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Role of Genetic Counselors in Prenatal Zika Care

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Abstract:

Zika virus (ZIKV) was first identified in 1945 in Uganda's Zika forest. The 2015 Brazil outbreak identified the ZIKV as a teratogen, leading to a heightened awareness in prenatal care in the United States. ZIKV is primarily transmitted via mosquitoes; however, vertical transmission from mother to fetus has also been reported. Intrauterine fetal infection is associated with Congenital Zika Syndrome, characterized by severe microcephaly with loss of brain tissue, macular atrophy, postnatal hypertonia and limited joint movements. Given their expertise in prenatal education and teratogen counseling, genetic counselors (GCs) may be uniquely suited to provide prenatal ZIKV care. Our goal was to assess the role of GCs in prenatal ZIKV care. A survey was distributed to practicing GCs through the National Society of Genetic Counselor's member listserv. The survey focused on the GCs' knowledge of ZIKV care, comfort providing ZIKV counseling, their current role in their institution, and their opinion on the role of a GC in prenatal ZIKV care. Other demographics were collected to investigate other possible correlations. The study showed that GCs with experience in providing ZIKV counseling were more comfortable providing prenatal ZIKV care. However, this comfort did not correlate with their tested knowledge.

Key words: Zika Virus, Congenital Zika Syndrome, Genetic Counselors, Microcephaly, Teratogen, Prenatal

Introduction

Virus discovery and migration

Zika virus (ZIKV) was first identified in 1945 in Uganda's Zika forest. In April 1947, Dick GW et al isolated ZIKV from feverish sentinel rhesus macaque (*Macaca mulatta*) while collecting data for a serosurvey of the area for Yellow Fever (Dick, 1952; Faizan et al., 2017). Antibodies against ZIKV were found among residents with no evidence of the disease. In 1953, MacNamara reported the first human ZIKV infection in three patients in Nigeria (1954). The virus then spread to the Yap Islands in 2007 affecting approximately 73% of the island's inhabitants. This was followed by the outbreak in French Polynesia in 2013-2014, where it was first correlated with neurological problems in newborns and Guillain-Barré syndrome in adults (Besnard, Lastere, Teissier, Cao-Lormeau, & Musso, 2014). GBS is an autoimmune disorder affecting the myelin sheath of the peripheral nervous system, impairing the muscle-brain neuronal signals ("Guillain-Barré Syndrome Fact Sheet | National Institute of Neurological Disorders and Stroke," n.d.).

In 2014, the Va'a World Sprint Championship canoe race held in Rio de Janerio marked the entry of the ZIKV to Brazil (Musso, 2015) resulting in 1.3 million suspected cases. By October 2015, the disease had spread to Columbia with 65,338 suspected ZIKV cases by April 2016. By January 12, 2017, ZIKV infections were documented in 48 different Pan American countries and territories(Yun & Lee, 2017). From 2015 to March 20, 2018, 2,286 laboratory tested pregnancies were reported to have possible ZIKV infection in the United States. Of these laboratory tested pregnancies, 114 liveborn infants were affected by a ZIKV associated birth defect(s) and 9 resulted in pregnancy loss related to ZIKV associated birth defects ("Pregnancy Outcomes | Zika and Pregnancy | CDC," n.d.).

Transmission

The primary vectors transmitting the ZIKV are the *Aedes* mosquitoes (Frankel, Pandya, Gersch, Siddiqui, & Schneider, 2017). Gilda Grard *et al* highlighted that amongst the mosquitoes that carry ZIKV, only those of the *Aedes* genus were seen to infect humans. Although, *Aedes hensilli* and *Aedes polynesiensis* were associated with the Yap and French Polynesian outbreaks (Duffy et al., 2009); *Aedes aegypti* and *Aedes albopictus*, native to Africa and Asia respectively, were involved in the 2015 – 2016 outbreaks in the Americas (Grard et al., 2014).

ZIKV can also be transmitted through sexual contact and prenatally from mother to fetus. The virus has been detected in other bodily fluids such as breast milk, blood, saliva, vaginal secretions, and respiratory droplets, but transmission of the virus through these fluids is still under investigation (Besnard et al., 2014; Darwish, Hoogstraal, Roberts, Ahmed, & Omar, 1983; Dick, 1952; Kilbourn et al., 2001). Foy et al was first to report sexual transmission of ZIKV infection in 2008, followed by another study by Musso et al in Tahiti reporting the presence of ZIKV particles in human semen. The virus survives longer in sperm with high copy number of the viral RNA longer than 62 days after the onset of symptoms (Foy et al., 2011; Musso et al., 2015). However, it is unclear how viral shedding takes place within both male and female reproductive tracts and associated fluids. ZIKV shedding may occur in phases, which may result in a false negative test due to the virus shedding at a later period of time ("Exposure, Testing & Risks | Zika and Pregnancy | CDC," n.d.). Several studies have reported the vertical transmission of the ZIKV from infected mothers to fetuses during pregnancy. Miner *et al* isolated ZIKV from placental trophoblasts suggesting trans-placental infection. Melo *et al and* Calvet *et al* identified the presence of ZIKV using reverse transcription polymerase chain reaction (RT-PCR) in the amniotic fluid of fetuses with microcephalic heads on the ultrasound.

ZIKV has been identified in brain and placental tissues of affected fetuses as well as tissue samples of infected products of conception (Calvet et al., 2016; Miner et al., 2016; Oliveira Melo et al., 2016).

