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# Vertical Transmission of Oropouche Virus in a Newly Affected Extra-Amazon Region: A Case Study of Fetal Infection and Death in Ceará, Brazil

Carlos Garcia Filho, Antônio Silva Lima Neto, Ana Maria Peixoto Cabral Maia, Luiz Osvaldo Rodrigues Silva, Robson da Costa Cavalcante, Higor da Silva Monteiro, Kamilla Carneiro Alves Marques , Rebeca de Souza Oliveira, Sami de Andrade Cordeiro Gadelha, Deborah Nunes de Melo, Anacelia Gomes de Matos Mota, Shirlene Telmos Silva de Lima, Karene Ferreira Cavalcante, Larissa Maria Façanha Duarte, Ítalo José Mesquita Cavalcante, Leda Maria Simões Mello, Carlos Henrique Alencar, Andre Ricardo Ribas Freitas, Luciano Pamplona de Góes Cavalcanti

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The moderation of this preprint received the endorsement of:
Maria Rita Donalisio (ORCID: https://orcid.org/0000-0003-4457-9897)

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Author listing
Carlos Garcia Filho[§] (1) carlos.garcia@saude.ce.gov.br
https://orcid.org/0000-0002-0345-6033
Antônio Silva Lima Neto[§] (1,2) antonio.limaneto@saude.ce.gov.br
https://orcid.org/0000-0003-2798-6730
Ana Maria Peixoto Cabral Maia (1,3) ana.maia@saude.ce.gov.br
https://orcid.org/0000-0001-5205-2417
Luiz Osvaldo Rodrigues da Silva (1) luizuva@gmail.com
https://orcid.org/0000-0003-1574-9148
Robson da Costa Cavalcante (1) robsondcavalcante@gmail.com
https://orcid.org/0000-0002-4661-7343
Higor da Silva Monteiro (1,4) higor.monteiro@saude.ce.gov.br
https://orcid.org/0000-0002-7342-9137
Kamilla Carneiro Alves Marques (1, 3) kamilla-carneiro@hotmail.com
https://orcid.org/0009-0009-1593-1258
Rebeca de Souza Oliveira (1) rebeca.oliveira@saude.ce.gov.br
https://orcid.org/0009-0008-8598-8826
Sami de Andrade Cordeiro Gadelha (5) samigadelha@gmail.com
https://orcid.org/0000-0001-5214-6771
Deborah Nunes de Melo (2,6) deborahnmb@gmail.com
https://orcid.org/0000-0002-7950-0424
Anacelia Gomes de Matos Mota (5) anaceliagomesm@yahoo.com.br
https://orcid.org/0000-0002-5477-7929
Shirlene Telmos Silva de Lima (7) shtlima@hotmail.com
https://orcid.org/0000-0003-4738-9626
Karene Ferreira Cavalcante (7) karene0979@gmail.com
https://orcid.org/0000-0001-5411-7149
Larissa Maria Façanha Duarte (7). larissamariafd@gmail.com
https://orcid.org/0009-0003-8838-7050
Ítalo José Mesquita Cavalcante (7) ítalo.cavalcante@lacen.ce.gov.br
https://orcid.org/0009-0000-5044-0053
Leda Maria Simões Mello (7) ledamsimoes@gmail.com
https://orcid.org/0000-0002-8108-4124
Carlos Henrique Alencar (3,6) carllosalencar@ufc.br
https://orcid.org/0000-0003-2967-532X
André Ricardo Ribas Freitas[‡] (8) andre.freitas@slmandic.edu.br
https://orcid.org/0000-0003-0291-7771
Luciano Pamplona de Góes Cavalcanti[‡] (3,6,9) pamplona.luciano@gmail.com
https://orcid.org/0000-0002-3440-1182
§ These authors contributed equally to this work
‡ ARRF and LPGC also contributed equally to this work.

Correspondence author: André Ricardo Ribas Freitas. E-mail: andre.freitas@slmandic.edu.br

Institutions:
1. Secretaria de Saúde do Estado do Ceará, Fortaleza, Brasil.
2. Centro de Ciências da Saúde. Universidade de Fortaleza, Fortaleza, Brasil.
3. Programa de Pós-graduação em Saúde Coletiva, Universidade Federal do Ceará, Fortaleza, Brasil.
4. Departamento de Física, Universidade Federal do Ceará, Fortaleza, Brasil
5. Serviço de Verificação de Óbitos do Ceará Dr Rocha Furtado, Brasil
6. Programa de Pós-graduação em Patologia da Universidade Federal do Ceará, Fortaleza, Brasil.
7. Laboratório Central de Saúde Pública do Ceará, Fortaleza, Brasil.
8. São Leopoldo Mandic, Campinas, São Paulo, Brasil.
9. Escola de Saúde Pública do Ceará Paulo Marcelo Martins Rodrigues, Fortaleza, Brasil.

# Vertical Transmission of Oropouche Virus in a Newly Affected Extra-Amazon Region: A Case Study of Fetal Infection and Death in Ceará, Brazil

## Abstract

The spread of Oropouche virus (OROV) to new regions, along with an increase in cases and the emergence of severe, previously unrecognized forms, has raised significant public health concerns. A 40-year-old pregnant farmer at 30 weeks of gestation developed fever, myalgia, and headache, with OROV infection confirmed by RT-qPCR. Initially, both maternal and fetal assessments showed no complications. However, the following week, the patient noticed decreased fetal movements, and ultrasound confirmed fetal demise. Molecular diagnostics detected OROV RNA in multiple fetal specimens. This case of vertical transmission underscores the urgent need to protect pregnant women, incorporate OROV in the differential diagnosis of febrile illnesses, and further investigate the virus's potential pathogenic mechanisms.

Keywords
Oropouche virus, vertical transmission, fetal death, placental pathology, maternal-fetal health

## Introdution

Oropouche virus (OROV) is an arbovirus of the genus Orthobunyavirus, serotype Simbu, primarily transmitted to humans by the bite of the midge Culicoides paraensis, although other insect vectors have also been implicated (Wesselmann, 2024). Initially identified in Trinidad and Tobago in the 1950s, OROV has been largely restricted to the Amazon Basin and neighboring areas, where transmission occurs primarily in wild and rural environments, with occasional small outbreaks in peri-urban regions[1].

