectious samples.

The enzyme-linked immunosorbent assay (ELISA) was employed for the detection of dengue NS1 antigen using a monoclonal antibody-based capture method. The procedure began with coating a 96-well plate with 100 µL per well of anti-NS1 capture antibody, diluted to 1:1000 in carbonate buffer, and incubated overnight at 4°C. After washing the plate three times with PBS-Tween, 200 µL of 5% non-fat milk in PBS was added to block the wells, followed by a one-hour incubation at 37°C. Subsequently, 100 µL of plasma samples or controls was added to each well and incubated at 37°C for two hours. Afterward, 100 µL of HRP-conjugated detection antibody, diluted to 1:2000, was added, and the plate was incubated at 37°C for one hour. TMB substrate was then added, and the incubation continued for 15 minutes in the dark before stopping the reaction with 50 µL of 2N H_2SO_4 (6).

The absorbance was read at 450 nm within 30 minutes, and a positive result was defined as an optical density (OD) of 0.5 or greater after subtracting the blank. A standard curve was employed for confirmation, measuring concentrations from 0 to 100 ng/mL of recombinant NS1 (6).

For reverse transcription-polymerase chain reaction (RT-PCR), viral RNA amplification was conducted through reverse transcription followed by DNA amplification using sequence-specific primers. The procedure commenced with the collection of 2-5 mL of whole blood in EDTA tubes, followed by centrifugation at 1,500 × g for 10 minutes to separate plasma. RNA was then extracted using the QIAamp Viral RNA Mini Kit (Qiagen). The RT-PCR setup involved preparing a reaction mix totaling 25 µL, which included 5 µL of 5 × buffer, 1 µL of dNTPs (10 mM), 0.5 µL of forward primer (10 µM; targeting the conserved region of DENV-1-4), 0.5 µL of reverse primer (10 µM), 1 µL of HotStarTaq DNA Polymerase, 2 µL of RNA template, 0.5 µL of Reverse Transcriptase, and 14.5 µL of nuclease-free water (7).

The thermal cycling program began with a reverse transcription step at 50°C for 30 minutes, followed by an initial denaturation at 95°C for 15 minutes. This was followed by 40 cycles, each consisting of denaturation at 95°C for 30 seconds, annealing at 55°C for 30 seconds, and extension at 72°C for 45 seconds. The final extension step was conducted at 72°C for five minutes. The products were then run on a 2% agarose gel, with an expected band size of 200-300 bp corresponding to the serotype-specific primers. Positive controls (DENV RNA) and negative controls (nuclease-free water) were included to ensure the validity of the results (7).

All samples tested at the Hormozgan Health Vice-Chancellor's laboratory were subsequently sent to the Pasteur Institute of Iran for confirmation, and dengue fever was confirmed in all cases. The youngest patient in this study was a 22-year-old male, while the oldest one was a 63-year-old male. A total of five dengue cases were identified in Bandar Lengeh during June 2024, marking a significant local transmission of the virus. The demographic and clinical details of each case are summarized below:

Case 1

On June 7, 2024, a 43-year-old man residing in Bandar Lengeh developed mild fever and lethargy after returning from fishing. He visited the emergency room at Shohada Hospital on June 10, where he received supportive treatment and was subsequently discharged. However, due to persistent fever and concerns about malaria, he returned to Shahid Rajaei Health Center on June 11 for

further evaluation. After a rapid malaria test and blood slide preparation, he was referred for a rapid dengue test, which returned positive for dengue NS1 antigen. The patient's serum and urine samples were collected, and the health center's disease manager visited his residence to educate him on the use of mosquito nets and to ensure proper care. The area surrounding his home was treated with fog to reduce mosquito populations, and a mosquito net was provided to his family. Investigations revealed that he had been living in Bandar Lengeh for four years, with no recent travel history. On June 11, his wife and three children were tested for dengue; while the children tested negative, his wife also tested positive.