Clinical Symptoms

Clinical symptoms associated with a ZIKV infection include fever, fatigue, myalgia, headache, rashes, conjunctivitis, retro-orbital pain (Faizan et al., 2017), and arthralgias (Brasil et al., 2016). There have also been reports of genitourinary symptoms (hematospermia, hematuria, perineal pain and prostatitis) and digestive tract symptoms (nausea, diarrhoea and aphthous ulcers of the mouth) (Foy et al., 2011; Ioos, Goffart, Gauthier, Cardoso, & Herida, 2014; Moloney, Kmush, Rudolph, Cummings, & Lessler, 2014; "Symptoms | Zika virus | CDC," n.d.). Clinical symptoms arise after the incubation period, usually last up to 2 weeks and 80% of infected individuals are asymptomatic or with mild symptoms (Duffy et al., 2009). The World Health Organization (WHO) reported an increase in the incidence of GBS and congenital microcephaly in 13 countries and territories with ZIKV outbreaks (2017).

Congenital Zika Syndrome

A teratogen is a foreign element that can disturb the normal development of an embryo or fetus. Its harmful effects vary based on the type of teratogen, the gestational age at the time of exposure and the dose and duration of exposure (Recommendations, 2017). ZIKV belongs to the flaviviridae family and its molecular structure is similar to dengue and chikungunya viruses of this family. It utilizes humans, monkeys and mosquitoes as hosts for replication ("ArboCat Virus: Zika (ZIKAV)," n.d.).

Sonja A. Rasmussen *et al* compared the documented clinical symptoms to both Shepard and Bradford Hill's teratogenic criteria and further supported the association of prenatal ZIKV

infections and congenital abnormalities (2016). After the outbreak in Brazil, the predicted risk for developing Congenital Zika Syndrome (CZS) was estimated as 1-13%. A study showed that 11% of the fetuses exhibited signs of congenital abnormalities when infected within the first trimester (Honein et al., 2017), which is the time frame for fetal neurological development. In multiple human cases, traces of the ZIKV were found in the placenta and amniotic fluid of fetuses with microcephaly. When human cortical neural progenitor cells were induced with the ZIKV, they were susceptible to ZIKV infection, thus supporting its neurotropic nature. It is believed that the infection affects the regulation of key facilitating genes for autophagy and apoptosis resulting in neural degradation and/or impairment (Faizan et al., 2017; Cugola1 et al., 2016; Tang et al., 2016).

Studies show fetal abnormalities can occur regardless of the gestational age at the time of ZIKV exposure or severity of maternal symptoms. Case reports from the USA show that 15% of first trimester infections resulted in birth defects (Reynolds et al., 2017). While data from US territories, show ZIKV infection resulted in 8%, 5% and 4% birth defects in the first, second and third trimester respectively (Shapiro-Mendoza et al., 2017). Reynolds *et al.* also reported that in the USA, 8% of symptomatic and 12% of asymptomatic women had babies with birth defects. However, Sharpiro *et al* reported that in US territories 5% of symptomatic and 7% of asymptomatic women had babies with birth defects.

ZIKV infection causes fetal growth restriction, microcephaly, malformations of the brain and central nervous system, polyhydramnios, placental insufficiency, miscarriages and intrauterine fetal demise later in the pregnancy (Bayer et al., 2016; Martines et al., 2016; Mlakar et al., 2016). CZS is characterized by severe microcephaly with loss of brain tissue, macular atrophy, severe postnatal hypertonia and limited joint movements such as clubfoot (“Birth

Defects | Zika virus | CDC," n.d.). Neonates with CZS might also present with low-birth weight, redundant scalp skin, arthrogryposis, swallowing difficulties, neurological (cerebral lesions, brainstem dysfunction, polymalformation syndrome) and ophthalmic (cataract, asymmetrical eyes, intraocular calcifications optic nerve hypoplasia, lens subluxation) abnormalities. The correlation between ZIKV and microcephaly, observed during the outbreaks in French Polynesia and Brazil, raises concerns for infections during the first trimester (Cauchemez et al., 2016; de Araújo et al., 2016; Jouannic, Friszer, Leparc-Goffart, Garel, & Eyrolle-Guignot, 2016). Soares de Souza *et al* studied two women infected in their third trimester and found that their fetuses presented with brain abnormalities such as subependymal cysts and lenticulostriate vasculopathy but no microcephaly (2016).

Testing Methods

The CDC has issued guidelines for ZIKV testing, Fig 1, that vary based on an individual's location, pregnancy status, symptoms, and exposure type. ZIKV exposure is defined as living in, traveling to, or having sexual relations with someone recently exposed. The CDC recommends anyone presenting Zika-like-symptoms to be tested for Zika ("Testing Guidance | Zika Virus | CDC," n.d.). It is advised for any male or female with possible ZIKV exposure to avoid pregnancy for a minimum of six months or eight weeks respectively regardless of symptoms. Pregnant women with abnormal ultrasound findings consistent with ZIKV infection should be tested as soon as possible or within 12 weeks of symptom onset or possible exposure.

Testing for ZIKV includes both a serum ZIKV Immunoglobulin (IgM) serology and a ZIKV nucleic acid test (NAT) on serum and urine. Cerebrospinal fluid, plasma, amniotic fluid, tissue, and whole blood can be used for testing. Diagnosis of ZIKV can be challenging due to cross reactivity with other flaviviruses like dengue and chikungunya. This cross reactivity may

be overcome by using a plaque reduction neutralization test (PRNT), a serologic test to utilize antibody properties to neutralize targeted viral samples from forming plaques on artificial substrate. The number of observed Zika or dengue plaques helps differentiate if the infection is due to ZIKV or another flaviviruses. However, PRNT can also give inconclusive results (Frankel et al., 2017; "Plaque Reduction Neutralization Tests (PRNT) - LabCE.com, Laboratory Continuing Education," n.d.; Rabe et al., 2016; Recommendations, 2017).