Since late 2023, however, OROV has experienced a significant expansion in its transmission area. The virus has spread to more than a dozen Brazilian states outside the Amazon and has reached countries that had not previously reported autochthonous cases, such as Bolivia and Cuba, with several regions being affected simultaneously. Travel-related cases have also been identified among European travelers[2]. Genomic analyses suggest that this expansion is driven by a monophyletic viral lineage that emerged after a genetic reassortment event, leading to the rapid displacement of previous OROV lineages[3–5].

OROV typically causes a dengue-like illness, characterized by fever, headache, myalgia, and rash, with rare neurological complications, and, until recently, no fatalities or vertical transmission had been documented[1]. However, reports of severe cases in 2024 have raised significant concerns among health authorities. Two fatal cases in Bahia involved young women who, despite having no preexisting conditions, presented with high viral loads and severe hemorrhages associated with coagulopathy and liver involvement—complications never documented before[6,7]. Additionally, cases of vertical transmission of OROV associated with severe fetal outcomes were reported in Brazil. Four cases of fetal death and one case of spontaneous abortion were reported in Pernambuco, and one case of vertical transmission with severe malformations in the newborn, who died at 47 days of life, was reported in Acre[7].

In response to this evolving situation, the Pan American Health Organization (PAHO) issued a statement on August 3, 2024, raising the risk level for the Americas from medium to high in its "Public Health Risk Assessment Related to Oropouche Virus (OROV) in the Region of the Americas"[7]. Here, we present a report of a case of vertical transmission of OROV confirmed by direct methods and associated with fetal death, which was investigated using minimally invasive autopsy techniques.

Epidemiological and Environmental Framework

The first case of Oropouche fever in Ceará was retrospectively confirmed on June 21, 2024, through active laboratory surveillance of serum samples that initially tested negative for urban arboviruses transmitted by *Aedes aegypti* (dengue, Zika, and chikungunya). This case involved a patient who began presenting symptoms on May 19. Following this confirmation, a symptom alert was issued to all municipalities in the state, prompting the initiation of systematic surveillance in the patient's area of residence. This included home visits and active case searches in several municipalities, leading to the identification of patients with symptoms suggestive of Oropouche fever. A total of 171 cases were confirmed through laboratory testing, with no serious cases reported except those related to vertical transmission.
The cases were concentrated in the Baturité Massif, spanning seven small municipalities with a median population of 11,224 inhabitants (range: 10,242 - 35,218, CENSO, 2022)[8]. These areas are situated in valleys where crops such as banana and chayote predominate, creating shade and contributing to the accumulation of organic matter. These crops are often interspersed with natural vegetation very close to residences. The region is located within the Caatinga biome, characterized by semiarid and tropical climates with a distinct dry season (Köppen-Geiger classification BSh and As, respectively) and diverse phytoecological types, including caatinga, humid forest, and dry forest (Figure 1)[8]. A notable concentration of cases was observed in a small area known as Serra do Vicente, located in Capistrano,

where the first case of vertical transmission was subsequently diagnosed (27 georeferenced cases are shown in Figure 2).

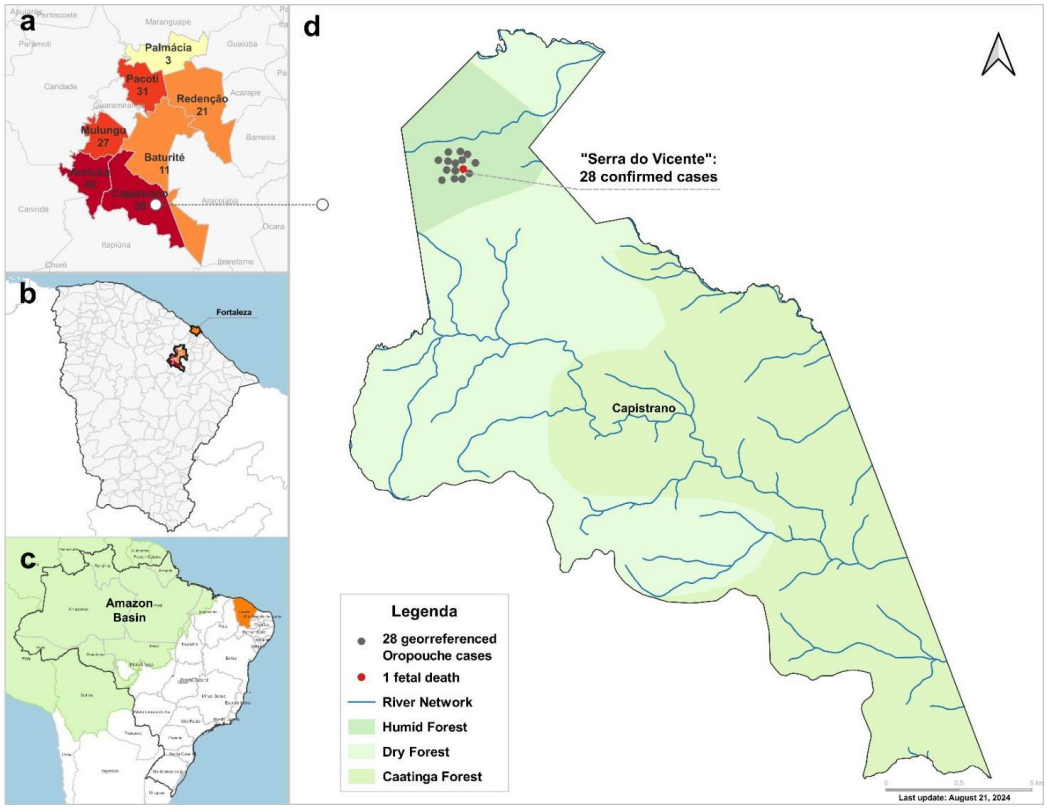


Figure 1. Spatial Distribution of Oropouche Cases and Fetal Death in the Maciço de Baturité Region, Ceará, Brazil, 2024.
(A) Spatial distribution of Oropouche cases across seven municipalities in the Maciço de Baturité mountain region of Ceará, Brazil. Each municipality is shaded according to the number of cases. (B) Location of the Maciço de Baturité region relative to the state of Ceará and its capital, Fortaleza. (C) Map of Brazil and part of South America, showing the location of Ceará in relation to the Amazon Basin. (D) Geographic distribution of 28 georeferenced Oropouche cases in the Serra do Vicente region of the municipality of Capistrano, including the case of vertical transmission resulting in a fetal death (red marker). The map also shows the river network and ecological zones within Capistrano, including areas of humid forest (most associated with the cases), dry forest, and Caatinga forest.

