The Zika virus: an opportunity to revisit reproductive health needs and disparities

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Abstract

First isolated in 1947, the Zika virus was initially connected only to limited or sporadic human infections. In late 2015, the temporal clustering of a Zika outbreak and microcephaly in newborn babies from northeastern Brazil, and the identification of a causal link between the two, led to the characterization of the congenital Zika syndrome. In the wake of the epidemic, several countries from Latin America advised women to postpone pregnancies for periods ranging from six months to two years. These recommendations initiated critical conversations about the challenges of implementing them in societies with limited access to contraception, widespread socioeconomic inequalities, and high rates of unplanned and adolescent pregnancies. The messaging targeted exclusively women, despite a high prevalence of imbalances in the relationship power, and addressed *all* women as a group, failing to recognize that the decision to postpone pregnancies will impact different women in different ways, depending on their age at the time. Finally, in several countries affected by the Zika epidemic, due to restrictive reproductive policies, legally terminating a pregnancy is no longer an option even at the earliest time when brain malformations as part of the congenital Zika syndrome can be detected by ultrasonography. The virus continued to circulate after 2016 in several countries. Climate change models predict an expansion of the geographical area where local Zika transmission may occur, indicating that the interface between the virus, teratogenesis, and reproductive rights is a topic of considerable interest for medicine, social sciences, and public health for years to come.

Keywords **Zika virus, teratogenesis, public health, reproductive rights.**

Introduction

The Zika virus is an emerging arthropod-borne virus or arbovirus[1,2] that belongs to the genus *Flavivirus* from the family *Flaviviridae*.[3] The virus was first isolated in 1947 from a febrile rhesus macaque monkey in the Zika Forest from Uganda, and while there is some controversy about the first time when it was isolated from humans, this appears to have been in 1964 in Uganda.[4-10] For over half a century, the Zika virus only caused limited or sporadic human infections in Africa and Asia until the 2007 outbreak from Yap Island in Micronesia, the western Pacific.[6,11] Only 14 cases of Zika virus disease were documented worldwide before this outbreak.[12] During the 2007 outbreak, it was estimated that 73% of the residents three years and older on the island became infected.[11] This was followed by an October 2013 outbreak in the French Polynesia, which extended until April 2014 and from where the virus spread, around the same time, to Easter Island, where it caused a 2014 outbreak, and to the Americas.[13-15]

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In May 2015, the local transmission of Zika was reported in the Americas for the first time, when the virus emerged in northern Brazil.[7,16,17] Based on phylogenetic analyses and molecular clock studies, it was estimated that the virus was introduced to the Americas in the second half of 2013.[18] By the time it was recognized that the virus may cause severe congenital disease, it has already spread from Brazil to >40 countries.[19] Local mosquito-borne transmission of the Zika virus in the US was first reported in December 2015 in Puerto Rico.[20] In the continental US, the first instance of local transmission was reported in July 2016 in Florida[21] and then in November 2016, in Texas.[22] The sequencing of Zika viruses isolated from patients and infected mosquitoes showed that the virus was introduced into Florida on multiple independent occasions, at least four, but possibly as many as 40, and that probably its local transmission began in the spring of 2016, months before the virus was first detected.[23] The World Health Organization (WHO) declared the Zika virus epidemic a Public Health Emergency of International Concern (PHEIC) on February 1, 2016[24,25] and, as of July 2019, 87 countries or territories reported local transmission.[26-29] Viral genomics and travel surveillance found that an outbreak occurred in Cuba in 2017, at a time when circulation of the virus was already waning in other places in the Americas.[19] After the period of Public Health Emergency of International Concern ended in November 2016, >100,000 cases of Zika virus infection were reported in Brazil[30] and >150,000 cases were reported in the Americas by the end of September 2021.[30] The virus was detected in other locations that include Mexico,[31] Gabon,[32] India,[33-35] Papua New Guinea,[36] and countries in the Caribbean.[37] The first laboratory-confirmed case of Zika in India was confirmed in November 2016[38] and the virus was still circulating in several states in India in 2021.[33,35,39] Some of the historical milestones of the Zika virus emergence and spread are presented in Table 1.

