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Reproductive Health Sequelae of Female Ebola Virus Disease Survivors in Sierra Leone

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Abstract

We study the prevalence of reproductive health sequelae among female Ebola virus disease (EVD) survivors in Sierra Leone. Nearly five years after deadly 2014 EVD outbreak, many women and men infected with virus continue to live with post-EVD complications, that are both physical and psychological in nature. This study examines the prevalence of post-EVD reproductive sequelae among a small cohort of female survivors in Freetown. We utilized a cross-sectional study of 25 EVD female survivors to determine the prevalence of reproductive complications and types. Quantitative data was collected using semi structured questionnaire and demographic data on EVD survivors was collected. Three out twenty-five female survivors (12 % prevalence rate) reported pregnancies ending in still births, whereas one out of 25 (4 % prevalence rate) reported having spontaneous abortion. Prior to EVD infection, 22 (92%) out of 25 female survivors reported having regular menstruation. Post-EVD infection, 60% (15) of the survivors reported irregular menstruation with unknown reason, 4% (one person) reported irregular menstruation with known reason, and 36% (9) experienced regular menstruation. Post-EVD at the time of data collection, 15 (60%) of them reported regular menstruation, nine (36 %) reported irregular menstruation for known reasons, one (4%) reported irregular menstruation based on an unknown reason. Two (8%) of control and EVD survivor participants reported having amenorrhea. In addition, oligomenorrhea, dysmenorrhea, and menorrhagia were reported by female EVD survivors at 16% (4 out of 25), 44 % (11 out of 25), and 32 % (8 out of 25), respectively. Despite the small sample size of the data to warrant definite conclusions, the trends in the data show higher prevalence of reproductive sequelae among female EVD survivors compared to a corresponding control sample from the general population.

Keywords: Ebola, Reproductive Health Sequelae, Ebola Survivors, Prevalence

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INTRODUCTION

The 2013-2014 Ebola Virus Disease (EVD) outbreak in West Africa was the largest in magnitude and devastation in Africa. The magnitude of infections greater than 28,000 registered for the outbreak in Guinea, Liberia, and Sierra Leone was higher than all previous outbreaks combined. The total number of cases and deaths reported for Liberia was 10,600 cases and 4,800 deaths (CDC/VHF Ebola history), Guinea 3,814 confirmed cases with 2,544 deaths, and Sierra Leone having the highest number of confirmed cases, recorded at 14,124 with 3,956 deaths.

'Post-Ebola Syndrome' is a diagnosis reported on a handful of Ebola survivors. It consists of both physical and psychological sequelae that have hindered the life process for these survivors. In August 2014, a national household survey conducted in Sierra Leone showed that 96% of respondents held at least one discriminatory attitude towards Ebola survivors. Five years after the end of the Ebola outbreak, EVD survivors continue to suffer the debilitating effects of post-infection complications that include abdominal pain, ocular complications, depression, insomnia, and several mental health issues (WHO- Interim guidance). For instance, Ebola virus persistence has been reported in semen, breast milk, and vaginal fluid of some female survivors (Fischer WA et al. 2017).

It is evident that post sequelae complications are numerous and pose serious health challenges for EVD survivors, especially women. Over 5,000 of the total infected case outbreaks in West Africa occurred among women of reproductive age. The EVD outbreak of 1978 in Yambuku, DR Congo recorded 46% of 82 infected pregnant women, of whom 73 (89%) died, which is

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like the overall epidemic mortality rate of 88% in 1978 (Lisa, M.D et al.).

The study conducted in 2020 aimed to understand the nature, types and prevalence of reproductive health sequelae among a small sample of EVD female survivors in Sierra Leone. A study conducted among EVD female survivors in Liberia reported a range of reproductive health complications ranging from stillbirths, spontaneous abortions, and several menstrual irregularities like Amenorrhea, oligomenorrhea, Dysmenorrhea, or menorrhagia (Godwin et al, 2019). Most research published focused on pregnant females infected with the virus during the outbreak. Research specifically documenting the incidence of Reproductive Health Sequelae among female survivors in Sierra Leone is underexplored. Therefore, we sought to investigate as objectives the, 1) the prevalence of failed pregnancies (miscarriage or stillbirth) and menstrual irregularities among EVD female survivors in Sierra Leone, 2) compare the prevalence of failed pregnancy (miscarriage or stillbirth) and menstrual irregularities among EVD female survivors and non- EVD female survivors, 3) compare stillbirth prevalence between the general population in the western area (urban and rural) with prevalence among female EVD survivors, and 4) accurately describe menstrual irregularity outcomes of the Female EVD survivors after EVD.