## Patient History

A 40-year-old small-scale banana farmer from the Baturité Massif region of Ceará was in her third pregnancy. Her last menstrual period (LMP) was on December 24, 2023. Her obstetric history included a first-trimester miscarriage 16 years earlier, followed by a successful pregnancy resulting in the birth of a healthy child. She received regular prenatal care and underwent four routine ultrasound examinations, from 8 weeks and 2 days to 27 weeks and 2 days of gestation, all of which revealed no abnormalities in fetal or placental morphology (Table 1, images collected during these ultrasound examinations are available in the Supplementary Appendix). The

patient was also on metformin therapy for gestational diabetes mellitus, with no other complications noted during this pregnancy.

Table-1: Ultrasound Biometric Measurements, Morphological Findings, and Parameters Across Gestational Age

| Ultrasound Parameter | 2024-03-26 | Parameter Status or Percentile* | 2024-07-02 | Parameter Status or Percentile* | 2024-07-29 | Parameter Status or Percentile* | 2024-08-05 | Parameter Status or Percentile* |
|---|---|---|---|---|---|---|---|---|
| Gestational age | 13 week 2 days | | 27 week 2 days | | 31 week 1 days | | 32 week 1 days | |
| Crown-Rump Length (CRL) | 82 mm | Normal | N/A | | N/A | | N/A | |
| Occipitofrontal Diameter (OFD) | N/A | | 93 mm | Normal | N/A | | 103 mm | Normal |
| Biparietal Diameter (BPD) | N/A | | 71 mm | 66.3 | 81.4 mm | 73.1 | 78.0 mm | 37.9 |
| Head Circumference (HC) | N/A | | 264 mm | 76.1 | 296 mm | 70.5 | 296 mm | 46.4 |
| Abdominal Circumference (AC) | N/A | | 233 mm | 51.5 | 303 mm | > 97.5 | N/A | |
| Femur Length (FL) | N/A | | 56 mm | >97.5 | 64 mm | 97.4 | 63 mm | 78 |
| Estimated Fetal Weight (EFW) | N/A | | 1,314 g | 86.7 | 2,269 g | >97.5 | N/A | |
| Nuchal Translucency (NT) | 1.3 mm | Normal | N/A | | N/A | | N/A | |
| Cephalic Index (CI) | N/A | | 0.77 | | N/A | | 0.76 | |
| HC/AC Ratio | N/A | | 1.13 | | 0.98 | | N/A | |
| FL/AC Ratio | N/A | | 0.24 | | 0.21 | | N/A | |
| Fetal Heart Rate (FHR) | 156 bpm | Normal | 145 bpm | Normal | 137 bpm | Normal | Fetal death | |
| Spontaneous Fetal Movements | Present | Normal | Present | Normal | Present | Normal | Fetal death | |
| Nasal Bone | Present | Normal | N/A | | N/A | | N/A | |
| Ductus Venosus | Positive Wave A | Normal | N/A | | N/A | | N/A | |
| Umbilical Artery (PI - Pulsatility Index) | | | 0.9 | Normal | | | | |
| Amniotic Fluid Aspect and Volume | Normal | Normal | Normal | Normal | Normal | Normal | | |
| MVP (Maximum Vertical Pocket) | | | 50mm | Normal | 50.7mm | Normal | | |
| Placenta (insertion) | | | Posterior and corporal | | Posterior and corporal | | | |
| Echotexture | | | Heterogeneous, Grade I | | Heterogeneous, Grade I | | | |

*Percentiles for key biometric measurements are calculated according to the Kiserud T. et al.. The World Health Organization Fetal Growth Charts: A Multinational Longitudinal Study of Ultrasound Biometric Measurements and Estimated Fetal Weight. PLOS Medicine 2017 Jan 24;14(1):e1002220 (https://www.who.int/teams/sexual-and-reproductive-health-and-research-(srh)/areas-of-work/interactive-tools)

"N/A" means: "Not Applicable" or "Not Available", depending on the context.

Images collected during these ultrasound examinations are available in the Supplementary Appendix.

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## Clinical Presentation

At 30 weeks and 3 days of gestation, the patient developed fever, chills, generalized myalgia, and severe headache on the evening of July 24, 2024. The following day, she noticed mild vaginal bleeding with a scant dark discharge but remained stable at home. She sought medical attention two days later, on July 27, at a local hospital. During her evaluation, arboviral infection was suspected, and laboratory tests for dengue, chikungunya, and Zika viruses were ordered, along with a comprehensive obstetric assessment.

On July 29, the patient returned to the hospital for reevaluation. Blood samples were collected for molecular testing of arboviruses. Given the epidemiological context, Oropouche and Mayaro viruses were also included in the investigation through active laboratory surveillance at the Central Public Health Laboratory of Ceará (LACEN). An obstetric ultrasound performed at that time indicated fetal macrosomia, with the estimated fetal weight above the 97.5th percentile for gestational age. The placenta was observed to be posterior and corporal with a heterogeneous Grade I echotexture, without signs of pathological alterations (Table 1). The amniotic fluid was within normal limits, and the fetal heart rate was normal, with spontaneous fetal movements noted. General biochemical tests, including blood glucose and hemoglobin A1c (HbA1c), were normal, with HbA1c at 5.6%. A complete blood count was also normal.

On August 7, molecular diagnostics using a Real-time RT-qPCR protocol for Mayaro (MAYV) and Oropouche virus (OROV), following PAHO-recommended protocols[9,10], confirmed the presence of Oropouche viral RNA, while ruling out Mayaro virus. Additionally, tests for urban arboviruses (dengue, Zika, and chikungunya) were conducted using both direct and indirect methods. The results for dengue, Zika, and chikungunya were negative, as confirmed by a multiplex RT-qPCR assay (BIOMOL ZDC for Zika, dengue, and chikungunya, IBMP®). Furthermore, IgM antibody testing was performed using commercial ELISA kits: Dengue IgM Capture ELISA (Panbio®), Anti-Zika Virus ELISA (IgM) (Euroimmun®), and Anti-Chikungunya Virus ELISA (IgM) (Euroimmun®), all of which returned negative results. Further laboratory investigations showed a negative urine culture, negative indirect Coombs test, normal TSH, and ruled out infections such as syphilis, toxoplasmosis, herpes, cytomegalovirus, rubella, HIV, and hepatitis B and C.