The Zika virus can be transmitted to humans by infected mosquitoes,[40] sexually by infected male or female partners,[41] perinatally,[42] by blood transfusion,[43,44] through laboratory exposure,[45] or as a result of organ transplantation.[46] Even though the virus was detected in breast milk, its transmission through breastfeeding was not yet documented as of 2021.[47-49]

The congenital Zika syndrome

Until October 2015, Zika was generally considered a benign disease.[47] In adults, the Zika virus infection is symptomatic in approximately 20-25% of the infected individuals and causes a mild and usually self-limiting flu-like illness[50] lasting for 7-10 days, usually without long-term consequences.[6,51] However, it was also linked to subcutaneous bleeding,[50] cardiovascular changes such as myocarditis, heart failure, and arrhythmia,[52-54] conjunctivitis, uveitis,[55] arthralgia,[52] Guillain-Barré syndrome, and meningoencephalitis.[56]

In October 2015, reports from northeastern Brazil revealed an increase in the number of babies born with microcephaly and this, together with their temporal clustering, led to the hypothesis that microcephaly was caused by the Zika virus.[57] Because historically the Zika virus was not linked to birth defects, and due to disparities in the incidence of microcephaly in different geographical locations, the initial increase in microcephaly cases was thought to be caused by environmental chemicals.[58,59] Subsequently, several studies provided epidemiological evidence that linked Zika virus exposure during pregnancy to microcephaly.[60-63] An analysis that used data collected from the Brazilian Information System on Live Births (SINASC) showed that between 2000, prior to the circulation of the virus, and 2015, there was a 9.8-fold increase in the annual average number of microcephaly cases.[64]

The virus was isolated from the brain of infants with microcephaly who died, and from the placenta of women who had miscarriages and suspected Zika infections.[50] In a pregnant woman who was infected in week 11 of her pregnancy, the fetal head circumference percentile decreased between week 16 and week 20 from the 47th to the 24th percentile. After her pregnancy was terminated at 21 weeks, viral-like particles were isolated from the fetal brain, and Zika virus

Table 1. Key events in the history of the Zika virus. Data are based on references[4,7,9-13,20-22,30,35,38,39,67,68,248-263]

Year	Event
April 1947	The first isolation of the Zika virus from a febrile sentinel rhesus monkey in Uganda
January 1948	The first isolation of the Zika virus from *Aedes africanus* mosquitoes
1956	The first demonstration that the Zika virus replicates in *Aedes aegypti* mosquitoes
1964	The first report of Zika virus infection in humans in Uganda
1966	The first isolation of the Zika virus from *Aedes aegypti* mosquitoes outside of Africa, in Malaysia
2007	The beginning of the Zika virus outbreak on Yap Island, the Western Pacific
2008	The first report of human-to-human transmission through intercourse
2013	The first report of Guillain-Barré syndrome (GBS) after an infection with the Zika virus
2013-2014	The Zika virus outbreak from French Polynesia
early 2014	The first confirmation of local transmission of the Zika virus in the Americas on Easter Island, Chile
early 2015	Detection of the Zika virus in Brazil
October 2015	The complete Zika virus genome was recovered from a fetus with microcephaly, in a woman who returned from Brazil to Slovenia
late 2015	Description of microcephaly in Brazil Detection of Zika virus RNA in the amniotic fluid of pregnant women with fetal microcephaly
December 2015	First local transmission of the Zika virus in a US jurisdiction, in Puerto Rico
February 2016	The WHO declares Zika a Public Health Emergency of International Concern (PHEIC)
February 2016	The first sexual transmission of the Zika virus in the US, from a traveler who returned from Venezuela to Texas
July 2016	The first recognized outbreak of mosquito-borne transmission of Zika virus in the continental US in a neighborhood from Miami-Dade County, Florida
November 2016	The first instance of locally transmitted Zika in Texas
2016	The first link between Zika virus and the acute motor axonal neuropathy variant of GBS supported by clinical and electrodiagnostic evidence
2016	The first laboratory cases of Zika virus infection reported in India
2017-2021	Zika virus reported in 16 states/union territories from India

