

CPD

Spotting Zika spots: descriptive features of the rash used in 66 published cases

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Summary

Zika virus (ZV) is an important emerging infection. Rash is a key feature, but the summative literature lacks description of the rash beyond 'maculopapular'. Our aim was to identify the cutaneous features described in the published literature. A literature search using defined terms for ZV cases reports and series was performed on the OVID, Clinical Key and University of Dundee's e-library journals databases in December 2016; a later case report was included while the paper was under review. Diagnosis in all cases was via PCR. Exclusion criteria were Zika cases without rash or omitting any description of the rash. Ocular features (conjunctivitis) were not included. In total, 42 publications with 66 cases met the criteria. The most frequent descriptive features included maculopapular (59%), lower limb petechial purpura (11%) and erythematous/red (9%). Pruritus was described in 44% and tenderness in 3%. Lesions were located on the trunk (29%), limbs (5% arms, 11% both arms and legs), face (17%) and extremities (14%) or were diffuse/generalized (12%). There was facial sparing in 3%. Other features were centrifugal spread (6%), palmar and/or plantar involvement (6%), palmo-plantar desquamation (2%) and malar erythema with oedema (2%). Mucosal features included gingival bleeding (11%), oral haemorrhagic blisters (8%) and painful blisters/vesicles (4%). Oedema/swelling was described in the upper limbs (5%), lower limbs (5%) and both (3%). Mean rash duration was 6 days (range 3–11 days). The ZV exanthema is most frequently maculopapular, pruritic, sometimes with centrifugal spread from the trunk to extremities. This may include lower limb petechial purpura, palmo-plantar lesions, oedema of limb extremities, and gingival bleeding or painful oral bullae. As ZV becomes more prevalent, recognition of the clinical features will enable earlier diagnosis and appropriate testing.

Introduction

Zika virus (ZV) is an important emerging infection. The March 2017 World Health Organisation (WHO) Situation Report¹ recorded 84 countries with evidence

of mosquito-borne transmission of ZV, 13 with person-to-person transmission (including returning travellers or their sexual partners), 31 with microcephaly cases and 23 with associated Guillain–Barré syndrome.

Zika virus is a flavivirus spread by the *Aedes* mosquito.² As an arthropod-spread infection, it is also known as an arbovirus. Sexual and maternal–fetal transmission has also been reported.² ZV was first detected in Uganda in 1947, followed by spreading to the Americas³ and elsewhere. Figure 1 shows countries with ZV and those at risk based on the March 2017 WHO report.¹ *Aedes aegypti* is the main vector in

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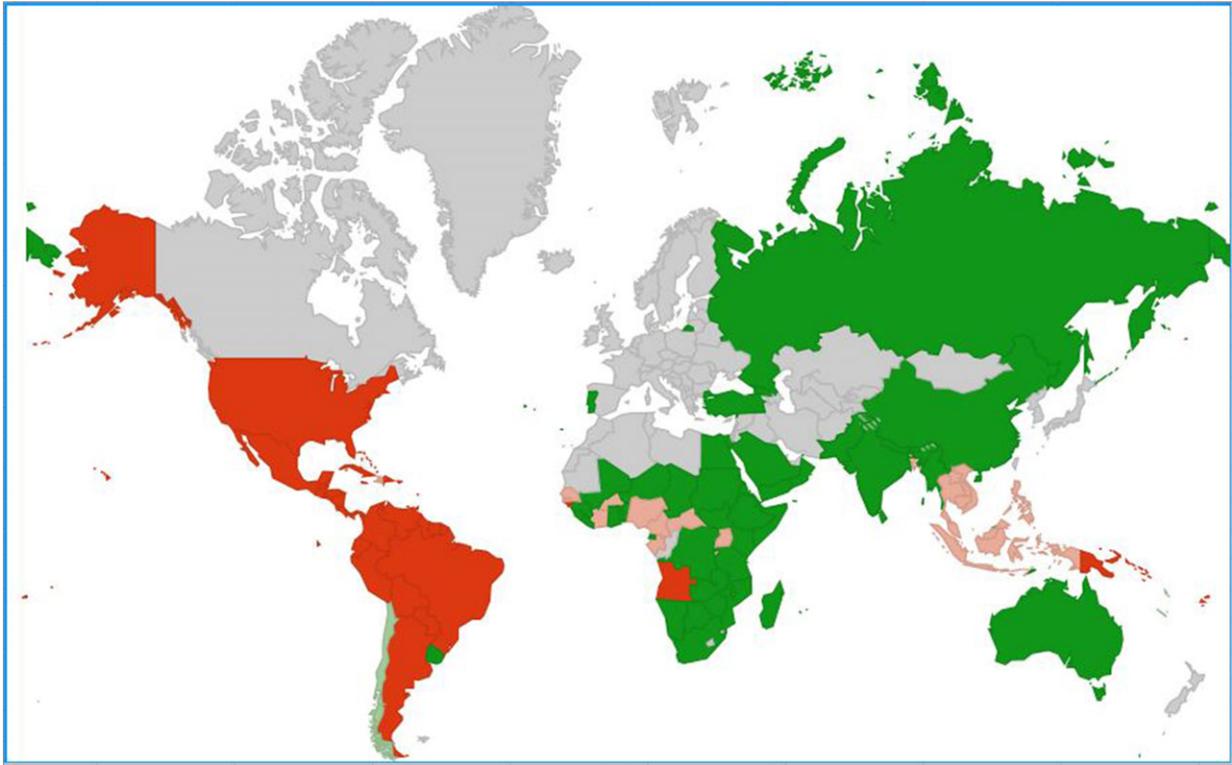