The results of the research will serve as a preliminary study that will help create awareness about the female survivors' unique post complications. Good reproductive health is a state of complete physical, mental, and social well-being in all matters relating to the reproductive system, as defined by the United Nations Fund for Population Activity (UNFPA). A fundamental right these survivors do not enjoy. The research goal is

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to create a detailed profile of these women's various complications to gain the government and different partners' attention to provide access to health

facilities that can enhance their reproductive health's proper function. It will also help citizens understand these women's plight and help female non-survivors relate to their reproductive health experiences and possibly help in better communication and non-stigmatization of this group of people. Most people, especially government officials, are not aware of the complications faced by these survivors post-Ebola. Sufficient research to document these women's complications is not available. This research will shed light on the disease's reproductive health effect on female survivors' post-Ebola.

METHODOLOGY

Study Setting

This study was conducted at the Sierra Leone Association of Ebola Survivors (SLAES) headquarter situated at 40 jui. After the outbreak ended, the SLAES was established to successfully integrate survivors living in different regions in the country.

Study Design

Twenty-Five (25) female EVD survivors aged 18-45 participated in this research, alongside 25 females who did not contract the disease used as a controlled study. This research is a retrospective case-control study, allowing a formulation of hypotheses about possible associations between the groups' outcomes. The controlled study was carried out using the same questionnaire as the treatment.

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Participant recruitment and eligibility

Recruitment for this was done in a study at the SLAES office; it was random. Participants only had to be 18-45 years with an Ebola treatment Unit discharge certificate issued by the Ministry of Health.

A meeting was held at the SLAES national headquarter conference room before the study took off to inform the administration about the research and educate and encourage them to take part.

Data Collection

Data was collected via the use of a detailed questionnaire administered during one on one interview at the SLAES office.

Data Analysis

The chi-squared test was used to analyze the data collected for this study, inputted in Microsoft Excel using the statistical package for social science (SPSS).

Chi-Square Test of Independence

The Chi-Square test of independence is used to determine if there is a significant relationship between two nominal (categorical) variables. Each category's frequency for one nominal variable is compared across the categories of the second nominal variable. The data can be displayed in a contingency table where each row represents a category for one variable, and each column represents a category for the other variable.

Hypothesis:

Null hypothesis: Assumes that there is no association between the two variables.

Alternative hypothesis: Assumes that there is an association between the two variables.

Hypothesis testing: Hypothesis testing for the chi-square test of independence as it is for

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other tests like ANOVA, where a test statistic is computed and compared to a critical value. The chi-square statistic's critical value is determined by the significance level (typically .05) and freedom degrees. The chi-square degrees of freedom are calculated using the following formula: df = (r-1) (c-1) where r is the number of rows, and c is the number of columns. If the observed chi-square test statistic is greater than the critical value, the null hypothesis can be rejected

Definitions/Measures

Assessment of Pregnancy outcome

All data collected were self-reported by the study participants. Each woman was asked if they were pregnant at the time of the outbreak; if the participant responded 'Yes,' she was then asked what the outcome of the pregnancy, based on the answer given, it will be recorded as either live birth, stillbirth, spontaneous Abortion, elective induced abortion or unknown was. Suppose participants report an affirmed live birth further question of 'how long did the baby live for?', in this category. In that case, different periods are listed as a speculated time for the life length of the baby, including a 'still living' checkbox.