replication was detected in a cell culture inoculated with the fetal brain sample.[65] A study that followed another woman, who was infected during her first trimester, documented progressive changes in the fetus upon imaging, and later in the newborn, including ventriculomegaly, cerebral calcifications, and a reduction in the head circumference.[66] A 2016 case report described a pregnant woman who learned after a 29-week ultrasonography about the presence of fetal microcephaly together with fetal and placental calcifications, and after her pregnancy was terminated, fetal autopsy showed that the Zika virus was present in the fetal brain, and the complete viral genome was recovered.[67] The viral genome was also detected in the amniotic fluid of two women whose fetuses presented microcephaly, a finding that strengthened this connection and confirmed the ability of the virus to cross the placenta.[68] It was suggested that the Hofbauer cells of the placenta, which are large vacuolated placental macrophages that appear on day 18 of the pregnancy,[69-71] may play a role in the transmission of the virus to the fetal brain.[72] Collaborative, multi-disciplinary approaches were critical in causally linking Zika virus to microcephaly.[58,73-75]

It was estimated that the risk of microcephaly was about 1-13% for infections that occurred during the first trimester of the pregnancy.[76,77] In an observational analysis of >4 million births from Brazil, the relative risk to develop microcephaly with structural changes in the brain was on average 16.80 if infection happened during the first two trimesters of pregnancy.[78] It was shown that the substitution of a single serine to asparagine in prM, one of the three structural proteins of the Zika virus, increased its infectivity in human and murine neural progenitor cells, the severity of the microcephaly in mice, and mortality in newborn mice. Phylogenetic and molecular clock analyses revealed that this

mutation emerged for the first time in May 2013, just months prior to the outbreak in French Polynesia, and was maintained subsequently as the virus spread to the Americas.[79]

Zika virus infection during pregnancy led to fetal manifestations that extended beyond microcephaly[80] and included growth restriction,[81] cerebellar hypoplasia,[82] calcification of the subcortical region and basal nuclei,[83,84] ventriculomegaly,[66] decreased brain volume,[84,85] and fetal death.[60] The Zika virus emerges as the newest member of the TORCH pathogens, and the most teratogenic window for Zika is the first trimester of pregnancy.[77,86] Based on the association between Zika virus infection and the multiple serious congenital manifestations, it was recommended that TORCH be renamed TORCHZ[66] or TORZiCH.[87]

Family planning recommendation in the wake of the Zika epidemic

On November 11, 2015, the Brazilian Ministry of Health recognized the Zika virus outbreak as a national public health emergency.[88,89] In January 2016, the health ministries from several countries issued advisories for women to postpone pregnancies by 6 months to 2 years.[90] Countries where such recommendations were made include Jamaica,[51,91-93] Panama,[93] Colombia,[51,93-95] Brazil,[51,94,95] El Salvador,[51,93-96] and Ecuador.[51,94,95] Subsequently, in June 2016, the World Health Organization recommended individuals of reproductive age, residing in areas that had local Zika transmission, to be *correctly informed and oriented to consider delaying pregnancy*, but the language about delaying pregnancies was later removed in an updated guidance in September of the same year.[97-100] In this context, the epidemic reignited discussions about family planning,[101,102] contraception,[103] and safe abortion.[104-107]

Criticism of the family planning recommendations

Advisories that recommended women to avoid or postpone pregnancies in the wake of the Zika epidemic have been extensively criticized for several reasons. In all the countries that issued these advisories, close to half or sometimes over half of the pregnancies are unintended,[90,108-112] sometimes with marked within-country variations.[113] Up to 50% of the women from Latin American countries give birth for the first time in adolescence[114] and 15-19-year-old adolescents from Latin America and the Caribbean account for 16% of the fertility among women of reproductive age, the highest rate worldwide.[115] Moreover, conversations about sexuality and family planning are considered a cultural taboo in several countries that were affected by the outbreak.[114,116-119] While the use of modern contraceptives in Latin America increased in recent decades, several gaps persist, and these include high out-of-pocket costs;[120] disparities for marginalized groups,[121] indigenous women, those from rural areas, and poor populations;[122] and a slow uptake of long-acting reversible contraception methods.[123] Poor access to healthcare in general, and particularly to reproductive healthcare, creates major barriers in the ability of women to utilize family planning services.[51,101,103,124-127] Burke and Moreau describe an overlap between areas where the risk of Zika virus infection is highest and those where the access to reproductive and family planning is most restrictive.[101]