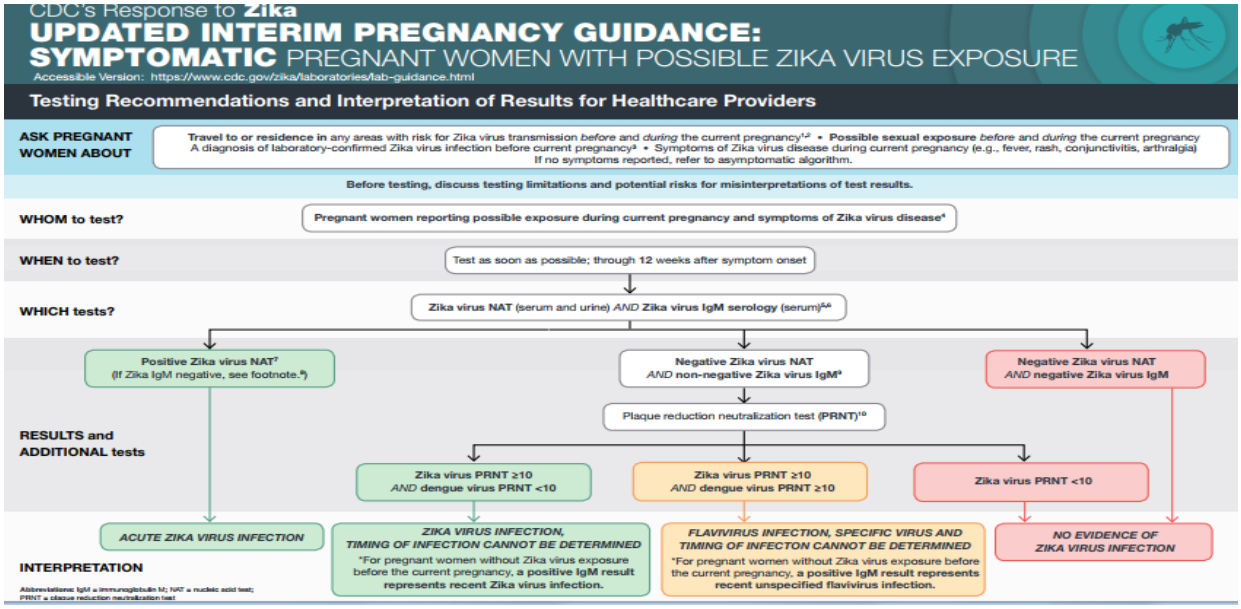

Fig1: CDC testing recommendation for symptomatic pregnant women

It is not typically recommended to test asymptomatic pregnant women who are not continuously exposed to the ZIKV. Testing should be considered on a case by case basis and followed according to guidelines for a symptomatic pregnant woman (Recommendations, 2017). For asymptomatic pregnant women with an ongoing ZIKV exposure, ZIKV NAT on serum and urine three times during the pregnancy upon initiation of prenatal care is recommended. A positive result would support an acute ZIKV infection, while a negative NAT concludes that no ZIKV RNA was detected. However, this result does not rule out a ZIKV infection during the pregnancy (Fig 1).

Teratogen counseling

A healthcare provider needs to complete a thorough medical, pregnancy, and travel history on the patient, address the patient's concerns, look up and understand appropriate resources, and counsel the patient. A study by Eleanor *et al* on the perception of physicians on teratogenic counseling discussed barriers faced in providing teratogenic counseling. It concluded time to be the main limiting factor (2009).

Services such as Teratogenic Information Services (TIS) and Organization of Teratology Information Specialist (OTIS), now called Mother to Baby, are available to public and medical professionals. Many health care providers refer patients to TIS or other specialists for teratogenic counseling (Hancock, Ungar, Einarson, Goodstadt, & Koren, 2008). However, there are some healthcare providers unaware of these services.

Genetic counselors (GCs), as described by National Society of Genetic Counselors (NSGC), are trained to educate patients, assess and cater a counseling session according to patient needs, and provide non-directive counseling. They have the flexibility to focus on these goals and spend more time with the patient. GCs bring a skill set that is equipped with critical thinking, problem solving, psychosocial and communication skills (Monaghan et al., 2016). The educational requirements of the Accrediting Board of Genetic Counselors have incorporated teratology and associated counseling techniques into the genetic counseling training curriculum (Accreditation Council for Genetic Counseling, 2013).

Methods

The survey consisted of multiple choice, likert scale, and open-ended questions to assess the current role, comfort, perceived knowledge, and tested knowledge of GCs in providing prenatal ZIKV care. Personal demographics such as age, ethnicity, earned degrees, clinic

location, specialty, years of practice, experience in providing ZIKV counseling, and personal opinions for who should provided teratogen counseling were also collected to consider possible correlations. The study was approved by the Sarah Lawrence College Institutional Research Board as exempt from full review due to the nature of the data collection and targeted participant group.

The participants were restricted to self-reported practicing GCs, determined by an initial question that prevented non-practicing GCs from proceeding further. The link to the survey was distributed via email by the NSGC to their member email listserv. The participants were informed that their responses were anonymous and that by completing the survey they were consenting to be a part of the study. The first notification was sent on a Thursday, January 25, 2018 and a reminder email was sent two weeks later. Data collection continued until February 23, 2018.

The data was downloaded from SurveyMonkey into SPSS version.24 for statistical analysis. In the analysis of continuous variables, t-tests were used in comparing 2 groups and One-way Anova was used for more than 2 groups. In addition to ANOVA, Tukey's Post Hoc analysis to determine where the mean differences were when there were more than 2 groups. Cross tabular analysis and Chi-square were used to examine the relationship between 2 categorical variables.