Figure 1 Map of Zika virus situation in countries categorized 1–4 based on World Health Organization situation report.¹ ■ Category 1: Area with new introduction or re-introduction with ongoing transmission; ■ category 2: area either with evidence of virus circulation before 2015 or area with ongoing transmission that is no longer in the new or re-introduction phase, but where there is no evidence of interrupted transmission; ■ category 3: area with interrupted transmission and with potential for future transmission; ■ category 4: area with established competent vector but no known documented past or current transmission. *Note the entire countries are marked, not the individual subregions e.g. Zika virus has not been reported in Alaska. [Colour figure can be viewed at wileyonlinelibrary.com]

tropical regions. *Aedes albopictus*, an invasive species to Europe, may carry ZV, so there is a risk of ZV becoming established in Europe. *Aedes albopictus* originated in Southeast Asia and has spread through eggs transmitted in used tyres and bamboo plants, further helped by climate change.⁴ *A. albopictus* was first reported in Albania in 1979, and has now been reported to be reproducing as far north as Germany.^{4,5} The WHO⁶ recently evaluated Europe to be at low to moderate risk for ZV.

Zika virus can be diagnosed by reverse-transcription (RT)-PCR testing or serological testing of ZV antibodies. Public Health England⁷ advises that RNA detected in any sample is sufficient to diagnose infection, but a negative result does not exclude previous infection. RT-PCR can be performed on serum, urine, saliva, semen and amniotic fluid.⁷ Antibody testing is complicated by crossreactivity with other flaviviruses and by previous infection or immunization.⁸ Therefore, testing for antibodies to dengue, chikungunya and other endemic arboviruses is also required. Table 1⁹

summarises the possible differential diagnoses. If ZV IgM is detected, then it usually indicates ZV infection.⁷ IgG plus IgM usually indicate ZV infection as ZV IgM is frequently undetectable in those with previous dengue.⁷ ZV IgG without IgM is difficult to interpret, and may indicate ZV infection, cross-reactivity or nonspecific reactivity⁷.

Zika virus is a spreading problem in both developing and developed countries. It may present in travellers, migrants and refugees. Dermatologists should be prepared to recognize cases: a rash is a key feature of ZV infection, but the summative literature is lacking description of the rash beyond 'maculopapular'. Singh *et al.*¹⁰ and Anderson *et al.*¹¹ have summarized features from a few articles.