Socioeconomic inequalities, prevalent in Latin America,[122,128,129] and also pervasive in the US,[125,130,131] additionally restrict access to reproductive health services. In most countries where the recommendations were issued, the most impoverished women have the lowest access to antenatal care.[132] This becomes even more relevant, considering that the risk of unintended pregnancies is higher among impoverished communities,[133-135] and minorities, poor, and pregnant women are more susceptible to vector-borne diseases.[103,136-139] Velez and Diniz refer to the inequalities in sexual and reproductive health as a *hidden pandemic*: hidden because it is largely ignored, and pandemic because it impacts subgroups of women in a generalized manner.[96]

Hodge et al. point out that recommendations to avoid or postpone pregnancies are not purposeful if access to contraception, prenatal care, and safe abortions are not provided.[95] However, 95% of women from Latin America live in a country where access to abortion is

legally restricted,[140] and even in countries where it is legal, many women face barriers in safely accessing the services.[141-143] After a total ban on abortions was instituted in El Salvador in 1997, a constitutional amendment passed in 1999 defined life as beginning at the moment of conception.[144] In El Salvador abortion is considered, without exception, a criminal offence,[96] it is not allowed even for victims of rape or incest, or when the woman's life is in danger and, based on this law, women have been prosecuted and convicted with prison sentences of up to 40 years.[144-147] Analyses of newspaper articles and court documents found that many of the women convicted of reproduction-related "crimes" had in fact stillbirths that occurred late in pregnancy.[144] In July 2017, a 19-year-old woman who became pregnant as a result of rape and delivered a stillborn baby received a 30-year prison sentence under an "aggravated homicide" charge.[147] She was subsequently acquitted in 2019 after a new trial.[148,149] In another example, a 21-year-old woman with systemic lupus erythematosus, pre-eclampsia, and renal failure, whose fetus presented anencephaly, had to wait for over a month before learning that the Salvadorian Supreme Court denied her petition to have an abortion in 2013. The doctors eventually performed a premature induction of birth via hysterotomy at 27 weeks of gestation. The newborn died and the mother survived, and anti-abortion advocates pointed out that this example illustrates that an abortion is not necessary to save a pregnant woman's life.[150,151] In Colombia, abortion has become available for all women infected with Zika,[152,153] but it was reported that this was not widely publicized.[107]

Another shortcoming of the recommendations made in the wake of the Zika epidemic was that with the exception of the WHO advisory, which also included men,[154] advisories issued early on were generally directed at women and inherently placed on them the entire burden and responsibility for delaying pregnancies. In a study of items from public health communication campaigns that intended to raise awareness about the Zika virus in Brazil, Coutinho et al. found that the messages on avoiding the mosquito vector and preventing the disease largely excluded men, reinforcing traditional gender roles.[155] Osamor and Grady relevantly point out that most attention in the wake of the Zika outbreak was directed at mosquito control, the pregnant population, and the summer Olympics, but largely omitted the role of men in behaviors related to viral transmission.[156] Even though both men and women are involved in reproductive decisions, family planning has historically focused on women,[157] and major gaps persist in incorporating male reproductive responsibilities into initiatives that target reproduction.[158] An analysis of media coverage related to Zika in 186 articles published in two major Brazilian newspapers revealed two sub-frames of the dominant "war" against the virus. One of them supported vector eradication, and the other one emphasized the need to control microcephaly, but placed the burden of prevention on women.[159] Efforts to include men in reproductive health decisions have increased in recent years, but much improvement in the gender-inclusive family planning programs is still needed.[160]