Results

The survey collected information on the participants' reported comfort levels on five areas of ZIKV care, their perceived knowledge on seven areas of ZIKV care, their years of experience in providing ZIKV care and being a GC, the frequency of providing ZIKV care, and the resources they use to educate themselves on ZIKV. Additionally, information on who

provides ZIKV care and who in their opinion should provide it was also collected. This data was compared with their responses to the four hypothetical case scenarios to assess how far their reported responses stand true to their tested knowledge and to find any additional correlation. Basic demographic information was also collected.

Sample Demographics

Overall, 58 practicing GCs covering 28 different states and Washington D.C. in the United States completed the survey. See Table 1 for demographic information.

GC role in ZIKV counseling

41 (71%) of the respondents reported prior experience in providing prenatal ZIKV counseling. Of these 41 respondents, 18 (30%) reported counseling 1-5 ZIKV patients in total, 11 (19%) reported counseling 1-5 per year, 10 (17%) reported counseling 1-5 per month, 3 (5%) reported counseling 1-5 per week, 1 (2%) reported counseling 1-5 per day and 15 (26%) reported not applicable.

31% (18) of the respondents indicated that GCs provide ZIKV care at their site, 12% (7) reported a collaborative approach between GCs and other healthcare providers, 40% (23) reported that other healthcare providers provide the counseling, and 17% (10) were unsure. However, when asked who they think should provide ZIKV counseling, 20% (11) indicated GCs, 3% (2) indicated GCs plus other healthcare providers, and 12% (7) were unsure; these percentages are decreased in relation to current practice. Conversely, the percentage of respondents who indicated that other healthcare providers are the ideal professionals to provide ZIKV counseling increased to 65% (38). These other providers included maternal fetal medicine specialist (MFM; 29, 76%), general OB/GYN (8, 21%), and Infectious Diseases specialists (1, 2%).

Table 1: Participants' Demographics	
Number of Participants	N=58
Sex of GCs	
Females	56
Males	2
Ethnicity	
Caucasian	53
Asian	3
Hispanic/Latino	2
Age Range	
20 - 30	33
31 - 40	13
41 - 50	9
51 - 60	1
60+	2
Years of experience	
<1	7
1-5	29
6-10	9
11-20	9
21-30	3
31-40	1
Workplace Setting	
University medical center	29
Private/Public hospital	20
Private practice	7
Laboratory	1
Telehealth	1
Specialization of participant	
Prenatal	31
Pediatric	5
Multiple specialties	14
Other	8
Clinic Setting	
Urban	39
Suburban	18
Rural	1
Reported Education	
MS in Genetic counseling or human genetics	58
Additional Masters degree	6
Additional Ph.D.	1

Table 1: The survey collected patient demographics to enable further correlations with the GC's reported knowledge, tested knowledge, reported comfort level, their role in providing ZIKV care in their clinic and who in their opinion should provide this care.

Table 2: Self reported knowledge on seven areas of ZIKV care							
	Areas with ongoing ZIKV transmission	Modes of transmission of ZIKV	Symptoms of ZIKV infection	Zika testing methods	Interpretation of results	Features of CZS	Risk for fetus to have CZS
No Knowledge	3.45% (2)	0% (0)	1.72% (1)	12.07% (7)	17.24% (10)	0% (0)	8.62% (5)
Limited Knowledge	70.69% (41)	50% (29)	51.72% (30)	65.52% (38)	67.24% (9)	55.17% (32)	68.97% (40)
Expert/ Significant knowledge	25.86% (15)	50% (29)	46.55% (27)	22.41% (13)	15.52% (9)	44.83% (26)	22.41% (13)

Table 3: Reported comfort levels based on five areas of ZIKV care					
	Chance the patient had ZIKV infection	Chance the fetus is/would be affected with CZS	Features of CZS	Options for further evaluation	Pregnancy termination ZIKV exposure
Not Comfortable	13.79% (8)	12.07% (7)	8.62% (5)	15.52% (9)	13.79% (8)
Somewhat uncomfortable / Unsure	34.48% (20)	43.10% (25)	29.31% (17)	29.31% (17)	32.76% (19)
Comfortable	51.72% (30)	44.83% (26)	62.07% (6)	55.17% (32)	53.45% (31)

Table 4: Tested knowledge using four board style case scenarios				
	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Correct	29.31% (17)	87.93% (51)	32.76% (19)	17.24% (10)
Incorrect	17.24% (10)	1.72% (1)	12.07% (7)	53.45% (31)
Not sure	53.45% (31)	10.34% (6)	55.17% (32)	29.31% (17)

Table 5: Correlation of number of years of practice and reported comfort levels					
	Chance the patient had the ZIKV infection	Chance the fetus is/would be affected with	Features of CZS	Options for Further Evaluation	Pregnancy termination due to Zika exposure