The aim of the current study was to perform a broad review and summarize the cutaneous clinical features described in published case reports and case series of ZV. Other already recognized features of ZV include fever, nonpurulent conjunctivitis, arthralgia, myalgia, headache and malaise.²

Table 1 Causes of rash and fever – tropical and cosmopolitan infections.

| Organism/disease | Rash (% cases) | Distribution | Vector/exposure risk | Associated features |
|--|----------------------|--|--|---|
| Dengue | M, MP, PP (50%) | Tropical, subtropical, worldwide | <i>Aedes</i> mosquito, urban and rural | Myalgia, haemorrhage, shock |
| Zika | MP | Africa, Asia, Oceania, Latin America, North America | <i>Aedes</i> mosquito, urban and rural, MTC, sexual, blood transfusion | Congenital Zika virus syndrome, Guillain–Barré syndrome |
| Chikungunya | M, MP (50%) | Tropical, subtropical African and Asia, Caribbean, South America | <i>Aedes</i> mosquito, urban and rural | Polyarthralgia, arthritis |
| African tick typhus | MP, PP, V (46%) | Sub-Saharan Africa | Ticks, rural/wilderness | Eschar common, headache |
| Mediterranean spotted fever | MP, PP (90%) | Mediterranean and sub-Saharan Africa, India | Ticks, urban, suburban | Eschar common |
| Rocky Mountain spotted fever | MP, PP (90%) | USA, Central and South America | Ticks, rural/wilderness | Eschar rare |
| Scrub typhus: <i>Orientia tsutsugamushi</i> | M, MP (35–90%) | Asia, Pacific Islands | Larvae of trombiculid mites (chiggers), rural | Eschar common |
| Typhoid fever: <i>Salmonella typhi/paratyphi</i> | M (rose spots) (20%) | Wherever risk of faecal contamination of water | Faecal–oral, poor sanitation | Prolonged fever, splenomegaly, GI perforation and haemorrhage, encephalopathy |
| Leptospirosis | M, MP, PP (20%) | Worldwide | Exposure to rat/rodent urine (fresh water) | Conjunctivitis, myalgia, jaundice |
| Schistosomiasis | U (Katayama fever) | Africa, Asia, South America, Caribbean | Freshwater snails | Eosinophilia, pulmonary infiltrates |
| Yellow fever | PP | Central and South America, Africa | Mosquito-borne, urban, rural | Jaundice, neurological involvement |
| Lassa fever | MP, PP | West Africa | Unknown, ?monkey bites, rural/wilderness | Pharyngitis, retrosternal pain, encephalitis, haemorrhage |
| Ebola/Marburg | MP, PP | West/Central Africa | <i>Culex</i> , mosquitoes, urban | Abdominal pain, diarrhoea and vomiting, haemorrhage |
| South American haemorrhagic fevers | PP | South America | Human | – |
| West Nile virus | MP | Africa, USA | Human | Encephalitis |
| Measles | MP | Worldwide | Human | Cough, conjunctivitis, Koplik spots |
| Varicella zoster virus | MP, V | Worldwide | Human | Coryza, pneumonitis |
| Epstein–Barr virus | MP, PP | Worldwide | Human | Pharyngitis, lymphadenopathy, splenomegaly |
| Cytomegalovirus | MP | Worldwide | Human | Pharyngitis, lymphadenopathy, splenomegaly |
| Toxoplasmosis | MP | Worldwide | Cats | Lymphadenopathy |
| Human immunodeficiency virus | MP | Worldwide | Sexual, IVDU, vertical transmission | Pharyngitis, lymphadenopathy, splenomegaly |
| Rubella | MP | Worldwide | Human | Coryza, arthralgia |
| <i>Staphylococcus aureus</i> | PP, E | Worldwide | Human, IVDU | Shock, heart murmur |
| <i>Streptococcus pyogenes</i> | E | Worldwide | Human | Pharyngitis, cellulitis, shock |
| <i>Neisseria meningitidis</i> | PP | Worldwide | Human | Shock, meningitis |
| <i>Neisseria gonorrhoeae</i> | PP | Worldwide | Sexual | Septic arthritis |
| Syphilis: <i>Treponema pallidum</i> | MP, PP, Pu, V | Worldwide | Sexual | Genital ulceration |

E, erythrodermic; GI, gastrointestinal; IVDU, intravenous drug use; M, macular, MP, maculopapular; MTC, mother-to-child; PP, petechial/purpuric; Pu, pustular; U, urticarial; V, vesicular. The % values given for frequency of rash in particular infections are derived from case series. Adapted from Sharma H *et al.*⁹ with permission from Elsevier (licence code: 4280360114492; Crown Copyright 2017, published by Elsevier Ltd).