The WHO defines stillbirth as fetal death occurring at, or after 28 weeks of gestation, including neonates born with no sign of life (Nayonga, M. et al., 2015). Precisely for this study, the term 'stillbirth' was self- described by each woman rather than by estimated gestational age. Miscarriage, according to WHO, is fetal loss occurring before 28 weeks of gestation. For this study and analysis, elective induced and spontaneous abortion are placed under this category

Assessment of Menstrual irregularities

The course of this assessment was divided into two, menstrual status before EVD and

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after EVD. For each question, a list of possible responses was translated to the participant in the local language. Participants were asked to describe in their own words their menstrual status before EVD based on the description, the response was categorized as either 'Regular' or 'Irregular.' Further questions of a story of menstrual status after EVD was asked, three list of possible response were listed; 'Regular' which for this study means, participant reports having menstruation both before and after Ebola infection; 'Irregular, for a known reason,' means participant was experiencing regular menstruation before Ebola but had irregular or no menstruation after Ebola due to use of hormonal contraceptives, menopause, breastfeeding, etc.; 'Irregular menstruation, for unknown reasons,' indicates that the participant reported having regular menstruation before Ebola, along with irregular menstruation, menstruation more or less frequently than once a month, or no menstruation post-EVD and did not identify a reason for this change (i.e., pregnancy, hormonal contraceptives, experiencing menopause, etc.)

Based on a qualitative description of their menstrual change, participants who reported irregular menstruation for unknown reasons were further categorized. This included: Amenorrhea (missed menstrual period three times in a row), Oligomenorrhea (irregular and inconsistent blood flow, 'light flow,'' reduced duration of flow,' and 'scanty flow'). Dysmenorrhea was described as having abdominal pain or cramps with menstruation. Menorrhagia is defined as having 'heavy flow' and 'long duration of flow.' For this study, 'TREATMENT' is referred to female Ebola survivor participants and 'CONTROL' refers to the female non-Ebola participants.

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Ethics Statement

Participants were provided with a written consent form during the interview, which was explained to each individually in Krio (local language) for better understanding before signing their names. A request to take photos for identification was made. Permission to take photos was a requested questionnaire used during this research and was approved by the Institutional Review Board (IRB) and an MOU with SLAES BOARD.

RESULTS

Fifty (50) women participated in this study, comprising 25 Ebola virus disease survivors and 25 non-survivors. A retrospective study was purposely chosen to accurately compare the prevalence of the two groups' reproductive health outcomes. The mean age at the time of EVD infection of survivors was 34.56 years and 36 years after EVD. This data was collected approximately four years after the outbreak. Different data were collected concerning study participants' characteristics, e.g., educational level, relationship status, habitation status. Relative to the control study, only the reproductive health descriptions (pregnancy outcomes and menstrual irregularities) will be compared with the case, as it is the study's focus. A summary of characteristics is presented in Table 4.1

Pregnancy Outcomes

Data recorded for this section was collected for both during EVD and after EVD; 12% (3/25) of pregnant women during the outbreak; each experienced elective induced abortion, stillbirth, and live birth, respectively. The participant who gave live birth reported a baby who lived for only 8 weeks. Elective induced abortion was offered as the only option to another participant as the virus had infected her fetus fatally. Of the 25 survivors, 40% (10) got pregnant after the

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outbreak; 10% (1) experienced spontaneous abortion, 30% (3) reported stillbirth, and 60% (6) had a live birth. All six live births are still living. Meanwhile, for the control study participants, 32% (8) disclose being pregnant at the time of EVD, 5 (62.5%) reported live birth, 1 (12.5%) experienced spontaneous abortion, and 2 (25%) had a stillbirth. These findings are presented in Table 4.2.

Menstrual Irregularities

The data for this part of the study was collected before EVD and after the outbreak. Of the 25 survivors, 22 (92%) reported having regular menstruation. After the Ebola virus outbreak, 60% (15) reported irregular menstruation but with unknown reason, 4% (1) irregular, for a known reason, and 36% (9) experienced regular menstruation. Control study participants reported 92% (23) of regular menstruation before EVD, 10% (1) irregular for unknown reasons, 16% (4) irregular for a known reason, and finally, 60% (15) reported regular menstruation after EVD. Findings are presented in a chart in Figure 2.1

DISCUSSION

Five years after the West African Ebola outbreak, many survivors experienced clinical sequelae related to Ebola. Arthritis, abdominal pain, uveitis, skin disorders, and impaired vision are a list of complications reported by survivors. These sequelae are various fatal pregnancy outcomes and menstrual irregularities that specifically female survivors of reproductive age experience. This study aims to mainly document the prevalence of pregnancy outcomes and menstrual irregularities among female EVD survivors. The study design is retrospective and explicitly uses a controlled group to compare the study outcomes, making this research unique.