		CZS			
R(58)	.28, p< .05	.31, p< .01	.24, p< .05	.32, p< .01	.21, p<.05

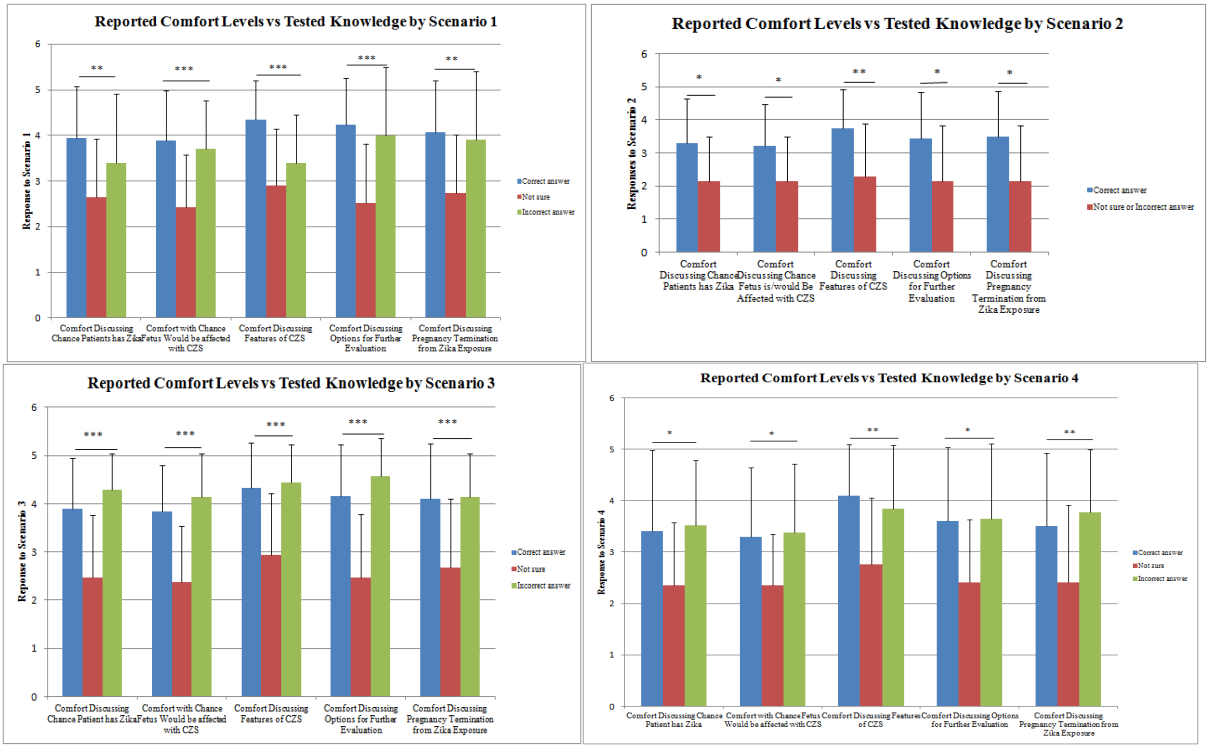

Fig 2: Comparison of reported comfort levels and tested knowledge by four different case scenarios