The patient was informed of the diagnosis and remained in the maternity ward for 48 hours, during which misoprostol was administered in an attempt to induce labor for intrauterine fetal demise. After unsuccessful induction, a cesarean section was performed on August 9. The family was advised to refer the fetus for autopsy, but they declined. Instead, they consented to a minimally invasive autopsy (MIA)

performed by a team of pathologists from the Death Verification Service (VSO), with a detailed timeline presented in Figure 2.

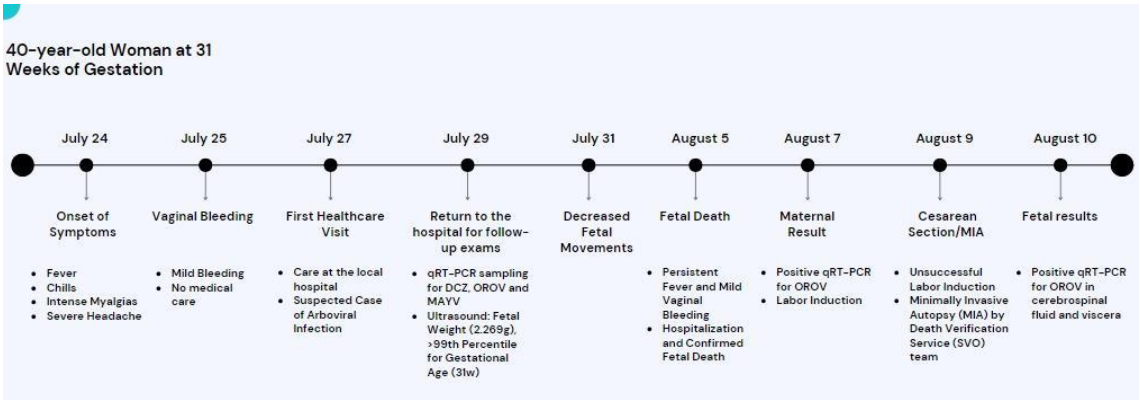


Figure 2. Timeline of events of a 40-year-old woman, 31 weeks pregnant, infected with Oropouche virus with fetal death. The timeline begins on July 24, 2024, with the onset of symptoms, including fever, intense myalgias, and severe headache and concludes on August 10, 2024, with the detection of Oropouche virus RNA in the fetal cerebrospinal fluid and viscera via RT-qPCR.

## Post-Mortem Examination

### Placental Examination:

The placenta weighed 354 g, corresponding to the 10th percentile for the estimated gestational age of 33 weeks in male fetuses. It exhibited features suggestive of placental infarctions affecting approximately 30% of the maternal surface. The umbilical cord measured 55 cm, with a paracentral insertion, containing two arteries and one vein. The chorioamniotic membranes were translucent.

### Macroscopic Fetal Examination:

The stillborn male exhibited level III maceration with no apparent external malformations. The fetus weighed 2,190 g, with key measurements including a crown-heel length of 45 cm, foot length of 6.5 cm, head circumference of 32 cm, chest circumference of 30 cm, and abdominal circumference of 24 cm. These morphometric parameters were consistent with a gestational age of approximately 33 weeks.

### Minimally Invasive Autopsy (MIA) Procedures:

MIA was conducted using 20 cm, 14-gauge percutaneous biopsy needles, and a syringe with a 1.2 x 40 mm hypodermic needle. Cerebrospinal fluid (1.0 ml) was obtained via occipital puncture. Brain cores were collected by inserting the biopsy needle through the nasal cavities and piercing the cribriform plate of the sphenoid bone. Both lungs were punctured between the third and fourth intercostal spaces, and cores were collected from each. Similarly, cores were taken from the heart

through the fifth intercostal space and from the liver through the right 11th intercostal space. Attempts to obtain cores from the spleen and kidneys were unsuccessful. These procedures were conducted as part of a study approved by the Research Ethics Committee under protocol CAAE 27162619.1.0000.5049, number 3.851.684 (Almeida et al., 2024). The collected samples were sent to the Central Public Health Laboratory of Ceará (LACEN-CE) for further testing, including RT-qPCR analysis for urban arboviruses (dengue, Zika, and chikungunya), as well as Oropouche and Mayaro viruses, following PAHO-recommended protocols[9,10].

Microscopic Examination:
Histopathological analysis was hindered by significant autolysis of the fetal tissues, a result of the delay between fetal demise and cesarean section (Figure 3). The placental tissue showed increased syncytial knots, reduced intervillous spaces, and frequent foci of fibrin deposition—findings consistent with the macroscopic evidence of infarction. Histopathological analysis of fetal tissues was limited due to extensive autolysis.

Molecular Findings:
Molecular analysis confirmed the presence of Oropouche virus RNA in all sampled specimens, including cerebrospinal fluid (Ct 21), brain, heart, lungs, liver, umbilical cord, and placenta. RT-qPCR tests for dengue, Zika, chikungunya, and Mayaro viruses returned negative results in all samples.

## Discussion

This case provides clear evidence of vertical transmission of Oropouche virus (OROV) with confirmed fetal infection, a phenomenon not previously documented before the current outbreak. The presence of OROV RNA in various fetal samples, including cerebrospinal fluid, brain, heart, lungs, liver, umbilical cord, and placenta, unequivocally demonstrates that the virus can cross the placental barrier and infect the fetus. This finding represents a significant advancement in our understanding of OROV's pathogenic potential, particularly in the context of pregnancy. The use of minimally invasive autopsy (MIA) in this case proved invaluable in confirming vertical transmission, offering a less invasive alternative to investigate the pathogenesis of OROV and other emerging arboviruses, especially in settings where conventional autopsy may not be feasible.