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In this study, two-fifth of the study population of survivors reported being pregnant after the outbreak, of which four (4) reported conception resulted in miscarriage or stillbirth; furthermore, more than half experienced menstrual irregularities; in comparison with findings from non-Ebola survivors, half of the participants reported being pregnant after the outbreak only three (3) experienced failed pregnancies (miscarriage or stillbirth). Additionally, two-fifth (10/25) reported menstrual irregularities, of which 90% (9/10) experienced irregular menstruation with known reasons. These findings are consistent with earlier reports by Godwin et al, 2019 of reproductive health sequelae among female EVD survivors in Liberia. Fallah and other fellow researchers conducted a study in 2016, findings from this study found an increase in post-EVD failed pregnancy (22.1% miscarriage, 5.8% stillbirths) (Flamigni and Giacomucci,1996). Additionally, this research is consistent with the study done by Christine L Godwin and colleagues in 2018, which results documented 8.7% (2/23) reported stillbirth, and 47,8% (11/23) reported spontaneous abortion (Godwin et al., 2018). The frequency of these outcomes reported in this research should be considered higher as the sample size is small compared to previous studies.

However, this study includes a control group, of which every outcome of the two main factors (Pregnancy and Menstrual irregularities) is studied. Meanwhile, 48% (12/25) reported having conceived post-EVD; only two (2) reported failed pregnancy with a distribution of one spontaneous abortion and one stillbirth (Table 4.2). Compared to the treatment group, the incidence of failed pregnancy outcomes is higher, which backs up the conclusion of previous research stating that adverse

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pregnancy outcomes are frequent among EVD survivors. Further research containing a larger sample size should be done with a control group to accurately record the incidence of these outcomes in Female EVD survivors in Sierra Leone.

The findings for menstrual irregularities for this study reports 92% (23) of female survivors experiencing regular menstruation, 64% (16/25) now reports irregular menstruation with fifteen (15) experiencing menstrual irregularity due to unknown reason. No national data was found on any form of menstrual irregularities in Sierra Leone. This study comparison will be made directly using the control group. All the female non-survivors reported having regular menstruation before EVD; only nine (9) experienced irregular menstruation due to known reasons, of which more than half of them admitted to being using contraceptives or undergoing family planning. This estimates that menstrual irregularity following acute EVD infection compared to non-infected individuals is higher and very common. The research conducted in the Gambia among women in the rural area reported 16% of participants reported irregular cycles; hence, this research presents estimates suggesting an excess of menstrual irregularity in acute EVD proves to be accurate, compared to the general population of other West African countries.

Regarding the description of the menstrual cycle after EVD, in terms of the level of flow and extensive abdominal pain, Dysmenorrhea was the most frequent (44%) reported type of menstrual irregularity, followed by menorrhagia (32%) among the survivors. Dysmenorrhea is classified into two types; primary and secondary; the former is more common and experienced as menstrual cramps, not due to a disease. On the other hand, secondary dysmenorrhea is

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pain caused by a disorder in a woman's reproductive organs (Endometriosis, uterine fibroids, adenomyosis, or and infection). Based on the description of dysmenorrhea by participants, which was an unimaginable pain at the abdomen during menstruation, secondary dysmenorrhea could be concluded. However, a lack of complete diagnosis from an Obstetrician gynecologist cannot back up this conclusion; hence, further research should be done to understand these outcomes completely. More than half of the participants reported discharging heavy thick black blood with a pungent odor in addition to experiencing menorrhagia. Previously mentioned research by Christine L Godwin reported 14.8% (4 women) of the 27 women who reported Dysmenorrhea and/ or menorrhagia after EVD due to unknown reasons (Godwin et al. 2018), evidently backs up the result from this study.