The almost exclusive focus on women, as part of recommendations to delay pregnancies, becomes even more disconcerting considering that some of the countries where this recommendation was made overlap with the ones marked by a prevalent and pervading lack of power balance in the sexual relationship, and where sexual assault, violence between partners, and rape are common.[137,161,162] Velez and Diniz note that women affected by the Zika crisis live in *asymmetrical power relationships* and cannot freely make decisions about their bodies.[96] In many Latin American countries, as a result of the *machismo-marianismo* gender constructs, with males and females assuming more dominant and submissive gender ideals, respectively, females become more vulnerable to adverse sexual and reproductive health outcomes.[163-165] Referring to recommendations made by various countries affected by the epidemic, the UN pointed out that they fail to acknowledge that *many women and girls simply cannot exercise control over whether or when or under what circumstances they become pregnant*.[166] Wenham et al. underscore the

absence of gender in the policy response to an epidemic in which the gender dimensions were very obvious from early on and highlight that without including women's voices in the arbovirus control plans, the sustainability of this intervention could be questionable.[167]

In a survey of women from Fortaleza, Brazil, who were using exclusively the national public health care system, Stolow et al. found that participants perceived the recommendations about postponing pregnancies to be against their cultural norms and did not consider Zika as a reason to use contraception, except for women who self-identified as more affluent. This emphasized that recommendations to postpone pregnancies failed to adequately take social norms into consideration.[168]

The recommendation that women postpone pregnancies was criticized for another flaw. As Luna notes, the message addressed women as a group, but failed to take into consideration that during a woman's reproductive lifespan, a two-year delay of a pregnancy may have very different implications depending on the age group, and while it may be feasible for young women, it may hinder the ability of older women to ever have biological children.[146]

Zika and reproductive behaviors and outcomes

Various studies showed that women's reproductive behavior in response to the Zika outbreak changed in multiple and complex ways. Rangel et al. found a ~25% decline in the size of birth cohorts in Brazil ~18 months after the risk of viral infection peaked. The magnitude of this decline was larger than the one caused by other events that impacted pregnancies, such as the economic conditions during the 2008 recession from the US. Changes in reproductive behavior were larger for more educated and for older women.[169]

Using focus group data, Marteleto et al. found that during the first 18 months of the epidemic from Brazil, many women did not want to be pregnant but older women, many of them of higher socioeconomic status, and who had not yet achieved their desired family size, were an exception. Measures to minimize the risk of infection included attempting to conceive during the winter months, using mosquito repellent, living in neighborhoods with a low mosquito prevalence, and wearing long-sleeve shirts. Women of low socioeconomic status identified multiple obstacles in their ability to access contraception. Even though all participants expressed a willingness to seek abortion had they become infected, those of lower socioeconomic status reported predominantly having access to medical abortion, while those of higher socioeconomic status, to a combination of medical and surgical approaches. This highlighted that women of lower socioeconomic status were more likely to carry to term a pregnancy affected by the virus.[170]

An analysis of data from the non-profit organization Women on Web (WoW), an online platform available in five languages that operates worldwide and provides access to abortion medication in countries where this is not available safely,[171] found that after November 2015, when the Pan American Health Organization issued a Zika virus alert, the number of requests for abortion medication from several Latin American countries increased significantly, and more than doubled in Brazil and Ecuador. Almost half of the women accessing the services in Brazil were poor and younger than 25 years old.[172-174] In Brazil, abortion is allowed only in cases of rape, for pregnancies that pose a significant risk to the woman's life, and in cases of fetal anencephaly.[175-178]

The Zika virus and implications in the changing reproductive climate from the US

Anencephaly can be reliably diagnosed on ultrasound around weeks 10 to 14 of the pregnancy,[179,180] and microcephaly is usually recognized only later.[181] During the Zika epidemic, the WHO recommended a fetal anomaly scan between weeks 18 and 20 of gestation or as early as possible after 20 weeks.[182] In several countries, and in about half the US states, where the access to abortion was severely curtailed after the June 24, 2022 reversal of the *Roe v. Wade* 1973 landmark precedent,[183] and abortion is expected to become largely illegal,[184]

the pregnant population will have limited options, which include continuing a pregnancy with a severely affected fetus, or seeking reproductive care in other states or countries. As of mid-2022, several states in the US banned abortions either in almost all instances, except for when it is required to save the life of the pregnant person, or after six weeks of pregnancy, with civil or criminal penalties for violating the respective laws, and more states are expected to implement restrictions in the near future.[185-187] As a result of these and similar restrictions, at the time when anencephaly or microcephaly can be detected on ultrasound, terminating a pregnancy will already be prohibited by law in many US states.[188-191]

