

# Risk Factors for Lassa Fever Infection Among Survivors at Federal Medical Centre, Owo, Ondo State, Nigeria.

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## Research

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# Abstract

## Background

There exists paucity of information regarding successfully managed Lassa Fever (LF) patients. This study is aimed at determining the perceived risk factors for LF infection among patients who had been managed and on follow up at Federal Medical Centre, Owo, Ondo State.

## Methods

A cross sectional study of 101 LF survivors who had been managed and attending follow up clinic at Federal Medical Centre, Owo was done. Data were collected using semi-structured interviewer-administered questionnaire. Respondents were assessed for symptoms and factors that may have predisposed them to LF, and data analyzed with SPSS version 23. Those who had more than three identifiable risks were categorised as high risk. Descriptive statistics was done, and association between socio-demographic characteristics and high risk were explored using chi square test.

## Results

The median age of respondents was 33 years (range 8-85 years), 61.4% were males, 92.1% have heard of LF prior to being diagnosed, 55.9% heard through the mass media. The perceived cause of Lassa fever infection among respondents included consumption of food contaminated by rats' feces among 57(56.4%) persons, while 16 (15.8) attributed their infection to contact with LF-infected persons. Among respondents with primary education and below, 5 (29.4%) had high risk of Lassa fever infection compared to 7 (8.3%) with secondary education and above ( $p=0.014$ ).

## Conclusion

Mass media and other sources of information should be well harnessed in the communication of risks and preventive practices for LF. Health education should be intensified both in hospitals and schools to capture both young and old in LF prevention activities.

## Background

Lassa fever (LF) is an acute viral zoonotic illness caused by Lassa virus (an arenavirus), and characterized by fever, muscle aches, sore throat, nausea, vomiting, and chest and abdominal pain [1]. An estimated 29 imported cases of LF have been documented worldwide, one third of which was fatal [2–6]. LF is endemic in West African countries (Nigeria, Sierra Leone, Guinea, and Liberia). In Cote d'Ivoire, Ghana, Togo and Benin, sero-prevalence was found to be lower, but isolated cases show evidence of viral circulation [3–5]. Across this sub-region, LF affects about 3–5 million individuals yearly, and causes about 5,000 to 10,000 deaths [7, 8].

LF was first described in the 1950s in Sierra Leone and was identified as a viral infection in 1969, but was not named until the death of two missionaries in Lassa village, Nigeria, West Africa [9]. LF is caused by an enveloped, single stranded, bi-segmented RNA virus that belongs to Arenaviridae family and is a disseminated systemic primary viral infection [9]. The natural hosts for the virus are multimammate rats (*Mastomys natalensis*) that breed frequently and are widely distributed throughout west, central, and east Africa [9]. These multimammate rats are probably the most common rodent in tropical Africa that are found predominantly in rural areas, and in dwellings more often than in surrounding countryside [5].

The last decade has seen the emergence and re-emergence of Viral Hemorrhagic Fevers (VHFs) in Nigeria and indeed in the West African sub-region. Not unexpectedly, most imported cases of LF have originated from Nigeria, Sierra Leone, Liberia, or Guinea [10]. However, to-date, at least three imported cases have been identified from outside these four countries, suggesting a wider distribution of LF Virus and challenging the current dogma of LF endemicity [3]. VHFs pose a great challenge to public health globally due to the high infectivity, morbidity and mortality associated with this group of diseases.

Seasonal outbreaks of LF have continued in Nigeria with cases now being recorded in states that have not reported in the past. From 1st January to 19th July, 2020, a total of 5366 suspected cases were reported from 27 States including the Federal Capital Territory (FCT), Abuja. Of these, 1051 were confirmed positive, 14 probable and 4315 negatives. Since the onset of the 2020 outbreak, there have been 219 deaths in confirmed cases [10]. Case fatality ratio in confirmed cases is 20.8%. Twenty-seven (27) States and FCT (Ondo, Edo, Bauchi, Nasarawa, Ebonyi, Plateau, Taraba, Abia, Anambra, Adamawa, Gombe, Borno, Kaduna, Kano, Katsina, Benue, Rivers, Kogi, Enugu, Imo, Delta, Oyo, Kebbi, Sokoto, Ogun, Osun and Lagos) have recorded at least one confirmed case across 129 Local Government Areas and Ondo State contributing the highest of 34% of the total national figure [10].