Methods

A literature search, using defined terms of ‘Zika virus AND rash OR exanthema OR lesions’, was performed on journal

articles in the OVID, Clinical Key and the University of Dundee’s e-library databases. The search was carried out in December 2016. A further case report identified after this

date was included while the paper was under review. Zika cases without rash or omitting any description of the rash were excluded. Zika diagnosis had to be made using PCR. PCR tests were usually RT-PCR, but also quantitative reverse transcription PCR (RT-qPCR) and real-time reverse transcription PCR (rtRT-PCR). Cases diagnosed only with antibodies (IgM and/or IgG) were excluded, unless ZV was identified by PCR in person-to-person transmission where the subject would not have been able to acquire another flavivirus (e.g. PCR-detected ZV in a sexual partner who had stayed in an unaffected country and in the returning partner who had travelled but had IgM and/or IgG only, or PCR-detected ZV in a mother with IgG and/or IgM and a PCR-positive fetus).

The identified case reports and series were read by one data collector (JSD). The publication and paragraphs describing the rash were copied into a data collection file. The descriptive words for each publication were entered into a spreadsheet (Excel; Microsoft Corp., Redmond, WA, USA). Analogous terms were grouped (e.g. generalized, diffuse and disseminated) before tallying the descriptive features. Features were noted regarding lesion appearance, distribution, sensation, oral mucosal and oedema/swelling. Data on the duration of the rash were collected if mentioned. Conjunctivitis is a well-recognized feature, so ocular mucosal features were not included.

Results

Publications and cases

In total, 50 publications describing the rash were identified, and of these, 8 (reporting 15 cases) that did not meet the diagnostic criteria were excluded. The remaining 42 publications (see Data S1 online) described 66 cases. As far as could be determined, there were no duplicate reports. Mean age of the patients was 46 years (range 15–81 years). There were 26 males, 34 females and 6 not specified. There were four sexually transmitted cases and one possible transmission by monkey bite. Twenty countries/regions were reported as the source of the infection, including two patients who had travelled to multiple at-risk zones. Table 2 summarizes the demographic information.

Clinical features and duration

The descriptive rash features (Table 3) included maculopapular (59%), lower limb petechial purpura (11%), erythematous/red (9%), macular (3%), papular (3%) and blanching (3%). The distribution (Table 3) included

trunk/torso (29%), face (17%), extremities (14%), diffuse/generalized/disseminated (12%), limbs/arms and legs (11%), centrifugal spread (6%), palmar and/or plantar involvement (6%), abdomen (5%), back (5%), arms (5%), facial sparing (3%) and neck (3%). The sensation-related descriptions included pruritic/itchy (44%) and specified tender rash (3%). There was oedema of the hands and/or wrists (5%), oedema/swelling of the feet/ankles/lower limbs (5%), oedema of the hands and feet (3%) and malar/facial oedema (2%) (Table 3). Mucosal features (Table 3) included gingival bleeding (11%), oral haemorrhagic blisters (8%), painful blisters/vesicles (4%) and mucosal bleeding (3%). Although data were not collected on ocular features, there was one case of uveitis reported.¹² ZV infection may trigger an exacerbation of other dermatoses.¹³ The mean duration of the rash, available from 10 cases, was 6 days (range 3–11 days).

Discussion

The WHO² describes the features of ZV as being similar to those of dengue, and they include fever, cutaneous rash, nonpurulent conjunctivitis, arthralgia, myalgia, headache and malaise. ZV-infected individuals are often asymptomatic (19% symptomatic reported by Duffy *et al.*,¹⁴ 26% by Musso *et al.*¹⁵). Duffy *et al.*¹⁴ described 31 cases, using different diagnostic criteria, with symptoms, of which 90% had a rash, 65% fever, 65% arthralgia or arthritis, 55% nonpurulent conjunctivitis, 48% myalgia, 45% headache, 39% retro-orbital pain, 19% oedema and 10% vomiting. Mean duration of rash was 6 days (range 2–14 days).² The incubation period is unknown, but is thought to be a few days.² Associated complications include Guillain-Barré syndrome and microcephaly through maternal-fetal transmission.² We found a similar mean duration and range for rash. The incubation period was not clear in the case reports/case series that we identified.