The two main mosquito vectors that can transmit the Zika virus in the US are *Aedes (Stegomyia) aegypti* (L.) and *Aedes (Stegomyia) albopictus* (Skuse).[192] *Ae aegypti*, which most likely originated from Africa[193] and was first reported in the continental US in 1828,[194] is most abundant in the southeastern and southwestern US states.[195,196] *Ae. albopictus* originated in Asia, it was first detected in the continental US in 1985,[197] where it was probably introduced through the used tire trade,[198] and it was in addition found in several northeastern and northwestern states and along the Pacific coast.[196,199,200] Between 1995 and 2016, *Ae. albopictus* and *Ae. aegypti* were reported in 40 and in 28 US states and the DC, respectively[192,201] and, in 2016, local Zika transmission in the US was reported in Florida and Texas.[202,203] Were the Zika virus to return to the US, several states that could see local transmission, based on the distribution of the mosquito vectors, are among the most restrictive ones with respect to the access to abortion services.[98]

It is expected that Zika virus outbreaks may occur in the future in various countries, partly as a result of the warming climate.[204] An analysis that used existing data to model the transmission dynamics of the Zika virus between humans and vectors, and accounted for seasonal temperature variations, identified temperature as a dominant driver of the basic reproduction number and of the size of the epidemic. The model predicted that even though transmission would not occur when the temperature is constant at 23°C, which is representative of the annual average conditions in Rio de Janeiro, Brazil, it may nevertheless occur in locations with a mean temperature of 20°C if 10°C seasonal variations were present, which is close to the conditions that exist in Tampa, FL. These findings underscored the importance of incorporating climate change dynamics into prospective models, and the possibility that Zika outbreaks may impact broader areas than the ones predicted by static models.[205] In another climate change modeling study, Ryan et al. anticipated that >1.3 billion new people will likely be at risk for Zika virus by 2050.[206] The potential re-emergence of the Zika virus in previously affected locations, and its emergence in new geographical areas, continue to be of worldwide concern for several reasons, including the implications for reproductive health and rights.

Parallels with rubella

A virus causing congenital abnormalities to the extent of Zika was not seen since the rubella outbreaks in the 1950s.[207,208] Rubella was recognized as early as 1814 as a benign infectious disease characterized by rash, adenopathy, and fever.[209] In 1941 Sir Norman McAlister Gregg, an Australian ophthalmologist, reported that congenital cataracts and heart malformations were more frequent in the offspring of mothers who had rubella during pregnancy,[210] and subsequently added deafness as an additional manifestation,[211] defining what became known as the classic triad of the congenital rubella syndrome (CRS).[209,212-214] Infection can be associated with other complications, such as microcephaly, bone and dental lesions, cerebral calcifications, and hypospadias.[215] The rubella virus was the first teratogenic virus described[216] and it is the most teratogenic virus currently known[217] and, just like the Zika virus and two other TORCH pathogens, cytomegalovirus and *Toxoplasma gondii*, was also associated with congenital microcephaly.[218,219] The first trimester and the early second trimester of the pregnancy are the most vulnerable in terms of developing CRS, and it develops in almost all fetuses if

infection happens before 8 weeks of gestation.[220] Between 1964 and 1965, 12.5 million cases of rubella were documented in the US, and led to >11,000 therapeutic abortions or miscarriages and the birth of >20,000 infants with CRS.[221] An estimated 100,000 or more cases of CRS still occur globally every year, making it a global public health concern.[222-224] The rubella epidemic from 1964-1965 is one of the events credited with reforming abortion law in the US.[225,226]