Transmission of LF virus could occur via any of two ways: direct or indirect contact [11]. Infection through direct contact can be by means of contact with the droppings (feces or urine) of the multimammate rats, consumption of these rats (a delicacy among people in some areas). Secondary or person to person transmission could occur through contact with infected body fluids. This mode of transmission mostly occurs while caring for sick persons either by relatives or health care workers [11]. Indirect infection occurs through ingestion of foods contaminated by rat droppings [12]. Rats found in houses of infected people have been found to be seropositive for the virus about 10 times more than those in control houses [12]. Virus antibodies occur after a febrile illness in twice as many people who eat rats as in those who do not.

To our knowledge, there exists paucity of information regarding the perceived risk factors for LF infection among successfully managed cases. An identification of these factors is needed to provide uninfected persons with knowledge of LF risk factors, and to prevent further outbreaks among infected persons particularly in LF endemic areas. This study aimed at determining the perceived risk factors for LF infection among patients who had been managed and on follow-up at Federal Medical Centre Owo, Ondo State, Nigeria.

# Materials And Methods

## Study location

The study was conducted in Federal Medical Centre, Owo located in the Owo Local Government Area of Ondo state in Nigeria. The hospital, though a tertiary health institution, provides primary, secondary, and tertiary levels of healthcare to the people within its catchment areas; Ondo, Kogi, Edo, Ekiti, Osun, and neighbouring states. The Infection Control Ward (ICW) started out as a response to managing LF in January 2017. The ICW became LF Infection Control and Research Centre (ICRC) after the unprecedented outbreak of LF disease in the first few months of 2018. A-34-bedded facility was provided on 28th February, 2018 in this regard. The ICRC collaborates with other national and international organizations for research and management such as the Nigeria Centre for Disease Control (NCDC), Alliance for International Medical Action (ALIMA) and African Centre of Excellence for Genomics of Infectious Diseases (ACEGID). The activities of the ICRC are controlled through an Emergency Operations Centre (EOC) that was set up to serve as the command centre for all activities during an outbreak. Aside clinical management of cases, a follow-up clinic exists for discharged patients with an average number of 25 patients seen monthly.

## Study design

A descriptive cross-sectional study was employed.

## Study participants

The study participants were LF patients who had been successfully managed, discharged, and were attending LF follow-up clinic at ICRC of the hospital. All consenting adults were included in the study. Consent was obtained from parents for persons aged below 18 years. All confirmed persons who were dead at the time of this study were excluded.

## Sample size determination

The minimum sample size was calculated using the Leslie and Kish formula for descriptive studies [13]:

$$n = z^2 p (1 - p) / d^2$$

- Where n is the minimum sample size needed.
- d is the level of error that can be tolerated (0.05 chance of error)
- p is the proportion of households in a LF endemic community at risk of LF due to presence of rodent in their houses (96.1%)<sup>22</sup>

- $z$  is the standard variate corresponding to confidence level.

At confidence level of 95%,  $z = 1.96$

$$n = 1.96^2 \times 0.96(1-0.96) / 0.05^2$$

$$n = 3.8416 \times 0.96 \times 0.04 / 0.0025$$

$$n = 58.9$$

Minimum sample size was rounded up to 65 by adding a non-response rate of 10%. However, a total of 101 recovered persons were interviewed over four months from May to August 2019.

## Data collection

Data were collected by resident doctors in the Department of Community Medicine, Federal Medical Centre, Owo using semi-structured interviewer-administered questionnaire. Respondents were assessed for knowledge on LF, symptoms and factors that may have predisposed them to contracting LF and the behavioural modifications put in place after recovery to prevent recurrence among them and family members.

## Data analysis

Data were analysed with SPSS version 20.0. Descriptive results were presented using frequency tables and charts. Risk scores were computed using six questions with “+1” assigned for presence and “0” assigned for absence. Only those who had cumulative risk scores greater than 3 were categorised as high risk. Association between socio-demographic characteristics and risk factors were assessed using Chi-square test at 5% level of significance.