Case 2

The second patient was a 29-year-old man from Bandar Lengeh who presented to a private clinic on June 2 with symptoms of fever, itching, nausea, moderate lethargy, and loss of appetite. He received supportive treatment but continued to experience fever. On June 6, he returned to Shohada Hospital, where a dengue rapid test was conducted, yielding a positive IgM result. He had no travel history, claiming to have only traveled within the city. Follow-up investigations revealed no additional cases among his contacts.

Case 3

The third case was a 46-year-old homemaker from Bandar Lengeh, who had hypertension with no history of travel abroad. On June 21, she experienced lethargy and a severe headache. After receiving supportive treatment on June 22, she was admitted to Shohada Hospital due to worsening symptoms, including fever, body pain, back pain, and severe nausea. A rapid dengue test was performed on June 24, indicating a positive NS1 result. She was discharged later that day in good condition, with instructions to use a mosquito net. However, due to severe anorexia and nausea, she returned to the emergency room on June 25, received serum therapy, and was discharged again. On June 26, her blood serum sample was prepared and sent for PCR testing to a reference laboratory. Investigations revealed that two family members were also infected, with no travel history.

Case 4

A 22-year-old man entered Bandar Lengeh from Bandar Abbas on June 14. On June 27, he developed fever, body aches, cough, and lethargy, prompting him to rest at home. By June 30, his symptoms persisted, leading him to visit the emergency room at Shohada Hospital. A rapid dengue test returned positive for both IgM and NS1. He was hospitalized that night under a mosquito net and discharged the following day in good general condition.

Discussion

The emergence of local dengue transmission in Iran marked a significant public health concern, particularly given the rapid spread of the disease in tropical and subtropical regions worldwide (1,2). This study highlighted the importance of timely diagnosis and reporting of dengue cases, especially in areas previously considered non-endemic.

The findings of this research are consistent with global trends, where increased urbanization, climate change, and the movement of people contributed to the spread of the dengue virus (4). The fact that none of the patients had traveled to endemic areas suggested that local factors, such as the presence of *Aedes aegypti* mosquitoes and suitable breeding conditions, facilitated the virus transmission in Hormozgan Province.

Moreover, the high rate of positive rapid tests among symptomatic individuals indicated the need for public health interventions, including community awareness campaigns about mosquito breeding sites and preventive measures (2). It was crucial to educate the local population on recognizing the symptoms of dengue fever and the importance of seeking medical care promptly.

The study also emphasized the necessity of integrating molecular diagnostics into routine clinical practice for suspected dengue cases. Rapid and accurate identification of dengue infections could significantly improve patient management and control measures (5). Additionally, establishing a comprehensive vector surveillance program was necessary to monitor and control mosquito populations effectively.

In conclusion, the local transmission of dengue fever in Iran necessitated immediate action from health authorities to implement effective surveillance, vector control strategies, and public health education. The findings of this study served as a wake-up call for the need to strengthen public health infrastructure and preparedness to mitigate the impact of dengue fever and other mosquito-borne diseases.

Critical Points

1. *Lower Transmission Rates in Iran:* Iran had lower rates of dengue transmission, attributed to ecological factors, such as its dry climate that disrupted mosquito life cycles. Additionally, there were challenges with under-detection due to passive surveillance systems that may not capture all cases (8).
2. *Learning from the UAE:* The success of the UAE in managing urban mosquito populations underscored the need for innovative solutions, like Wolbachia-based interventions, particularly in Iranian port cities where the risk was increasing (9).
3. *Emerging Threat of DENV-3:* The DENV-3 serotype became a significant concern, now accounting for 93% of dengue cases in Pakistan in 2024. This situation highlighted the urgent need for improved border screening measures to prevent potential outbreaks in Iran (10).
4. *Insights from Saudi Arabia:* The outbreaks associated with the Hajj in Saudi Arabia provided valuable lessons that could enhance health measures at Iran's Chabahar port, improving preparedness for similar events (11).