Although vertical transmission of OROV is well supported, the potential causal relationship between this infection and the observed fetal death remains to be clarified. Histopathological examination of the placenta revealed infarcts affecting approximately 30% of the maternal surface, together with increased syncytial

nodules, reduced intervillous spaces and frequent foci of fibrin deposition. These findings are indicative of poor placental perfusion, a factor commonly associated with adverse fetal outcomes (Redline, 2021). The lack of adequate fetal material for histopathological and pathophysiological studies, together with maternal risk factors such as advanced maternal age, history of spontaneous abortion, gestational diabetes and fetal macrosomia, preclude the establishment of any definitive causal relationship. However, several hypotheses may deserve further investigation.

We hypothesize that maternal OROV infection could provoke inflammatory responses that trigger vascular phenomena, exacerbating the already compromised maternal vasculature and leading to placental insufficiency, ischemia, and infarctions. This vascular disruption could be a contributing factor to the adverse fetal outcomes observed. Additionally, OROV might directly infect placental cells, further contributing to these infarctions. Similar pathophysiological mechanisms have been observed in other viral infections, such as Zika and SARS-CoV-2, where placental inflammation and vascular malperfusion have been linked to adverse pregnancy outcomes[11,12]. Further studies are needed to elucidate how OROV impacts maternal, placental, and fetal health and to better understand the complex pathophysiological processes underlying this viral infection.

This case report is likely linked to the same recombinant OROV viral lineage that has emerged in several other regions outside the Amazon Basin, causing a dramatic increase in the number of cases.[3–5]. The emergence of severe forms may be partly attributed to the increase in the absolute number of cases and to improved access to etiological diagnostics. This possibility warrants further evaluation, particularly considering that experimental studies, both in vivo and in vitro, suggest that this new OROV lineage is associated with more extensive viral replication, increased pathogenicity in mammalian cell cultures, and the ability to evade antibodies generated by previous OROV lineages.[5].

A concerning and noteworthy parallel is with the Zika virus, which, before establishing urban transmission and global spread, was not associated with severe congenital anomalies or fetal death. Subsequent studies revealed that the emerging Zika lineage was indeed more pathogenic than the zoonotic African lineage[13]. Similarly, Schmallenberg virus (SBV), another orthobunyavirus of the Simbu serotype, closely related genetically to OROV and likely the result of genetic reassortment, emerged in Europe in 2011, causing abortions and congenital deformities in ruminants with significant economic impact[14].

The social and environmental context of the outbreak in Ceará underscores the role of local ecological factors in the transmission dynamics of OROV. The affected region, characterized by a dry tropical climate and humid forests, may provide a favorable environment for *Culicoides paraensis*, the primary known vector (with

entomological studies underway in the area). The geographic isolation of humid forest areas, surrounded by caatinga and semiarid regions, may indicate the emergence of new vector transmission patterns.

The recent changes in OROV transmission, coupled with the potential for serious outcomes such as vertical transmission and fetal death, demand urgent public health attention. These findings emphasize the need to include OROV in the differential diagnosis of febrile illnesses in pregnant women, particularly in regions where the virus is endemic or emerging. Enhanced epidemiological, entomological, and virological surveillance, along with further research into the pathogenic mechanisms of OROV, are essential to address and mitigate the impact of this emerging arbovirus, especially in recently affected regions.

## Consent

Written informed consent was obtained from the patient's parents for publication of this Case Report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## Conflict of Interest

The authors declare that there is no conflict of interest.

## Authors' Contributions

Description of each author's role in the research process and in preparing the manuscript:
CGF, AMPCM, ASLN, SACG, ARRF, LPGC - analysis and interpretation of data and writing of the article.
CGF, ASLN, SACG, ARRF, LPGC - were responsible for drafting the proposal, review of literature and writing the article.
CGF, AMPCM, ASLN, JAPB, OJN, HSM, KCAM, RSSO, LMSM, SACG, DNM, AGMM, STSL, KFC, ITMC, LMF, LORS, WMS, CHMA, ARRF, LPGC drafting the paper or substantially revising it and was responsible for overall direction conception and design of the study.

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## Informed Consent Statement

Informed consent was obtained from the family.

## Data Availability Statement

All other accessible data are available in the supplementary materials section.

## Supplementary Material

### Photographs of the Locality

Photographs depicting the geographical and environmental context of the affected region in Ceará, Brazil.

### Clinical and Epidemiological Characteristics

Detailed clinical and epidemiological characteristics of Oropouche virus cases in Ceará, Brazil, 2024.

### Ultrasound Images

Supplementary ultrasound images collected during the patient's prenatal care, the progression of OROV disease and confirmation of fetal demise.

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Supplementary Material


Figure 1: Photo on affected region https://www.saude.ce.gov.br/2024/06/27/saude-do-ceara-intensifica-acoes-de-prevencao-e-de-vigilancia-epidemiologica-da-febre-oropouche/