## Results

Table 1  
Sociodemographic characteristics of Lassa fever confirmed persons, Federal Medical Centre, Owo

<b>Variable (n=101)</b>	<b>Frequency</b>	<b>%</b>
<b>Age group (Years)</b>		
<25	23	22.8
25-39	42	41.6
40-59	26	25.7
≥60	10	9.9
<b>Sex</b>		
Male	62	61.4
Female	39	38.6
<b>Religion</b>		
Christianity	84	83.2
Islam	17	16.8
<b>Highest level of Education</b>		
Primary and below	17	16.8
Secondary	39	38.6
Tertiary	45	44.6
<b>Ethnicity</b>		
Yoruba	75	74.3
Ibo	14	13.9
Hausa	4	4.0
Others*	8	7.9
<b>Occupation</b>		
Business/Trader	42	41.6
Teacher/Civil Servant/Health worker	26	25.6
Student	24	23.8
Unemployed/retirees	9	8.9
<b>Marital Status</b>		

Single	32	31.7
Married	69	68.3
*: Urhobo, Igbira, and Igede		

A total of 101 respondents were interviewed among LF-infected persons visiting the Federal Medical centre, Owo, Ondo State. The median age of respondents was 33 years and ranged between 8 and 85 years, with 42 (41.6%) aged between 25 and 39 years. Among the respondents, 62 (61.4%) were males, and 45 (44.6%) had attained tertiary level of education. Other socio-demographic characteristics are as shown in Table 1.

Among the respondents, 93 (92.1%) have heard of LF prior to being diagnosed of it. Fifty-seven (56.4%) respondents perceived consumption of food contaminated by rats' feces as the cause of cause of their infection, while 16 (15.8%) attributed their infection to contact with LF-infected persons. Sixteen persons (15.8%) stated that LF was either due to unknown cause or the devil's attack, while 12 (11.9%) mentioned that LF was caused by the handling of rats.

The main sources of information regarding LF was either via the mass media (55.9%) or from friends (28%). 6 persons (6.5%) each got LF information from hospitals or school. Other sources of LF information are described in figure 1.

The presence of fever that is unresponsive to antimalarial and antibiotics was mainly reported among 97 (96%) respondents, while 78 (77.2%) stated headache as a symptom of LF infection. Sixty-two persons (61.4%) presented with body weakness, while forty-nine persons (47.5%) had cough following LF. Other symptoms of LF infection among respondents are as shown in figure 2.

Table 2

Recognized risk factors of Lassa fever and measures to prevent recurrence among respondents

<b>Risk Factors</b>	<b>Frequency</b>	<b>%</b>
Presence of bush around the house	63	62.4
Presence of multimammate rats in/around the house	59	58.4
Absence of rat proof containers for food storage	28	27.7
Recent contact with anyone who had fever or died of unknown cause	17	16.8
Spreading of food items on the ground	11	10.9
Consumption of rats in the family	2	2
No identifiable risk factor	2	2
<b>Risk Scores</b>		
0	2	2
1	26	25.7
2	32	31.7
3	29	28.7
4	12	11.9
<b>Measures put in place to prevent recurrence</b>		
Frequent clearing of bush/ Fumigation	58	57.4
Proper storage of food/avoidance of out-of-home meals	22	21.8
Regular handwashing	12	11.9
Change of residence/blocking of crevices	9	8.9

The presence of bush around the house was stated as a risk factor for LF among sixty-three persons (62.4%), while fifty-nine (58.4%) persons mentioned the presence of multimammate rats in/or around the house as a risk factor for LF. Twenty-seven persons (27.7%) reported the absence of rat-proof containers for food storage as a risk factor for LF. Frequent clearing of bush/fumigation was stated as a measure to prevent recurrence of LF among 58 (57.4%) respondents. Among the respondents, 2 (2%) had a risk score of 0 while 12 (11.9%) had a risk score of 4. Twenty-two (21.8%) persons prevented recurrence of LF by ensuring proper storage of food and avoidance of out-of-home meals. Other risk factors for LF and measures to prevent recurrence are shown in table 2.