Zika virus at the convergence of multiple disparities

The Zika virus epidemic disproportionately impacted marginalized and impoverished women, and it further accentuated disparities.[146,155,227] Nearly 39% of the Zika virus infections in Mexico occurred in the four states with the highest unmet need for contraception, where disparities in family planning and the ones to mosquito-borne diseases were shown to overlap. A criticism of the approach adopted by the Mexican government in the wake of the Zika outbreak is that it mirrored the approach used for other infectious diseases transmitted by *Aedes* mosquitoes, such as dengue and chikungunya, and the fact that, even though ~42% of the confirmed Zika cases occurred in women, the focus was placed on mosquito control but not on counseling about contraception. In the US, the geographical regions most likely to experience local Zika transmission overlap with the ones that have the highest rates of unintended pregnancies and where accessing contraception is most challenging.[103] Nearly 10 million US women live in a *contraception desert*,[228,229] which is defined as a county where less than one clinic exists for every 10,000 women who need publicly funded contraception,[230] and many groups, including minorities, low-income individuals, and those from rural areas, face large differences in their ability to access contraception.[228,231,232]

A study that enrolled 54 women who had children with confirmed or suspected congenital Zika syndrome, living in Alagoas, a state in northeastern Brazil with one of the highest rates of adolescent pregnancies, found that the outbreak initiated and accentuated inequalities that have existed in the country even before the epidemic. For example, 76% of the women did not return to work after the birth of their child, 55% of them depended on transportation provided by their municipality to take their infant to therapy sessions, and 53% of the families did not have resources to purchase prescription medication to control seizures.[233]

A Supreme Court case in Brazil, initially filed in 2016 to request protection for women and children affected by Zika, and scheduled for April 2020, was dismissed in the wake of the COVID-19 pandemic. The fact that women lived through two major public health crises, each of them disproportionately affecting minorities and poor populations,[233,234] accentuated the disparities and vulnerabilities that they faced.[227,233,235]

Wenham et al. point out that, for multiple reasons, the social and economic impact of Zika, COVID-19, and other infectious disease outbreaks predominantly affected women. These include the fact that women are disproportionately affected by decreased access to reproductive health services, have more responsibilities as caretakers, and are more frequently the victims of domestic violence.[236]

The interface between a teratogenic mosquito-borne virus and reproductive rights

The rubella epidemic catalyzed biomedical advances and social reforms that played important roles during the Zika virus outbreak. At the interface between a vector-borne teratogenic virus and reproductive rights, Zika is uniquely positioned to guide the management of other emerging and re-emerging infectious diseases with teratogenic potential.

When the Zika virus outbreak peaked in 2016 in the Americas, local transmission was reported in 87 countries and territories from tropical and subtropical regions.[28] The possibility that the virus will spread to more countries and/or that it will reemerge in places with prior transmission is an important consideration.[237,238] The framework to address the impact of the Zika virus should extend beyond classic healthcare interventions such as vector control and improving living conditions. It needs to empower women of reproductive age and their families,[239] incorporate sexual and reproductive rights,[240] and

account for structural inequalities that permeate healthcare.[241]

The authors are concerned with recent developments in the United States and several other countries that have eroded women's reproductive options.[242-245] We strongly support the autonomy of pregnancy capable individuals to make informed decisions regarding continuation or termination of a pregnancy, and this is particularly relevant when there is significant fetal damage due to Zika infection.[246,247]

Conclusions

As of mid-2019, the Zika virus showed autochthonous mosquito-borne transmission in 87 countries and territories, and opened a new chapter in the book of viral teratogenesis. One of the unique aspects of the Zika virus is that an emerging mosquito-borne infectious disease, which can have teratogenic effects, became intimately intertwined with the access to, and conversations about reproductive health and family planning. The epidemic brought into the public attention several long-known public health crises, including barriers in access to contraception and abortion; inequalities in reproductive health education and messaging; and gender-based violence, all of them playing decisive roles in women's ability to make reproductive decisions. In context of the teratogenic effects of the Zika virus, an emerging challenge is that in several countries that were affected, abortions are already banned at the time when microcephaly can be detected on ultrasound. In the US, the June 2022 reversal of *Roe v. Wade*, and the passage of abortion bans and restrictions in several states, along with predictions that broader geographical areas may be impacted in the future as the result of climate change, open important questions on the options that will be available for women with affected pregnancies. The Zika virus epidemic remains an ongoing concern and provides a unique and important case study that brings family planning and reproductive empowerment to the forefront of medicine and public health.

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