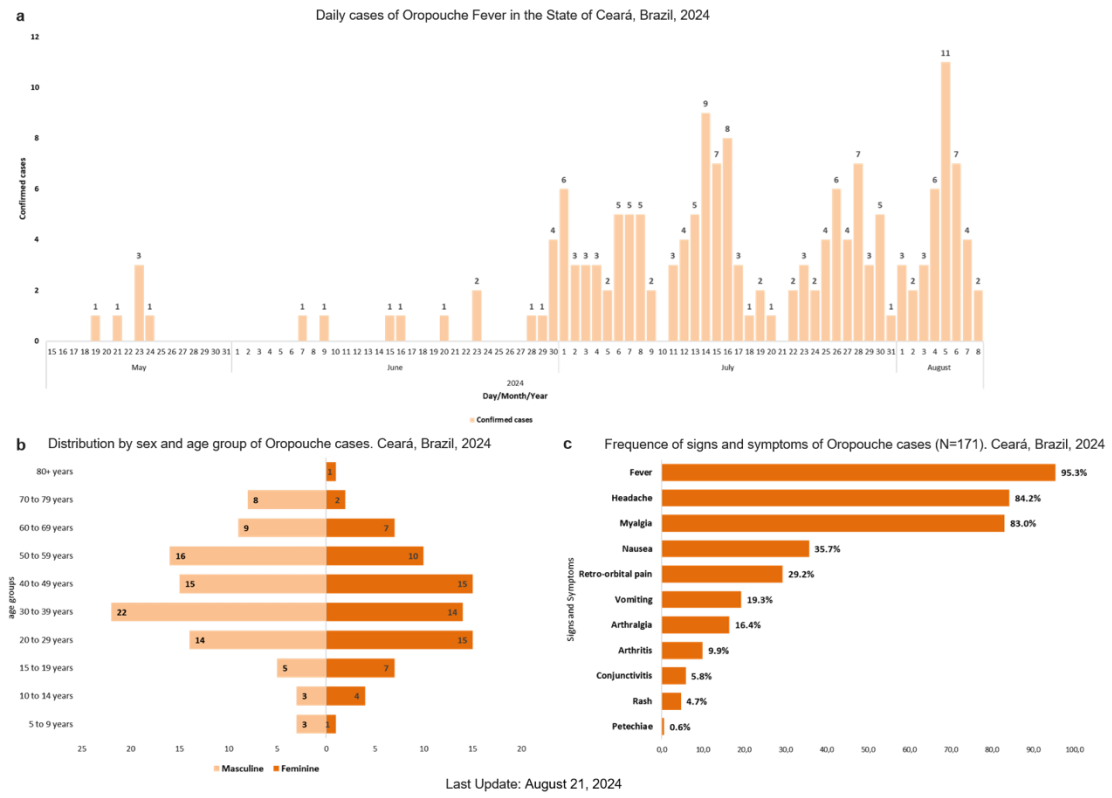



Figure 2. Clinical and Epidemiological Characteristics of Oropouche Virus Cases in Ceará, Brazil, 2024.

Comments

(A) Daily Oropouche cases from May to August 2024. The first confirmed case in Ceará was reported on June 21, 2024, with earlier cases identified retrospectively. Active surveillance following June 21 led to the identification of subsequent cases, resulting in a steady increase in cases over time, as shown in the epidemiological curve. (B) Age and sex distribution of Oropouche virus cases, showing that the virus affected a wide range of age groups, with a concentration in individuals aged 30 to 39 years, especially among men (22 cases). The observed distribution suggests that Oropouche virus transmission may not be confined to agricultural environments near plantations but could also be extending into households, affecting individuals of varying ages. (C) Percentage of reported signs and symptoms among confirmed Oropouche virus cases in the Maciço de Baturité region. Fever, headache, and myalgia were the most frequently reported symptoms, occurring in 95.3%, 84.2%, and 83.0% of cases, respectively, forming a common clinical triad for Oropouche infection. Despite increasing reports of rash associated with Oropouche virus in other regions of Brazil, this symptom was less frequently observed in cases from Ceará, with only 4.7% of cases reporting rash. Other symptoms such as retro-orbital pain, nausea, vomiting, and intense arthralgia were reported with varying frequency, while petechiae and conjunctivitis were notably rare.

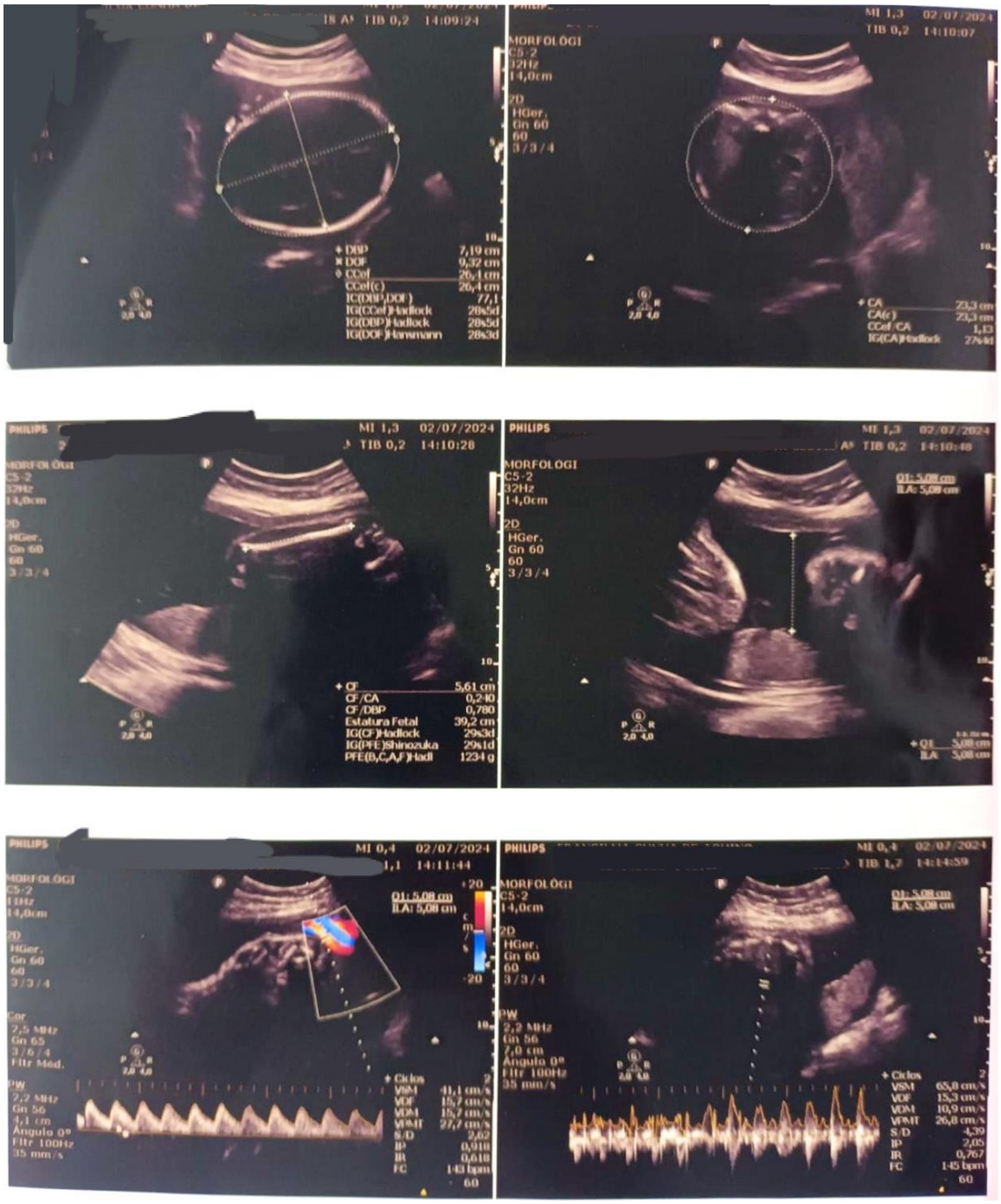



Figure 3: Ultrasound image taken on July 5, 2024, showing fetal biometric measurements at 31 weeks and 1 day of gestation. The scan shows any notable feature, with no abnormalities detected in fetal or placental morphology at this stage.