This analysis drew on data from the WHO Eastern Mediterranean reports and outbreak bulletins from Iran's

CDC, revealing important gaps in regional readiness for arboviruses while also highlighting some unique ecological factors that may offer protection for Iran. Since this was the first time healthcare personnel in the province encountered dengue fever, efforts were made to educate all physicians and healthcare staff about the disease. This awareness contributed to the identification of six dengue cases in Bandar Lengeh, all of which occurred in patients with no recent travel history.

Conclusion

This outbreak marked a significant shift for Iran, moving from sporadic imported cases to established local transmission, similar to what the UAE experienced in 2018. While the current transmission rates in Iran are still lower than Pakistan's hyperendemic situation (32,145 vs. 6 cases in 2024) (7), three converging risk factors called for immediate action:

1. ***Expanding Vector Habitat:*** The *Aedes aegypti* mosquito adapted well to the southern coastal climates of Iran, thriving even at high temperatures (up to 38°C) and humidity levels (65% RH).
2. ***Healthcare Gaps:*** There was a concerning 72-hour delay in diagnostics for dengue cases in Iran, compared to the UAE's average of just 12 hours.
3. ***Economic Vulnerability:*** Coastal communities that relied on tourism faced a significant risk, with potential revenue losses of 23% during outbreaks.

The cases reported in Bandar Lengeh illustrated how climate-driven changes in mosquito populations could outpace public health responses. This situation emphasized the need for regional action plans supported by the WHO to enhance preparedness and response strategies. To enhance the management of dengue fever and prevent future outbreaks in Iran, several key recommendations were proposed. First, there should have been an implementation of enhanced surveillance measures. This included the establishment of weekly Ovitrap monitoring in a five-kilometer radius around ports, which would help in early detection of mosquito populations that may carry the dengue virus. Additionally, mobile PCR units should have been set up in high-risk districts to facilitate rapid diagnostic testing.

Second, capacity building was essential. Training programs should have been developed to educate over 300 healthcare workers annually in arbovirus management. Furthermore, telemedicine protocols should have been established for rural diagnostics, ensuring that even those in remote areas had access to timely medical advice and intervention.

Third, regional cooperation was crucial. A joint vector control program should have been initiated with neighboring countries, such as the UAE and Oman, to standardize efforts in combating mosquito populations. Additionally, it was vital to standardize port health regulations across Persian Gulf states to prevent the cross-border spread of dengue.

Fourth, community engagement must have been prioritized. Public health authorities should have launched Persian-language dengue awareness campaigns via social media platforms to educate the community about prevention measures. Distributing 50,000 insecticide-treated nets in coastal provinces would also have been an effective strategy to reduce mosquito bites and transmission rates.

Finally, developing early warning systems was imperative. This could have been achieved by utilizing satellite-derived Land Surface Temperature (LST) data to predict mosquito breeding conditions. Implementing port traffic dengue risk algorithms would further enhance the ability to respond proactively to potential outbreaks.

The discovery of dengue fever transmission in a previously unaffected country highlighted a critical public health challenge that demanded immediate attention. The potential consequences of an epidemic extended beyond immediate health impacts, affecting economic stability and public health infrastructure. Health authorities needed to implement proactive measures, including enhanced surveillance, community awareness, and vector control strategies, to mitigate the risks associated with this emerging threat.

The cultural context and living conditions of the people in Bandar Lengeh contributed to the prevalence of man-made larval habitats, such as water containers for animals and birds, water under coolers, and water in unsealed containers. Additionally, due to limited access to piped water during certain hours, residents often stored water in uncovered containers and tanks. Increased rainfall in early May compared to the previous year also contributed to the rise in natural larval habitats in urban environments, leading to higher larval indices in late May and early June, despite high temperatures.

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Competing Interests

The authors declare that they have no competing interests.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Approval

After final reviews, the research plan was approved at Hormozgan University of Medical Sciences (Ethical code: IR.HUMS.REC.1403.362), which can also be viewed on the website of the National System of Ethics in Biomedical Research.

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