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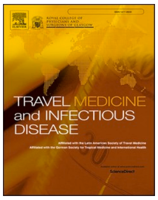

Zika virus infection in a German traveller to the Maldives, August 2025

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ABSTRACT

Background: Zika virus (ZIKV) is a neurotropic flavivirus associated with generally mild disease but the risk of congenital abnormalities when contracted during pregnancy. Reports from the Maldives are rare.
Methods: We describe a ZIKV infection in a traveller returning from the Maldives in August 2025, including clinical findings and molecular diagnostics with metagenomic sequencing and phylogenetic analysis.
Results: ZIKV ribonucleic acid was detected by reverse transcription polymerase chain reaction, and sequencing identified the ZIKV Asian lineage. However, the limited sequence length precluded precise phylogenetic placement.
Conclusion: This case underlines the ongoing risk of ZIKV transmission in areas where compatible arthropod vectors are present. Since there is no systematic surveillance in the Maldives, the detection of ZIKV infections in returning travellers is becoming increasingly important for assessing the epidemiological situation.

Zika virus is a flavivirus that became known due to a major outbreak on the American continent in the wake of the 2014 football World Cup in Brazil. The disease is typically characterized by a febrile phase accompanied by malaise and a generalized rash. Usually, symptoms are less pronounced than in dengue, one of the main differential diagnoses, and resolve within approximately one week [1].

Already in 2013, the neurotropism of the virus became evident during an outbreak in French Polynesia with a large number of Guillain-Barré-syndrome in infected persons [2]. Since 2015, microcephaly cases have been reported in the areas most affected by the Zika outbreak in northeastern Brazil. [3]. For this reason, WHO temporarily advised pregnant women against unnecessary travels to endemic regions [4]. After ZIKV became the focus of so much attention, reports of ZIKV infections emerged from many parts of the world, causing considerable concern among travellers wishing to have children. The WHO epidemiological data categorize countries into two groups based on the presence of *Aedes aegypti* mosquito vectors and documented autochthonous human infections, but provide no detailed regional risk assessment [5]. A recent article shows that the risk varies greatly between countries with autochthonous cases, both in terms of location and over time [6].

We report a case of ZIKV infection in a person after travel to the Maldives in August 2025.

In August 2025, the woman in her mid-thirties travelled to the Maldives for a total of nine days. She spent the first six days on Fulidhoo island, and continued her vacation for another three days on Maalhos island. On August 10th, one day after return to Germany, she noticed a swollen left-sided inguinal lymph node followed by fever (39.8 °C), fatigue and malaise the next day. On August 12th, she noticed a generalized rash with itching and burning sensations, as well as arthralgia, pronounced in hands and back. She presented to our tropical medicine outpatient department on August 13th, where blood sampling for diagnostic workup was conducted – three days after symptom onset. Laboratory parameters showed normal red and white blood count as well as normal platelets and liver enzymes. CRP was slightly elevated (5.1 mg/dl). A rapid test for DENV was negative, therefore, we decided to conduct multiplex-RT-PCR to enable detection of further arboviruses (BioFire Global Fever panel, BioMérieux, Marcy L'Étoile, France), which

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returned positive for ZIKV but negative for all other pathogens examined, including CHIKV, DENV, *Leptospira* and *Plasmodium spp.*

Since she travelled alone and reported no possible exposition within several months before the journey, sexual transmission was extremely unlikely. She was not pregnant, therefore, we counselled to use contraception for the following two months. No further follow-up appointments were necessary.

Real-time RT-PCR for confirmation (Altona diagnostics, Hamburg, Germany) revealed positivity for ZIKV RNA, with a C_t-value of 36. An attempt to culture the virus in Vero cells was unsuccessful. The ZIKV-RNA positive blood sample was subjected to unbiased metagenomic next-generation sequencing (mNGS). RNA extracted and purified from the blood sample was processed using an in-house mNGS pipeline established for virus discovery [7] and sequenced on a NextSeq 2000 platform (Illumina). The total number of reads was 10,578,256. Coverage of the ZIKV reference genome was 7.4%, with a sequencing depth between 0.1 and 0.3x. The obtained sequence is available at https://doi.org/10.55876/gis8.251123eu.

ZIKV genomic sequences were recovered from gisaid - epiarbo on November 22, 2025 using the filters complete CDS, complete collection date and high coverage (only entries with less than 5% NNs). Then sequences were aligned with mafft (https://mafft.cbrc.jp/alignment/server/) including the sequenced generated in this study. Phylogenetic reconstruction was performed using IQTREE 2 [8] and the results of this analysis are shown in Fig. 1.

According to a systematic literature research, only few cases of Zika in travellers to the Maldives were diagnosed in recent years, including one case in Finland in 2015 from Dhiffushi island [9], one case in Spain in 2016 from Nilandhoo island [10] and two cases in Korea in 2017 [11]. According to a situation report from the Maldives ministry of health from 26th December 2021, active surveillance of febrile patients revealed no Zika cases since January 2018, and only three cases before 2018 [12]. According to a press release, however, a Chinese tourist had been tested positive after travel to Maldives in 2018 [13], and two cases of returning travellers were reported from Taiwan in 2023 [6].