Table 3  
Association between Sociodemographic variables and risk category for Lassa fever among respondents

Sociodemographic Variable	Risk category		Chi-square	p-value
	High	Low		
	n (%)	n (%)		
<b>Age</b>				
<25	3(13.0)	20(87.0)	1.613	0.656
25-39	6(14.3)	36(85.7)		
40-59	3(11.5)	23(88.5)		
≥60	0(0.0)	10(100.0)		
<b>Sex</b>				
Male	5(8.1)	57(91.9)	2.234	0.135
Female	7(17.9)	32(82.1)		
<b>Religion</b>				
Christianity	10(11.9)	74(88.1)	0.000	0.987
Islam	2(11.8)	15(88.2)		
<b>Highest level of Education</b>				
Primary and below	5(29.4)	12(70.6)	6.000	<b>0.014</b>
Secondary and above	7 (8.3)	77(91.7)		
<b>Ethnicity</b>				
Yoruba	6(8.0)	69(92.0)	4.192	<b>0.041</b>
Others*	6(23.1)	20(76.9)		
<b>Occupation</b>				
Business/Artisan	6(14.3)	36(85.7)	2.518	0.472
Teacher/Civil Servant/Health worker	3(11.5)	23(88.5)		
Student	1(4.2)	23(95.8)		
Unemployed/ Retirees	2(22.2)	7(77.8)		
<b>Marital status</b>				

Single	2(6.2)	30(93.8)	1.419	0.234
Married	10(14.5)	59(85.5)		
*: Igbo, Hausa, Urhobo, Igbira, and Igede				

Among respondents with primary education and below, 5 (29.4%) had high risk of LF infection compared to 7 (8.3%) with secondary education and above ( $p=0.014$ ). Regarding ethnicity, 6 (8%) of the Yorubas had high risk for LF compared to 6 (23.1%) of other ethnic groups ( $p=0.041$ ). Pertaining to sex, 5 (8.1%) had high risk for LF compared to 7 females (17.1%), although these differences are not statistically significant. Other associations between socio-demographic characteristics and risk category are shown in Table 3.

## Discussion

Findings from this study revealed that the presence of bush around the house and the presence of multimammate rats in/around the house are potential factors with high risk for LF infection. Consumption of rats within the family was only identified as a risk factor for LF among 2% of respondents. This finding is unexpected because residents of Ondo State are known for their rat-hunting skills and love for consumption of rat meat [14]. We found that only 2% of respondents who were at no identifiable risk got infected. This highlights that individuals are less likely to be infected in the absence of risk factors. This finding also indicates the possibility of infection in the absence of any identifiable risk. Hence the need for all persons, either at high or low risk for LF, to adopt infection prevention and control (IPC) measures at all times.

Similarly, absence of rat-proof containers for food storage was well identified as a risk factor for LF infection among respondents. A significant association was found in a study between food storage in rat-proof containers and occurrence of LF [15] When containers are not covered with fitted lids, rats gain access to food items, and as such place individuals at risk for LF infection [16]. Similarly, studies conducted in Ebhodiza, South-west Nigeria point to the poor practice of rat prevention measures within home settings as a risk factor for LF infection [17]. A similar study conducted in Liberia corroborates the association between LF and poor waste disposal, accessibility of food preparation areas to rodents, and absence of rodent-proof containers for food storage [18].

The identification of recent contact with persons who died of fever or unknown cause is consistent with findings from a study where human to human transmission reinforced the known epidemiology of LF disease [16]. We also identified spreading of food items on the ground as a risk factor for LF. This was corroborated by the International Fund for Agricultural Development (IFAD) which stated that roadside drying of food produce could cause LF infection [19]. These findings are pointers to lifestyles which could place one at risk for LF.

We found that persons with primary education and below had higher risk of LF. This finding contradicts the findings from a similar study conducted in Edo State where about 90% of respondents had a minimum of secondary school education [20]. Our study highlights that all persons, educated or not are at risk for LF infection. We noted a higher risk of LF infection among artisans or those engaging in business. Farmers who are present in this category are involved in the production and sales of food items [21]. Hence, they could serve as transmitters of LF infections if precautionary measures are shunned.