This study found that the most frequently described ZV exanthema feature is a maculopapular pruritic rash, sometimes with centrifugal spread from the trunk to the extremities. This may include palmoplantar lesions, oedema of the limb extremities, and gingival bleeding or painful oral bullae. Pruritus was specified in 44%. Purpura with thrombocytopenia was observed as a later complication of the initial ZV symptoms.^{16–18}

Singh *et al.*¹⁰ and Anderson *et al.*¹¹ referenced 4 and 10 sources, respectively. We found 6% palmoplantar lesions; however, Singh *et al.*¹⁰ reported no palmoplantar involvement. They did not describe oral

Table 2 Demographic data of the cases.

| Patient | Reference* | Case number within reference† | Age | Sex | Diagnostic test | Country of suspected infection (or route of sexual transmission) | Country in which patient presented |
|---------|------------|-------------------------------|---------------|-----|---|---|------------------------------------|
| 1 | 1 | – | 43 | M | RT-PCR blood, urine, saliva, semen | Brazil | South Korea |
| 2 | 2 | 1 | Mid-20s | M | rtRT-PCR serum | Bora Bora (French Polynesia) | Japan |
| 3 | | 2 | 30s | F | rtRT-PCR urine | Bora Bora (French Polynesia) | Japan |
| 4 | 3 | 1 | 30s | F | rtRT-PCR serum, saliva and breast milk | French Polynesia | French Polynesia |
| 5 | | 2 | 40s | F | rtRT-PCR serum, urine and breast milk | French Polynesia | French Polynesia |
| 6 | 4 | – | 52 | F | PCR serum | Indonesia | Australia |
| 7 | 5 | – | NS | F | RT-PCR blood, urine, nasopharyngeal fluid | Thailand | Canada |
| 8 | 6 | 1 | 24 | F | RT-PCR urine and saliva | Vaginal/oral sexual transmission | France |
| 9 | | 2 | 46 | M | RT-PCR urine and semen | Brazil | France |
| 10 | 7 | – | 47 | F | RT-PCR urine | Brazil | Brazil |
| 11 | 8 | – | 51 | F | rtRT-PCR serum | Guatemala or El Salvador | Switzerland |
| 12 | 9 | 1 | 60 | F | PCR | Suriname | Netherlands |
| 13 | | 2 | 40 | F | PCR | Suriname | Netherlands |
| 14 | | 3 | 54 | M | PCR | Suriname | Netherlands |
| 15 | | 4 | 47 | M | PCR | Suriname | Netherlands |
| 16 | | 5 | 53 | F | PCR | Suriname | Netherlands |
| 17 | 10‡ | – | 38 | M | RT-PCR serum with BLAST analysis | Brazil | Brazil |
| 18 | 11 | – | Not specified | F | rtRT-PCR urine | Dominican Republic (vaginal/oral sexual transmission; partner had returned from DR) | USA, Maryland |
| 19 | 12 | 1 | 49 | F | PCR with BLAST analysis | Cook Islands | Australia |
| 20 | 13 | – | 68 | M | rtRT-PCR serum and semen | Cook Islands | UK |
| 21 | 14 | – | 26 | F | qRT-PCR serum, whole blood, urine, saliva, vaginal swab | Honduras | USA |
| 22 | 15 | – | 34 | M | RT-PCR serum and urine | Venezuela | China |
| 23 | 16 | – | 39 | M | RT-PCR | Brazil | Brazil |
| 24 | 17 | – | 40s | M | rtRT-PCR urine | Thailand | Japan |
| 25 | 18 | – | 26 | M | Real-time PCR serum | Puerto Rico | USA |
| 26 | 19 | – | 62 | M | RT-PCR serum | Honduras | Venezuela |
| 27 | 20 | 1 | 62 | M | RT-PCR (positive in partner's urine; patient IgM- and IgG-positive) | Martinique, Caribbean | France |
| 28 | | 2 | 60 | F | RT-PCR serum and urine | Martinique (possible sexual transmission likely from timeline, but had also been to Martinique) | France |
| 29 | 21 | 1 | 20s | F | rtRT-PCR serum and urine | Country NS | USA |
| 30 | | 2 | 20s | M | rtRT-PCR urine | Country NS (vaginal sexual transmission) | USA |
| 31 | 22 | 1 | NS | M | RT-PCR (positive in partner's serum; partner had not travelled) | Caribbean | USA |
| 32 | | 2 | NS | F | RT-PCR from serum | Country NS (vaginal sexual transmission) | USA |
| 33 | | 3 | NS | M | RT-PCR (positive in partner's serum; patient IgM-positive) | Central America | USA |
| 34 | 23 | – | Early 30s | F | rtRT-PCR serum | French Polynesia | Italy |