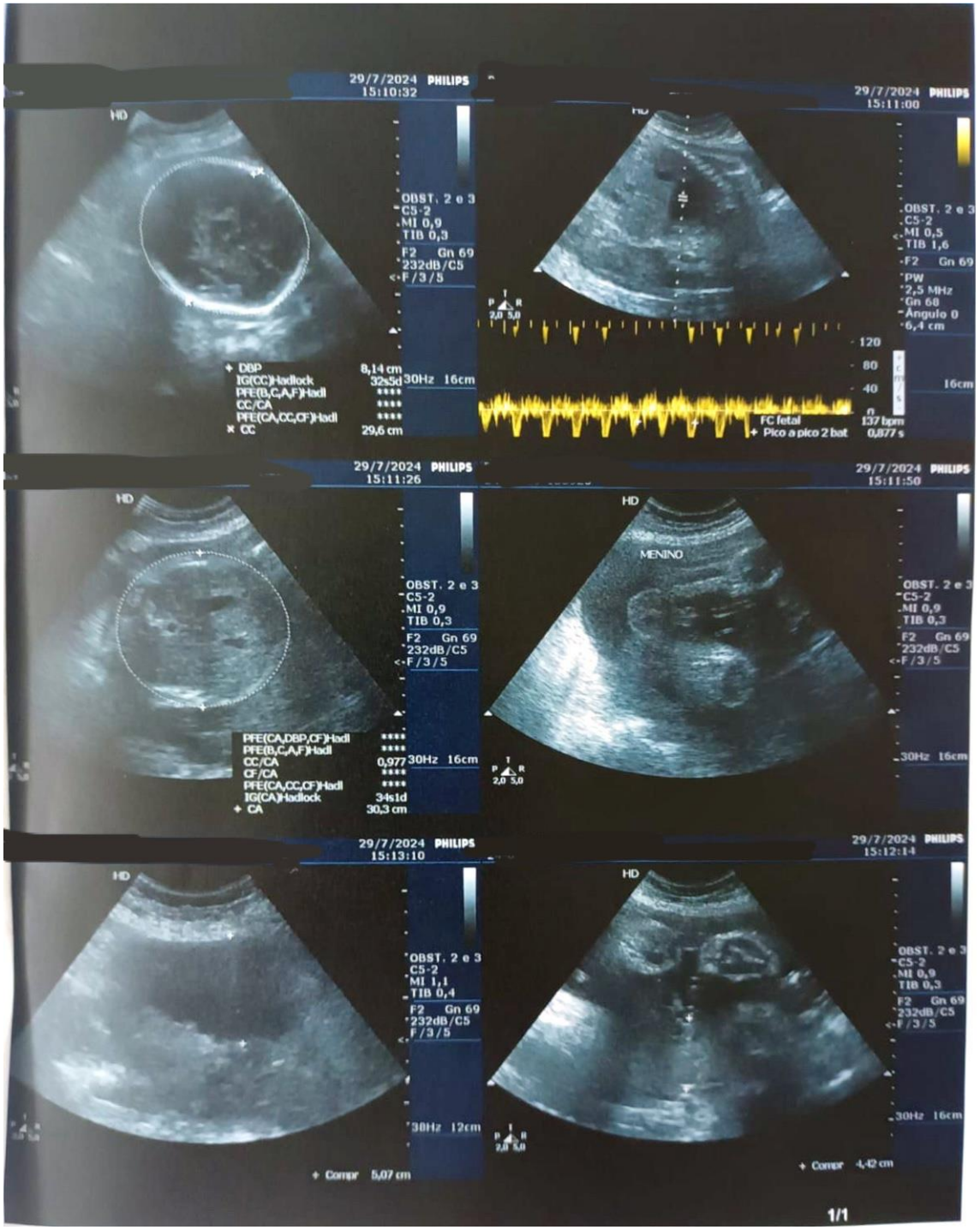



Figure 4: Ultrasound image taken on July 29, 2024, at 32 weeks and 1 day of gestation. The scan shows an Abdominal Circumference (AC) of 303 mm and Femur Length (FL) of 64 mm, both above the 97.5th percentile, indicating accelerated fetal growth. The Estimated Fetal Weight (EFW) was 2,269 g, also above the 97.5th percentile, with no additional abnormalities in placental or fetal morphology observed at this time.