This study aims to estimate the incidence of failed pregnancy and menstrual irregularity in Female survivors in Sierra Leone using national data and a control group to compare the frequency. Meanwhile, a control group comparing outcomes between treatments is a new approach towards this area, which can be exploratory through further research. This study can only serve as preliminary research in conducting large-scale studies due to the small sample size.

Results related to menstrual irregularities of this study can be susceptible to multiple interpretations, as it can be triggered by many underlying factors, e.g., Stress and loss of weight (Harlow and Ephross. 1995)

Limitations

There were several limitations to this study. The fact that the research was during the coronavirus pandemic took away the chance of socially interacting with the survivors,

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which could have helped make sure participants were comfortable enough to share their experiences yielding more first-hand information. All protocols concerning social distancing and safety prevention were observed. Most importantly, the lack of funds to incentify and recruit more participants contributed to the small sample size (25) used in the study. Data was self-reported by the study participants, so the accuracy depended on the survivor's recall. Memory issues are a well-recorded manifestation of post-EVD; hence the potential for error due to memory limitation might be of specific concern in this study (Christie, A. et al., 2015. Lee, Hand H Nishiura, 2017).

CONCLUSION

This study has documented a specific frequency of reproductive health sequelae experienced by survivors relating to several adverse outcomes (failed Pregnancy, menstrual irregularities).

More research is needed to understand how the EVD leads to survivors' reproductive health sequelae in Sierra Leone, most importantly if it is short term or long term. A serological test can be done on more advanced research. Research questions concerning other reproductive health issues (fertility, organ disorder, fibroid) can be asked to understand these survivors' menstrual irregularities completely. 'A woman's reproductive system is a delicate and complex system in the body. It is essential to take steps to protect it from infections and injury and prevent problems—including some long-term health problems (CDC., Women's Reproductive Health, 2020).

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Table 4.1: Demographic data of participants

Summary Table				
	CONTROL		TREATMENT	
Variable Labels	**At the time of EVD**	**After EVD**	**At the time of EVD**	**After EVD**
Mean Age	28.7	33	31.9	36
Mean admission per day	N/A	N/A	17.6	
Educational level				
	CONTROL Count (%)		**TREATMENT Count (%)**	
None	8 (32)		12 (48)	
Primary	5 (20)		2 (8)	
Secondary	7 (28)		10 (40)	
Tertiary	5 (20)		1 (4)	
Relationship Status				
	CONTROL Count (%)		**TREATMENT Count (%)**	
Not in a relationship	12 (48)		9 (36)	
In a relationship, not married	3 (12)		9 (36)	
In a relationship, married	10 (40)		7 (28)	
Habitation Status				
	CONTROL Count (%)		**TREATMENT Count (%)**	
Living alone	1 (4)		3 (12)	
Living with partner/family	24 (96)		22 (88)	
Husband a survivor				

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	CONTROL Count (%)	TREATMENT Count (%)
Yes	0	4 (57)
No	10 (100)	3 (43)

Table 4. 2: Assessment of Pregnancy

Pregnancy				
	CONTROL Count (%)		TREATMENT Count (%)	
	At the time of EVD	After EVD	Att time of EVD	After EVD
Yes	8 (32)	12 (48)	3 (12)	10 (40)
No	17 (68)	13 (52)	22 (88)	15 (60)
Pregnancy Outcome				
	CONTROL Count (%)		TREATMENT Count (%)	
	At the time of EVD	After EVD	At the time of EVD	After EVD
Live birth	5 (62.5)	9 (75)	1 (33.3)	6 (60)
Still Birth	2 (25)	1 (8.3)	0	3 (30)
Spontaneous Abortion	1 (12.5)	1 (8.3)	1 (33.3)	1 (10)
Elective Induce Abortion	0	0	1 (33.3)	0
Unknown	0	1 (8.3)	0	0
If live birth, how long does the baby live for?				
	CONTROL Count (%)		TREATMENT Count (%)	
	At time of EVD	After EVD	At the time of EVD	After EVD
2-4 weeks	0	0	0	0
2-5 months	0	0	1 (100)	0

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6-10 months	0	0	0	0
1 year	0	0	0	0
Less than all the above	0	0	0	0
Still Living	5 (100)	9 (100)	0	6 (100)