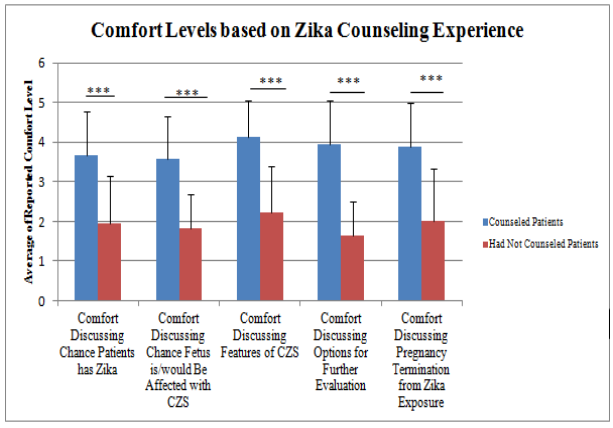

Fig 3: Comparison of comfort levels based on Zika counseling experience

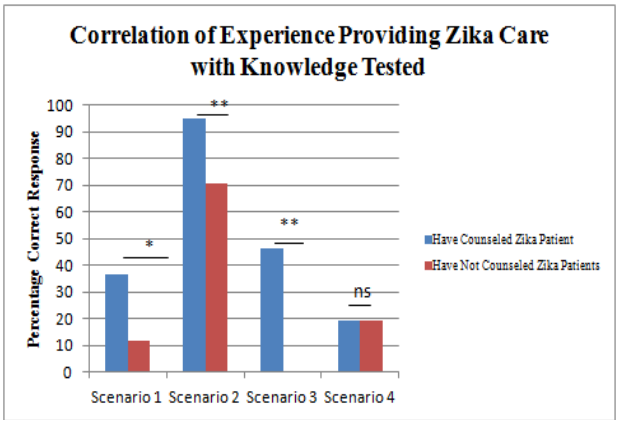

Fig 4: Correlation of experience providing Zika care and knowledge tested

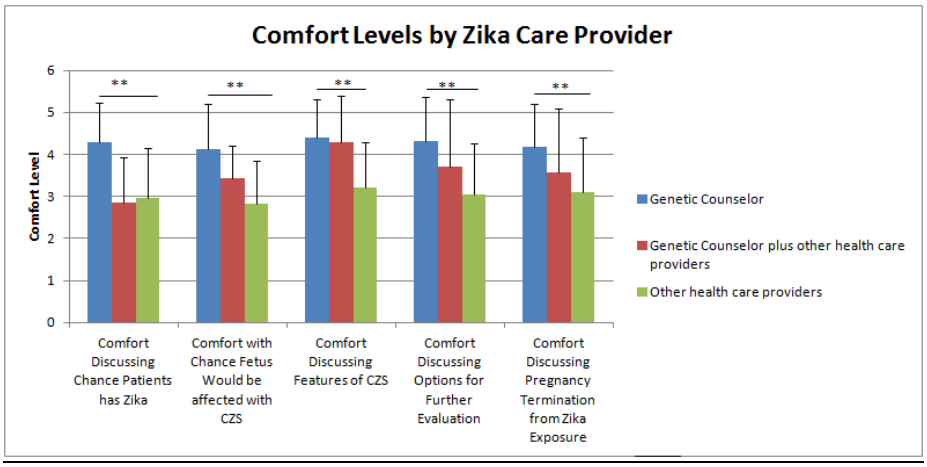

Fig 5: Comparison of comfort levels by the Zika care provider

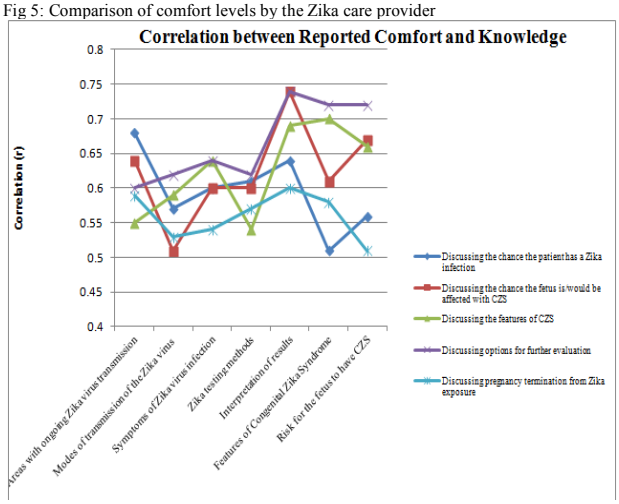

Fig 6: Correlation between reported knowledge and report comfort levels

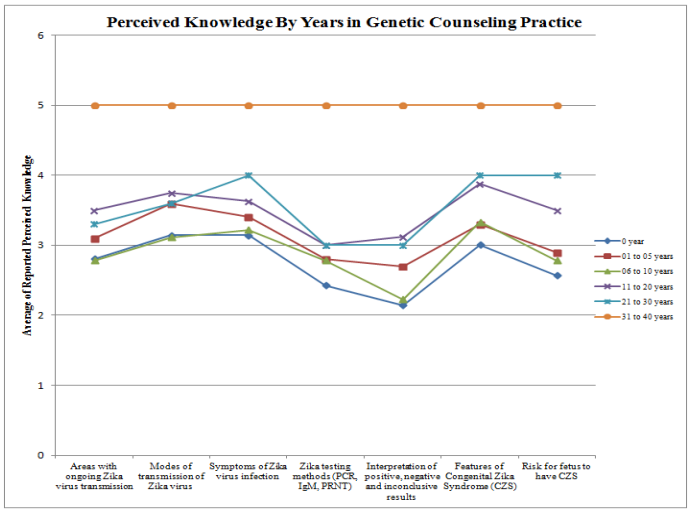

Fig 7: Association of years of experience in genetic counseling to perceived knowledge

Tested knowledge

Participants were presented with four clinical scenarios and were asked to answer boards-style questions to assess their knowledge regarding testing and counseling strategies (See table 4). Overall, only three participants chose the right answers to all the four scenarios.

Reported comfort levels and correct responses

In relation to the comfort levels for discussing ZIKV matters on the four case scenarios, there were significant differences for all the five comfort areas (Fig 2). One-way ANOVA was conducted and all F values were statistically significant (Fig 2). However, in every case, Tukey's Post Hoc analysis revealed the difference was in the comfort levels between those who were

unsure and those who had either the correct or the incorrect answer. The mean comfort levels of those with incorrect responses were as high as those with correct responses and often higher.

Reported knowledge and correct answer

In relation to the GCs' knowledge of ZIKV matters on the four case scenarios, there were significant differences for most of the seven knowledge areas by their answers. One-way ANOVA was conducted, except for case number two, where only one person who had the incorrect answer and only two categories and a t-test was used.

For case number one and three, all F values were statistically significant. Case number four, had six out of seven areas of knowledge were statistically significant and case number three, had five out of seven areas were statistically significant. However, in every case, Tukey's Post Hoc analysis revealed the difference was in the knowledge levels between those who reported unsure and those who had either the correct or the incorrect answer. The mean knowledge levels of those with incorrect responses were as high as those with correct responses and often higher. Participants unsure of their answers had lower perceived knowledge levels that were statistically significant.

Experience

The comfort level discussing all areas of ZIKV was positively correlated with how long GCs have been in practice. However, having counseled a ZIKV patient was not associated with years of experience. In addition, years in practice did not correlate with correct answers on the four cases scenarios.

GCs with ZIKV counseling experience had significantly higher comfort levels than those who had not (Fig 3). They were also more comfortable in all five areas. The mean scores for

those who had counseled a patient were usually around 4.00 or "Somewhat comfortable," while those without experience had mean scores around 2.00 or "Somewhat uncomfortable."

Three of the four cases showed significant differences where GCs with prior ZIKV counseling experience had more correct answers than those without (Fig 4). In the case of scenario 1, 36.6% (15) of those with experience had a correct answer while only 11.8% (2) without experience answered correctly (Chi-square = 3.57 (df=1), $p<.05$). For scenario 2, 95.1% (39) of those with ZIKV counseling experience had the correct answer, while only 70.6% (12) of those without experience answered correctly (Chi-square = 6.82 (df=1), $p<.01$). For scenario 3, 46.3% (19) of those with ZIKV experience had the correct answer and for those without did not have a correct answer (Chi-square = 11.72 (df=1), $p<.01$). The only difference that was not statistically significant was for scenario 4. 19.5% (8) of those with experience answered correctly, and 16.8% (2) without experience answered correctly (Chi-square = .51 (df=1), n.s.).

Perceived Knowledge based analysis

The GCs' perceived knowledge about all seven areas of Zika was positively correlated with years of practice (Fig 7). This includes knowledge about areas of ongoing ZIKV transmission ($r(58) = .29$, $p<.05$), modes of transmission of the ZIKV ($r(58) = .22$, $p<.05$), symptoms of ZIKV infection ($r(58) = .30$, $p<.05$), Zika testing methods (PCR,lgM,PRNT) ($r(58) = .23$, $p<.05$), the interpretation of results ($r(58) = .25$, $p<.05$), features of CZS ($r(58) = .40$, $p< .01$), and the risk for fetus to have CZS ($r(58) = .37$, $p< .01$).