Table 2. continued

| Patient | Reference* | Case number within reference† | Age | Sex | Diagnostic test | Country of suspected infection (or route of sexual transmission) | Country in which patient presented |
|---------|------------|-------------------------------|-----------|-----|---|--|------------------------------------|
| 35 | 24 | – | 31 | F | rtRT-PCR serum | Tahiti | Norway |
| 36 | 25 | 1 | 38 | F | RT-PCR urine | Guadeloupe | Guadeloupe |
| 37 | | 2 | 58 | F | RT-PCR urine and plasma | Guadeloupe | Guadeloupe |
| 38 | | 3 | 15 | F | RT-PCR urine and plasma | Guadeloupe | Guadeloupe |
| 39 | | 4 | 74 | F | RT-PCR urine | Guadeloupe | Guadeloupe |
| 40 | | 5 | 46 | F | RT-PCR urine | Guadeloupe | Guadeloupe |
| 41 | | 6 | 36 | M | RT-PCR urine | Guadeloupe | Guadeloupe |
| 42 | | 7 | 46 | M | RT-PCR urine | Guadeloupe | Guadeloupe |
| 43 | 26 | – | 45 | M | rtRT-PCR semen and urine | Brazil | UK |
| 44 | 27 | – | 54 | F | PCR urine and blood | Suriname | Netherlands |
| 45 | 28 | 1 | 26 | F | PCR urine | Martinique, Caribbean | Martinique, Caribbean |
| 46 | | 2 | 21 | M | PCR urine | Martinique, Caribbean | Martinique, Caribbean |
| 47 | 29 | 1 | 62 | F | RT-PCR and rtRT-PCR urine | Brazil | Portugal |
| 48 | | 2 | 57 | M | RT-PCR and rtRT-PCR urine | Brazil | Portugal |
| 49 | 30 | – | 81 | M | RT-PCR CSF | New Caledonia, Vanuatu, Solomon Islands, but also travelled to New Zealand (not identified as active for ZV) | France |
| 50 | 31 | – | Early 40s | M | rtRT-PCR urine, plasma, semen and saliva | Haiti | Italy |
| 51 | 32 | – | 20s | F | rtRT-PCR plasma, urine and saliva | Dominican Republic | Italy |
| 52 | 33 | – | 27 | F | RT-qPCR serum and breast milk | New Caledonia | New Caledonia |
| 53 | 34 | – | 27 | M | PCR (identified flavivirus on nasopharyngeal swab, then sequence identified Zika virus) | Indonesia (proposed monkey bite transmission) | Australia |
| 54 | 35 | – | 37 | M | rtRT-PCR urine with BLAST analysis | Maldives | Finland |
| 55 | 36 | – | 27 | F | RT-qPCR amniotic fluid | Brazil | Brazil |
| 56 | 37 | – | Early 30s | M | rtRT-PCR urine, saliva and semen | Haiti | Italy |
| 57 | 38 | – | 27 | F | rtRT-PCR blood, endocervical swab, cervical mucus | Guadeloupe | Guadeloupe |
| 58 | 39 | – | 25 | F | IgG in patient; RT-PCR of fetal autopsy tissue | Brazil | Slovenia |
| 59 | 40 | 1 | NS | NS | rtRT-PCR urine and serum | New Caledonia | New Caledonia |
| 60 | | 2 | NS | NS | rtRT-PCR urine and serum | New Caledonia | New Caledonia |
| 61 | | 3 | NS | NS | rtRT-PCR urine | New Caledonia | New Caledonia |
| 62 | | 4 | NS | NS | rtRT-PCR urine and serum | New Caledonia | New Caledonia |
| 63 | | 5 | NS | NS | rtRT-PCR urine | New Caledonia | New Caledonia |
| 64 | | 6 | NS | NS | rtRT-PCR urine and serum | New Caledonia | New Caledonia |
| 65 | 41 | – | 32 | F | rtRT-PCR serum, urine, CSF, saliva, vaginal swab | Dominican Republic | Italy |
| 66 | 42 | – | 68 | F | RT-PCR | Venezuela | Venezuela |