Genomic analysis has been performed from samples of the Finnish and Spanish patients, revealing different Asian lineages [9,10]. To the best of our knowledge, no further virus sequencing attempts have been made on samples from the Maldives. The Sequence obtained from our patient's samples was incomplete (545 bp in five fragments) as were the previously published sequences from the Finnish (160 bp) and the Spanish patients (637 bp). There was no overlap between the sequence fragments from our patient with the sequence from the Spanish patient. The Finnish sequence is not publicly available. Phylogenetic reconstructions allowed us to ascertain that the strain sequenced belong to the Asian lineage, however, since the strain position was not stable within the Asian lineage, likely due to the short fragments recovered, no major inferences about source of introduction can be made. Homologous recombination has been described for several flaviviruses and postulated for ZIKV [14]. Due to the lack of overlap of the two available sequences, it cannot be fully ruled out that these viruses are closely related. Fig. 1 shows the placement of the strain within the phylogenetic tree including other ZIKV strains.

The islands visited by our patient (Fulidhoo and Maalhos) are some of the less populated and less visited islands of the Maldives (511 and 750 registered inhabitants, respectively) [15]. Arbovirus outbreaks in closed populations such as islands are often characterized by a sharp rise in infections with subsequent widespread immunity, leading to spontaneous resolution of these outbreaks due to decreasing R0 values [16]. In the case of Zika, this is also reflected by the fact that despite sustained circulation of ZIKV in the Americas, many Caribbean islands have reported few, if any, cases after 2017 [17]. Although it is plausible, it is not known whether a similar development has taken place in the Maldives.

Mandatory reporting of ZIKV-infections in Germany started in May 2016, following the large outbreak in the Americas. From May to December 2016, 222 cases were reported, while in the entire year of 2017, only 72 cases were reported. Since then, the maximum reported cases in one year were 39 (2024) (Fig. 2) [18]. A similar development was observed in the entire European Union [19]. While microcephaly following intrauterine infection remains the greatest concern with ZIKV, very few cases of adverse birth outcome have been reported among European travellers, and no cases have become known in Germany [20]. Based on the current WHO recommendations, the German guideline on management of arbovirus infections from 2025 recommends special precautions for women of reproductive age and pregnant women, including thorough mosquito protection, but does not generally advise against travel to endemic areas [21].

For countries without systematic surveillance, detection in travellers is the backbone of epidemiological assessment. This is all the more evident in the fact that more cases have been identified among returning travellers from the Maldives, than through systematic surveillance of febrile patients in the Maldives conducted in the years 2016 and 2017. The absence of further reports of ZIKV infections in the Maldives in recent months is a hint that the virus is not circulating permanently. This

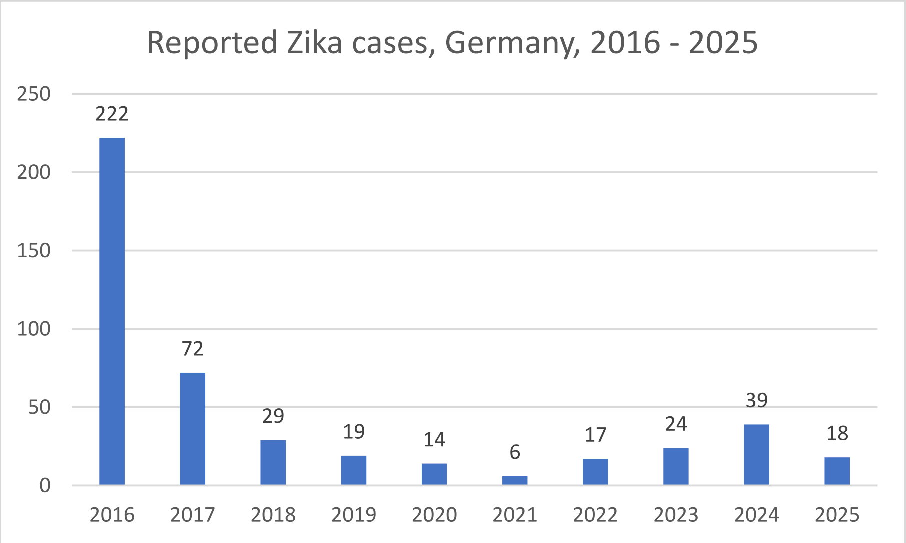

Fig. 1. Phylogenetic analysis of current (bold) and earlier ZIKV strains. The strain from our patient belongs to the Asian lineage, but due to the short fragments, the source of introduction cannot be clearly traced.