There were strong positive correlations between the GCs' comfort in discussing certain issues about ZIKV and their ratings of their knowledge in all areas of ZIKV information (Fig 6). Being comfortable discussing the chance the patient has a ZIKV infection correlated with

knowledge of areas with ongoing ZIKV transmission (r (58) = .68, p<.001), modes of transmission of ZIKV (r (58) = .58, p<.001), symptoms of ZIKV infection (r (58) =.60, p<.001), ZIKV testing methods (r (58) = .61, p<.001), interpretation of results (r (58) = .64, p<.001), features of CZS (r (58) = .51, p< .001), and risk for the fetus to have CZS (r (58) = .56, p<.001).

Being comfortable discussing the chance the fetus is/would be affected with CZS correlated with knowledge of areas of ongoing ZIKV transmission (r (58) = .64, p<.001), modes of transmission of the ZIKV (r (58) .51, p<.001), symptoms of ZIKV infection (r (58) =.60, p<.001), ZIKV testing methods (r (58) = .60, p<.001), interpretation of results (r (58) = .74, p<.001), features of CZS (r (58) = .61, p< .001), and risk for the fetus to have CZS (r (58) = .67, p<.001).

Comfort discussing the features of CZS was correlated with knowledge of areas of ongoing ZIKV transmission (r (58) = .55, p<.001), modes of transmission of the ZIKV (r (58) .59, p<.001), symptoms of ZIKV infection (r (58) =.64, p<.001), Zika testing methods (r (58) = .54, p<.001), interpretation of positive, negative and inconclusive results (r (58) = .69, p<.001), features of CZS (r (58) = .70, p< .001), and risk for the fetus to have CZS (r (58) = .66, p<.001).

Comfort discussing options for further evaluation was correlated with knowledge of areas of ongoing ZIKV transmission (r (58) = .60, p<.001), modes of transmission of the ZIKV (r (58) .62, p<.001), symptoms of ZIKV infection (r (58) =.64, p<.001), Zika testing methods (r (58) = .62, p<.001), interpretation of positive, negative and inconclusive results (r (58) = .74, p<.001), features of CZS (r (58) = .72, p< .001), and risk for the fetus to have CZS (r (58) = .72, p<.001).

Comfort discussing pregnancy termination from ZIKV exposure was correlated with knowledge of areas of ongoing ZIKV transmission (r (58) = .59, p<.001), modes of transmission

of the ZIKV (r (58) .53, p<.001), symptoms of ZIKV infection (r (58) =.54, p<.001), Zika testing methods (r (58) = .58, p<.001), interpretation of positive, negative and inconclusive results (r (58) = .60, p<.001), features of CZS (r (58) = .58, p< .001), and risk for the fetus to have CZS (r (58) = .51, p<.001).

ZIKV Care provider

Analysis of comfort levels by who provides counseling for ZIKV indicated that when it was the GC alone versus the GC plus other healthcare professionals versus other healthcare professionals, there were significant differences in comfort levels (Fig 5). The GC alone always had significantly higher comfort levels than the GC plus other healthcare professionals or other healthcare professionals. GCs had higher comfort levels in all five areas, the chance the patient had the ZIKV infection, the chance the fetus would be affected with CZS, the features of ZIKV, the options for further evaluation, and pregnancy termination from ZIKV exposure. Four out five categories of comfort levels have a $p<0.01$ and except comfort discussing pregnancy termination from ZIKV exposure has a significance of $p<0.5$.

Resources Used

In the case scenario 1, GCs who used a state or local Department of Health (DOH) source were more likely to have a correct answer, 38.7% (12) for those who used this source versus 18.5% (5) for those who did not. Most of those who did not use this source, 70.4% (19) were unsure of the answer, while only 38.7% (12) of those who used it were unsure of the correct response. (Chi-square = 5.82, (df=2) p<.05). The use of PubMed or other literature searches also had significant differences in this case (Chi-square = 5.42, (df=1), p<.05). 52.2% (12) of those who used PubMed or another literature search and only 20.0% (5) of those who did not use it

chose the correct answer. 80.0% (20) of those not using it and 47.8% (11) of those who used it were unsure of the answer.

In the case scenario 2, 40.2% (28) of those using PubMed or another literature search had the correct answer, while 76.7% (23) of those who did not use these sources had the correct answer (Fisher's exact $p < .05$). All seven respondents who were unsure or had an incorrect answer did not use these sources.

In case scenario 3, respondents who used PubMed or another literature search were more likely, 52.0% (13), to have the correct answer than the 23.1% (6) who did not use these sources. 76.9% (20) of those who did not use these sources were unsure of the answer, while only 48.0% (12) of those who did not use PubMed or another literature search were unsure of the answer (Chi-square = 4.50 (df=1) $p<.05$).

Discussion

The goal of the study was to assess the current and potential role of GCs in providing ZIKV care. This was assessed by analyzing their comfort levels, perceived knowledge, tested knowledge via 4 case scenarios, their years of experience in the field of genetic counseling, and their experience in providing ZIKV care. Additionally, the participants were asked who provides ZIKV care at their site and whom they think should ideally provide this care. Comparisons and correlations were made to verify the reported responses.