BLAST, Basic Local Alignment Search Tool; CSF, cerebrospinal fluid; NS, not specified. qRT-PCR, quantitative reverse transcription PCR; RT-PCR, reverse-transcription PCR; rtRT-PCR, real-time reverse transcription PCR. *References are provided in Data S1 online; †if > 1 case (note that some cases within one reference were excluded as they did not meet our criteria); ‡patient was human immunodeficiency virus-positive.

Table 3 Characteristics of the Zika virus rash in 66 cases.

| Characteristic | n | %* |
|--|----|----|
| Description | | |
| Maculopapular | 39 | 59 |
| Petechial purpura on lower limbs | 7 | 11 |
| Erythematous/red | 6 | 9 |
| Macular | 2 | 3 |
| Papular | 2 | 3 |
| Blanching | 2 | 3 |
| Subcutaneous haematomas on arms and legs | 1 | 2 |
| Mottled flat rash, later papular | 1 | 2 |
| Malar erythema | 1 | 2 |
| Distribution | | |
| Trunk/torso | 19 | 29 |
| Face | 11 | 17 |
| Extremities | 9 | 14 |
| Diffuse/generalized/disseminated | 8 | 12 |
| Limbs, arms and legs | 7 | 11 |
| Palmar and/or plantar involvement | 4 | 6 |
| Centrifugal spread | 4 | 6 |
| Arms | 3 | 5 |
| Abdomen | 3 | 5 |
| Back | 3 | 5 |
| Neck | 2 | 3 |
| Facial sparing | 2 | 3 |
| Palmoplantar desquamation | 1 | 2 |
| Hands | 1 | 2 |
| Upper arms | 1 | 2 |
| Upper extremities | 1 | 2 |
| Legs | 0 | 0 |
| Sparing of head | 0 | 0 |
| Sensation | | |
| Pruritic/itchy† | 29 | 44 |
| Slight itch | 6 | 9 |
| Moderate itch | 2 | 3 |
| Intense itch | 2 | 3 |
| Itchy hands | 1 | 2 |
| Specified as nonpruritic | 3 | 5 |
| Specified as tender rash | 2 | 3 |
| Specified as painless | 1 | 2 |
| Oedema | | |
| Of hands and/ or wrists | 3 | 5 |
| Oedema/swelling of feet, ankles, legs | 3 | 5 |
| Of hands and feet | 2 | 3 |
| Malar/facial | 1 | 2 |
| Mucosal features† | | |
| Gingival bleeding | 7 | 11 |
| Mucosal bleeding | 2 | 3 |
| Oral haemorrhagic blisters | 5 | 8 |
| Painful oral vesicles | 1 | 2 |
| Painful oral blisters | 1 | 2 |
| Hyperaemia of hard palate | 1 | 2 |
| Petechiae of hard palate | 1 | 2 |

*Out of 66 cases; †includes slight/moderate/intense/hand cases below and cases without intensity specified; the table does not include ocular features e.g conjunctivitis and uveitis.

bullae/vesicles (haemorrhagic or not), contrasting with 12% in our results.¹⁰ Anderson *et al.*¹¹ stated that ZV is usually not pruritic, contrasting with our finding of 44% with pruritus, and they did not describe petechial purpura, oedema or oral mucosal features.¹¹ Our results summarize the features clinicians should look for in suspected cases of ZV infection (Table 3).