Table 4.3: Assessment of Menstrual Irregularities

Menstrual status				
	CONTROL Count (%)		**TREATMENT Count (%)**	
	Before EVD	**After EVD**	**Before EVD**	**After EVD**
Regular	25 (100)	15 (60)	23 (92)	9 (36)
Irregular	0	Not applicable	2 (8)	Not applicable
Irregular known reasons	Not applicable	9 (36)	Not applicable	1 (4)
Irregular unknown reasons	Not applicable	1 (4)	Not applicable	15 (60)
Description of menstrual cycle after EVD (Level of flow)				
	CONTROL Count (%)		**TREATMENT Count (%)**	
Amenorrhea	2 (100)		2 (8)	
Oligomenorrhea	0		4 (16)	
Dysmenorrhea	0		11 (44)	
Menorrhagia	0		8 (32)	

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Table 6.1: National Data on Stillbirths in Sierra Leone

Period	2018				2019				Jan - July 2020			
Organisation unit / Data	Antenatal client 4th visit	Delivery conducted	Still birth - fresh	Still birth - macerated	Antenatal client 4th visit	Delivery conducted	Stillbirth – fresh	Stillbirth - macerated	Antenatal client 4th visit	Delivery conducted	Stillbirth	Stillbirth
Bo District	21,304	16,652	58	78	20,519	17,615	106	143	11,127	9,955	103	106
Bombali District	8,274	9,938	200	98	8,036	9,125	125	160	4,741	5,136	84	82
Bonthe District	5,554	6,373	24	61	5,556	5,774	19	48	3,082	3,248	24	59
Falaba District	4,842	5,232	32	121	4,312	5,121	338	44	2,552	2,709	3	
Kailahun District	13,141	14,144	65	90	13,094	14,697	51	243	8,202	9,531	28	33
Kambia Distri	9,415	10,860	232	168	9,710	10,701	219	135	5,970	5,711	146	89

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ct												
Karene District	6,743	7,934	34	40	7,311	7,805	6	40	3,868	4,176	10	1
Kenema District	18,124	19,026	87	381	17,632	19,366	185	2,705	9,863	10,140	105	244
Koinadugu District	4,656	4,560	27	79	4,276	4,207	514	93	2,597	2,686	46	49
Kono District	7,982	8,619	75	163	9,327	11,392	78	146	5,300	6,363	124	56
Moyamba District	13,416	13,793	50	183	13,733	13,966	46	92	7,411	7,357	17	33
Port Loko District	16,768	16,241	102	539	17,975	16,477	102	339	10,344	9,236	49	106
Pujehun District	10,359	11,866	101	132	11,430	12,344	75	82	7,826	7,951	26	33
Tonkolili District	13,429	13,981	126	382	14,894	13,125	125	534	7,842	7,095	60	70
Western Area	14,976	17,333	16	38	14,007	14,366	35	59	8,139	8,910	21	46

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Rural District												
Western Area Urban District	14,821	18,068	137	203	15,942	17,980	395	394	8,542	9,715	11	22
Total	183,804	194,620	1,366	2,756	187,754	194,061	2,419	5,257	107,406	109,919	857	1,029

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Chi-squared Calculations

Test Statistics

	CONTROL (PREGNANCY AFTER EVD)
Chi-Square	16.000[a]
df	3
Asymp. Sig.	.001
Exact Sig.	.002
Point Probability	.000

Test Statistics

	CONTROL (PREGNANCY AT TIME

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	OF EVD)
Chi-Square	3.250[a]
df	2
Asymp. Sig.	.197
Exact Sig.	.296
Point Probability	.154

a. 3 cells (100.0%) have expected frequencies less than 5. The minimum expected cell frequency is 2.7.

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Test Statistics

	PREGNANCY AT TIME OF EVD
Chi-Square	.000[a]
df	2
Asymp. Sig.	1.000
Exact Sig.	1.000
Point Probability	.222

a. 3 cells (100.0%) have expected frequencies less than 5. The minimum expected cell frequency is 1.0.

Test Statistics

	PREGNANCY AFTER EVD

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Chi-Square	3.800[a]
df	2
Asymp. Sig.	.150
Exact Sig.	.178
Point Probability	.085

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