The participants were asked to rate their comfort levels with respect to 5 areas of ZIKV counseling and the weighted average was 3.29 on a scale of 5. Comparing their individual responses to the comfort level and the 4 case scenarios revealed even though GCs may be comfortable with ZIKV counseling, their knowledge of what to do can be faulty. Their reported comfort does not always reflect proper understanding of the subject. With half of the participants

having 1-5 years of experience, the data supports a higher comfort level for GCs with more ZIKV genetic counseling experience. This shows that participants with more experience feel more confident in their abilities to counsel patients on relatively new topics, like ZIKV. However, years in practice was not correlated correct responses to the four cases. A GC's ability to identify appropriate resources and the prior availability of patient medical information, including ultrasound findings, for case preparation could be attributed to this trend. For instance, 25 to 30% of the participants, who reported CDC, DOH and/or PubMed and other literature as their primary resources chose the correct response to at least two case scenarios. It also shows that GCs are able to properly research topics of interest they may not have previous experience in counseling.

Although Accreditation Council for Genetic Counseling requires GCs to be trained for teratogen counseling, the survey indicated a drop from 52% (30) of GCs providing teratogen counseling to 31% (18) of GCs providing ZIKV care. This could infer GCs though trained to provide counseling for typical teratogens are not as comfortable with new teratogens. Additionally, 65% (38) of the participants thought ZIKV counseling should be provided by other healthcare providers. This could be because ZIKV is a relatively new teratogen that is not genetic. This calls for more guidance/recommendations/coordination among specialties on national and institutional levels supporting the need for multidisciplinary care for emerging issues.

The weighted average of participants' perceived knowledge about all seven areas of ZIKV was 3.12. It positively correlated with how long they have been in practice. When analyzing the perceived knowledge compared to tested knowledge, the mean knowledge levels of those with incorrect responses were as high as those with correct responses, and often even

higher. This indicates that counselors can rate themselves as knowledgeable in discussing ZIKV issue with their patients but their knowledge of what to do can be incorrect. This supports a stronger need for new teratogen education for health care providers.

Examining responses to the four case scenarios by whether or not GCs had counseled a ZIKV patient, three of the four cases showed significant differences. Those who had counseled patients had more correct answers, and significantly higher comfort levels than counselors who had no prior ZIKV counseling experience. This supports a stronger association for case specific experience to correlate to higher comfort and knowledge levels for GCs regardless of their years of experience, which is also found to have no association through the survey. This makes sense since ZIKV is a relatively new development and individuals with prior ZIKV experience would have done research to prepare for the case.

Significant differences were found when comparing accurate knowledge of GCs who have previously counseled patients regarding the ZIKV to GCs without previous experience. The responses to the four case scenarios were not related to who provided counseling on ZIKV at the center. However, there was a relationship between who provided the counseling at the center and who the respondents thought should provide the counseling (Fishers exact $p<.01$). All of the institutions (10) where the MFM provided counseling on ZIKV risks thought that the MFM should provide the counseling. When GCs provided the counseling, 53.9% (7) thought GCs should do the counseling, while 46.2% (6) thought the MFM should do the counseling. Analysis of comfort levels by who provides counseling for ZIKV indicated that when it was the GC alone versus the GC plus other healthcare professionals versus other healthcare professionals, there were significant differences in comfort levels (Fig 7). The GC alone always had significantly

higher comfort levels than the GC plus other healthcare professionals or other healthcare professionals.

Study Limitations

It is a self-reported study that targeted all practicing GCs irrespective of their prior experience in providing ZIKV counseling. This could have resulted in biased reporting of their knowledge and comfort levels leading to skewed data analysis. Credential verification was not required to participate in the survey. Although the case scenarios were used to access their knowledge, the scenarios were limited both in number and breadth of knowledge. The knowledge assessment was computed from four hypothetical ZIKV case scenarios, three of which focused on testing protocols for ZIKV related occurrences. When assessing comfort, perceived knowledge and tested knowledge, there was no consistency in the topics assessed. This would have enabled better and consistent correlation analysis.

This study is unique in itself without similar literature. However, it limits the results found due to the inability to compare the findings.

The sample size was small with 58 surveys completed, even though 85 individuals opened the survey yielding a 68% completion rate. The introductory email stated an estimated length of time to complete the survey as 15-20 minutes; however, Surveymonkey reported 4 mins as the average time individuals spent. This could have swayed individuals with a busy work life schedule from participating in the survey. Motivation to participate in the survey may have deterred further by lack of incentives such as gift cards.

ZIKV infections and its teratogenic nature is a relatively new topic and the frequency in the United States is not uniform throughout the country. This could have contributed to incorrect responses to the case scenarios, and the discrepancies in higher numbers of GCs being involved

in teratogen counseling than ZIKV counseling. Additionally, in the case of scenario 4, a couple of respondents requested clarification. This could have contributed to less respondents choosing the right answer.

Practice Implications

This study highlights the importance of education and communication regarding emerging counseling issues. Increasing awareness of the available resources and providing training with the identification of every new teratogen may boost confidence of GCs and expand their knowledge of approved protocols. Utilizing services such as OTIS when GCs or other health care providers are unsure or uncomfortable providing ZIKV care can ensure better service.

Research Recommendations

This study requires consistent metrics to assess the comfort and knowledge of GCs. To ensure better assessment of knowledge it is important to present case scenarios covering a broad spectrum of GCs role in ZIKV care. Pre and post educational surveys may better assess understanding and management of hypothetical case scenarios. Expanding the sample size may obtain stronger significance and better reflect the targeted population.

Conclusion

This study revealed GCs with experience are comfortable providing ZIKV counseling. This comfort, however, does not necessarily reflect their tested knowledge. This may be overcome by further training and increasing the availability and awareness of reliable resources.

Conflict Of Interest

Monisha Sebastin and Erica Poole declare that they have no conflicts of interest.

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