Other infections causing rash and fever are also summarized (Table 1). Paniz-Mondolfi *et al.*¹⁹ have suggested the term 'ChikDenMaZika syndrome' as a mnemonic for cases from South America. There are no clinically foolproof discerning features. Co-infection with more than one arbovirus increases complexity.¹⁹ A thorough travel history of the patient, sexual partners and symptomatic contacts is crucial in guiding investigation.

A recognized limitation of any analysis of pooled cases/case series is the bias for the cases selected for publication. However, this provides a dermatological starting point from which to build.

Conclusion

As ZV becomes more prevalent, recognition of the features of the rash will enable clinicians to consider the diagnosis and test for ZV and its differentials appropriately.

Learning points

- Clinicians should have a higher suspicion of ZV in recent travellers returning from at-risk sites presenting with a rash and other key features such as fever, arthralgia/myalgia and conjunctivitis.
- However, the clinical features alone cannot guarantee a diagnosis of ZV, as other infections can present similarly and should be considered in the diagnostic testing.
- Zika virus transmission can be sexual and maternal–fetal, therefore in a patient presenting with a maculopapular rash consider taking a sexual history and any recent travel locations of their sexual partners, and also ask women about pregnancy.
- If a Zika rash is suspected, look for oedema of the distal limbs, oral bullae and or gingival bleeding, and occasionally palmoplantar involvement. Additionally, look for ocular signs of nonpurulent conjunctivitis as it is an established feature; uveitis has also been described.

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CPD questions

Learning objective

To gain up-to-date knowledge about the signs and symptoms of Zika virus and important history-taking questions in cases.

Question 1

Which of the following oral signs has been observed most frequently with Zika virus?

- Haemorrhagic bullae.
- Gingival bleeding.
- Wickham striae.
- Chelitis.
- Koplik spots.

Question 2

A 28-year-old woman presents with fever, conjunctivitis and a maculopapular rash. She has not travelled abroad. What feature in her medical history would make you think this could be Zika virus?

- Mosquito bites while gardening in her backyard in the UK.
- Her husband recently returned from a business trip in Florida.
- A monkey bit her while she was working at the zoo.
- Her 3-year-old son has seen the GP for conjunctivitis.
- She had been riding a polo pony with mange, which had been imported from Brazil by a dealer.

Question 3

Which of the following clinical features is most common in Zika virus (ZV)?

- (a) Maculopapular rash.
- (b) Fever.
- (c) Arthralgia.
- (d) Conjunctivitis.
- (e) None of the above; the virus is asymptomatic.

Question 4

Which two mosquitos are known to be vectors for Zika virus?

- (a) *Aedes aegypti*, *Aedes triseriatus*.
- (b) *Aedes albopictus*, *Aedes koreicus*.
- (c) *Aedes koreicus*, *Aedes triseriatus*.
- (d) *Aedes albopictus*, *Aedes aegypti*.
- (e) *Anopheles plumbeus*, *Aedes albopictus*.

Question 5

A 40-year-old-man with a maculopapular rash has returned from a trip around the world. Which of the countries that he visited is classified by the WHO as having ongoing transmission of Zika virus?

- (a) China.
- (b) Australia.
- (c) Fiji.
- (d) Egypt.
- (e) Uruguay.

Instructions for answering questions

This learning activity is freely available online at <http://www.wileyhealthlearning.com/ced>

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures
- Reflect on the article
- Register or login online at <http://www.wileyhealthlearning.com/ced> and answer the CPD questions
- Complete the required evaluation component of the activity

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

This activity will be available for CPD credit for 2 years following its publication date. At that time, it will be reviewed and potentially updated and extended for an additional period.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. Additional references for paper in *Clinical and Experimental Dermatology*: Dobson JS, Levell NJ. Spotting Zika spots: descriptive features of the rash used in 66 published cases (<https://jdsresources.wordpress.com/>).