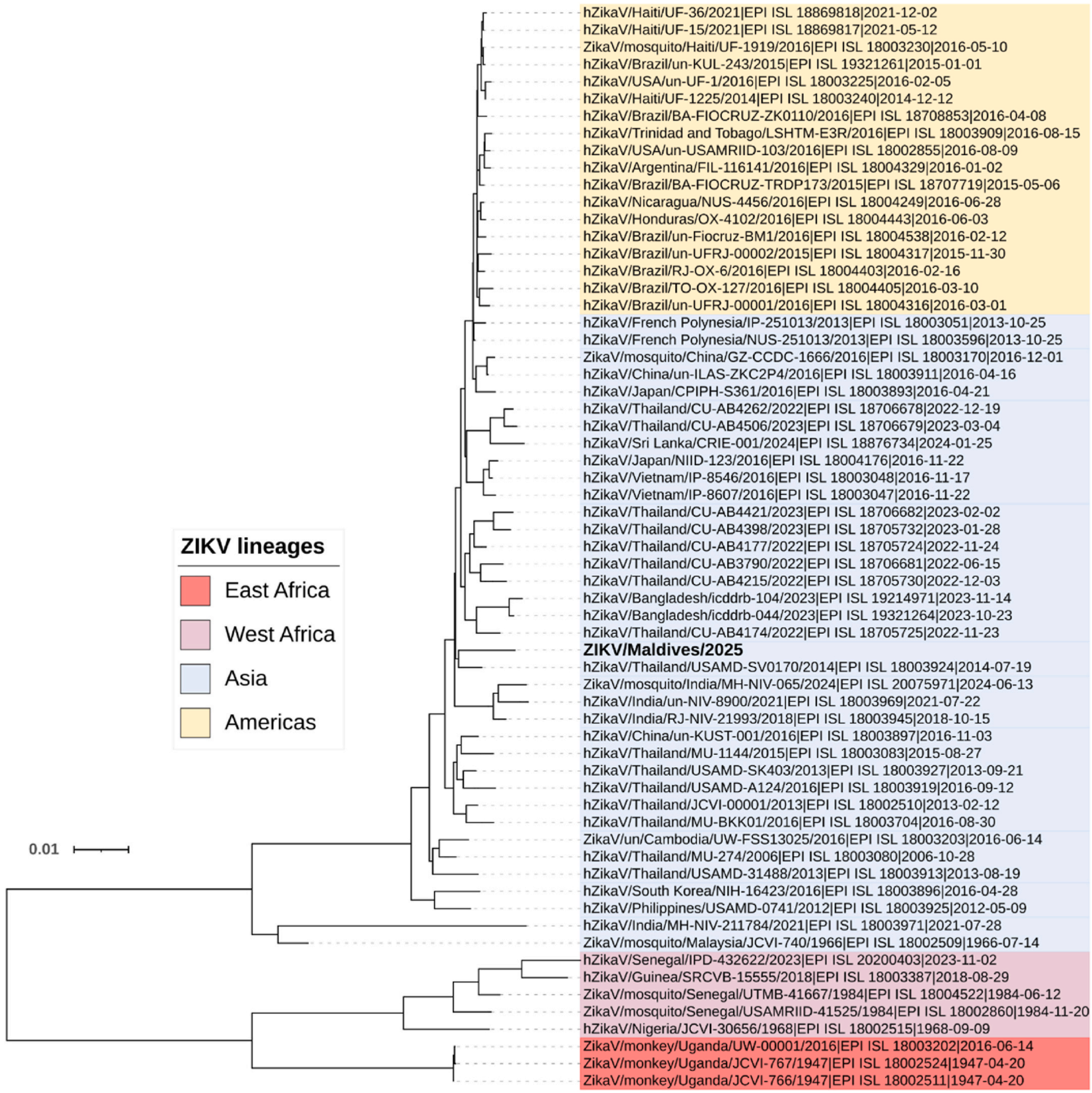

Fig. 2. Reported Zika cases in Germany from 2016 to 2025. Data source: Robert-Koch-Institute. Note: The column for 2016 contains only cases from May to December.

is also supported by phylogenetical analysis of the available ZIKV sequences from the Maldives, although all these sequences are fragmented and incomplete, and therefore permanent circulation of a single virus strain with possible evolutionary adaptations cannot ultimately be ruled out. Based on the available data, however, a sporadic case due to re-introduction appears likely.

Either way, this case shows that there is an ongoing risk of ZIKV infection in all regions where competent mosquito vectors exist. Consistent virus sequencing in returning travellers could help to better understand virus evolution and epidemiology and to assess the risk for travellers and residents.

1. Use of artificial intelligence tools

During the preparation of this work the authors used DeepL (https://www.deepl.com) in order to correct linguistic errors and improve readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

CRediT authorship contribution statement

Hans Martin Orth: Writing – review & editing, Writing – original draft, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **David Meierkord:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Martha Charlotte Holtfreter:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Tom Luedde:** Writing – review & editing, Formal analysis, Data curation. **Jonas Schmidt-Chanasit:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Torsten Feldt:** Writing – review & editing, Supervision, Formal analysis, Data curation.

Ethical statement

According to the ethical review board of the University of Düsseldorf, ethical clearance is not required. The patient gave written consent for publication.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

All clinically relevant data are included in this publication. The genomic sequence data collected in this publication are publicly available at https://doi.org/10.55876/gis8.251123eu.

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