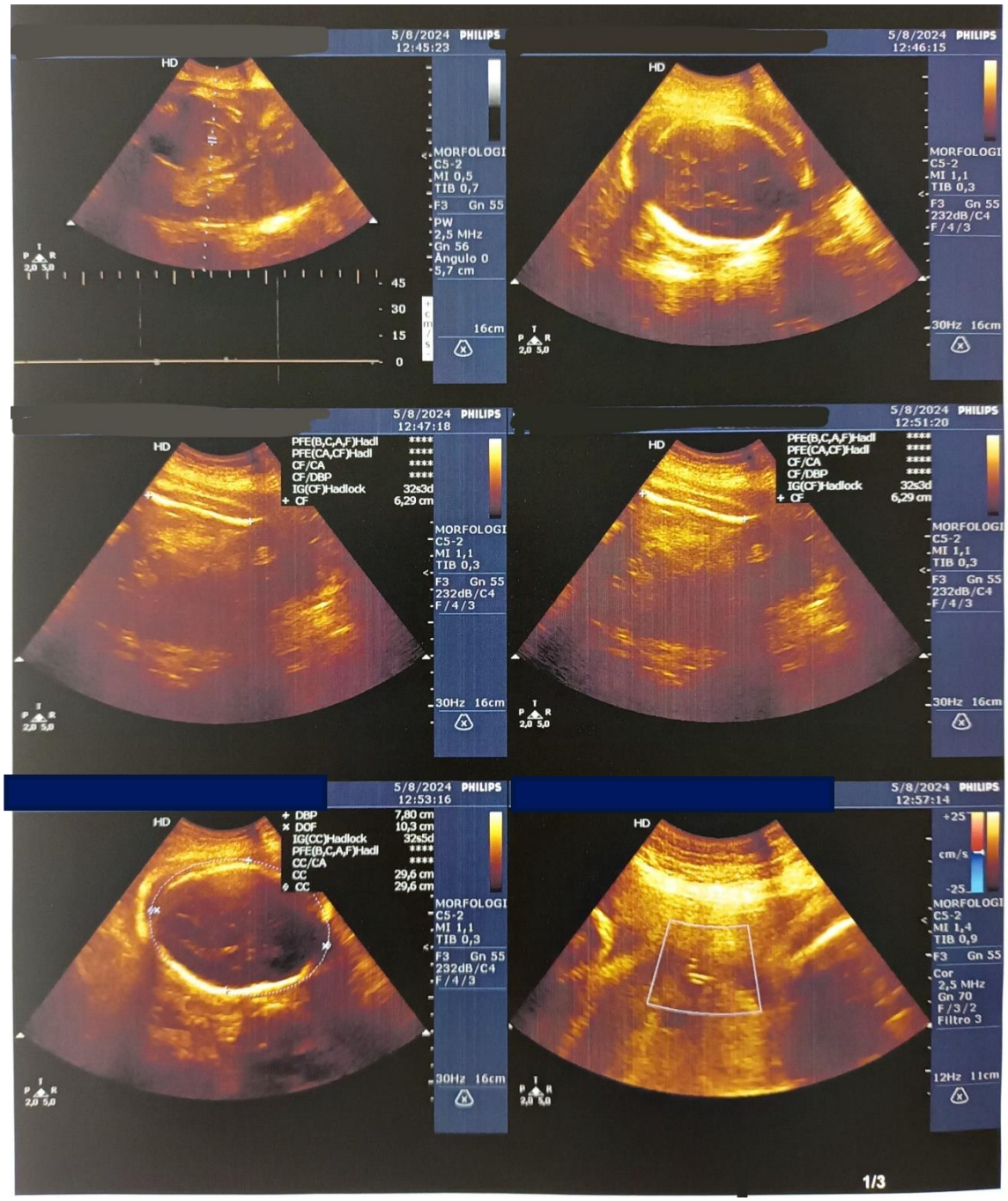
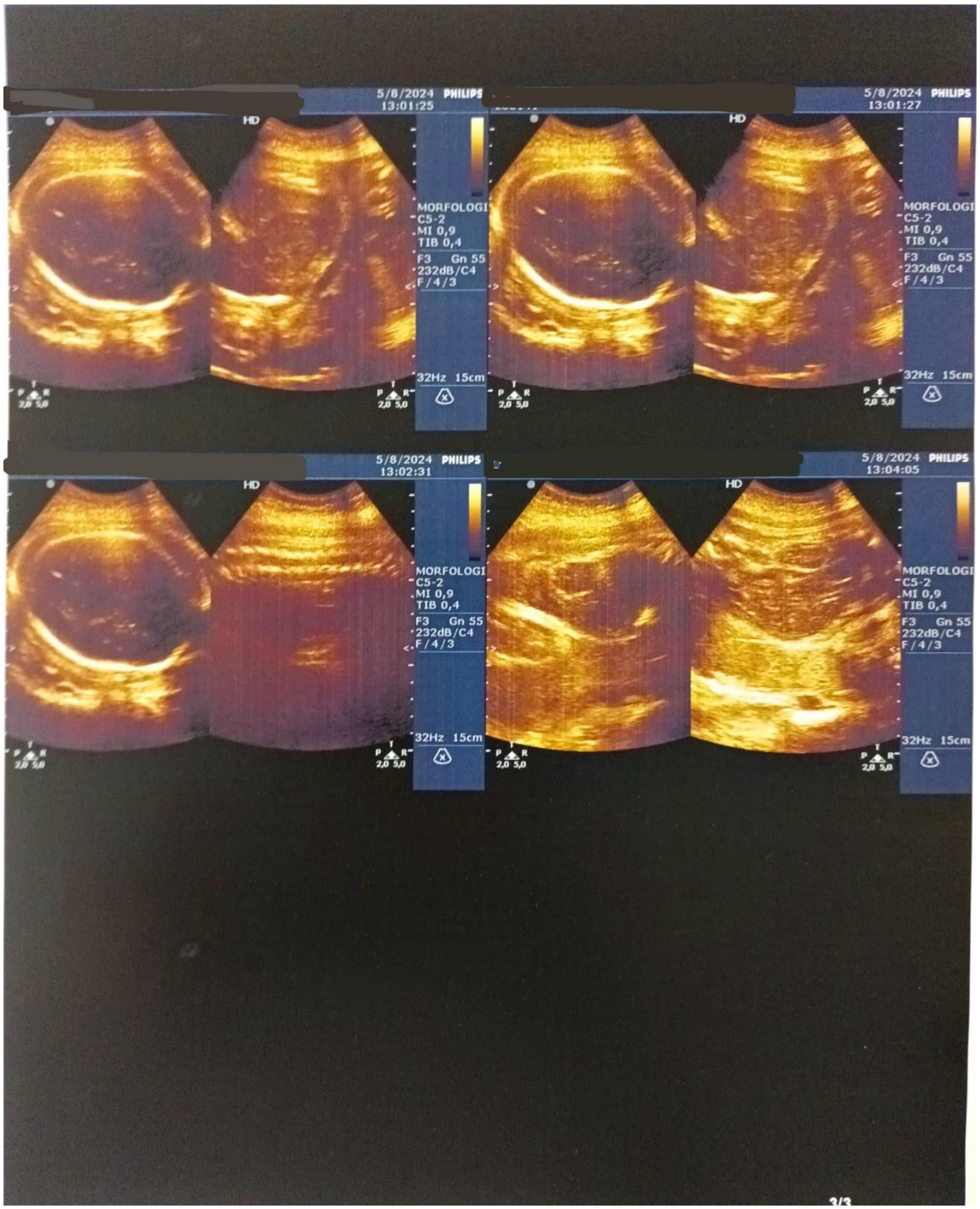



Figure 5: Ultrasound image taken on August 5, 2024, at 33 weeks and 1 day of gestation. The scan confirmed the absence of Fetal Heart Rate (FHR) and Spontaneous Fetal Movements, indicating fetal demise.

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