We found that mass media and friends were identified as the main sources of LF information among respondents. This finding is similar to findings from studies conducted in Edo and Oyo States [22, 23] It also agrees with the reports from Pulse which maintained in community information and mobilization for awareness generation on the role of rodents in the transmission of LF disease [24]. This consonance highlights the active involvement of the mass media in communicating health-related information, and prompting health-seeking behavior among individuals. These findings could have been due to the inclination towards high usage of the mass media among a larger number of persons in Ondo State.

The high proportion of information provided by friends highlight the need to providing social networks and unit leaders in the community with LF-rich information. This study revealed that hospitals and schools are not the main sources of information regarding LF. A few respondents obtained LF information from the hospitals. This finding is contrary to results in hospitals and schools conducted in previous studies [25]. This could have been due to the hospital-based setting in which this study was conducted. This finding is worrisome because hospitals and schools are known for enhanced communication of health information on non-LF illnesses [26, 27]. Findings from this study thus imply the need for interventions especially at health facilities in order to capture all visiting persons in LF education sessions.

Findings from this study reveal the symptoms of LF that respondents presented with. Leading LF symptoms included fever that is unresponsive to medications, headache, and body weakness. These symptoms were similarly reported in a study conducted in Abakaliki, Nigeria, a LF-endemic zone [25]. Also, pregnancy loss was similarly reported as the least identified symptoms in both studies. This highlights that similar presentations could accompany LF infection among different individuals.

Regarding measures in place to prevent recurrence of LF, frequent clearing of bush and fumigation of the environment was well reported among respondents. Evidence from existing literature places emphasis on poor environmental sanitation as a major driver for LF outbreak [20]. Also, decisions were made on the proper storage of food items and avoidance of out-of-home meals. IPC measures were also reported as preventive measures for repeat episodes of LF infection among respondents. The need for these measures were also reported in a similar study conducted among healthcare workers [28]. The decision to change residential apartments among respondents could be due to the proximity of current residences to dumping sites. Such proximity increases vulnerability to LF outbreak [20]. Hence it is needed that dumping sites are located far from residential areas.

This study is limited to LF survivors on follow-up visitations at Federal Medical Centre, Owo. The findings in this study could be different from future studies conducted in other LF endemic communities in Nigeria. Also, the cross-sectional nature of this study could have limited our findings. We therefore suggest that longitudinal research should be conducted among LF survivors.

## **Conclusion**

Identification of the risk factors for LF is central to preventing the infection. Lifestyle modifications on hygienic practices are required to prevent being infected. Also, mass media and other sources of information should be well harnessed in the communication of risks and preventive practices for LF across all population groups. Health education should be intensified both in hospitals and schools to capture both young and old in LF prevention activities. Infection prevention and control (IPC) measures need to be widely accepted and practiced both at home and public settings to prevent further outbreaks of LF.

## **Abbreviations**

LF: Lassa Fever

VHFs: Viral Hemorrhagic Fevers

FCT: Federal Capital Territory

ICW: Infection Control Ward

ICRC: Infection Control and Research Centre

NCDC: Nigeria Centre for Disease Control

ALIMA: Alliance for International Medical Action

ACEGID: African Centre of Excellence for Genomics of Infectious Diseases

EOC: Emergency Operations Centre

IFAD: International Fund for Agricultural Development

IPC: Infection Prevention and Control

## **Declarations**

***Ethics approval and consent to participate***

Ethical approval was obtained from the ethical review committee of Federal Medical Centre, Owo, Ondo State (FMC/OW/380/VOL. LXVII/187).

## ***Consent for publication***

Consent was gotten from all respondents prior to the commencement of data collection.

## ***Availability of data and materials***

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## ***Competing interests***

The authors declare that they have no competing interests.

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The research was fully funded by the authors.

## ***Authors' contributions***

OSI, OTO-L, and AJO conceptualized the study. OIS and AAA overtook data analysis. OSI, OTO-L, AJA, AAA, AOK, CA, and OOA read the first draft. All authors approved the final version of the manuscript.

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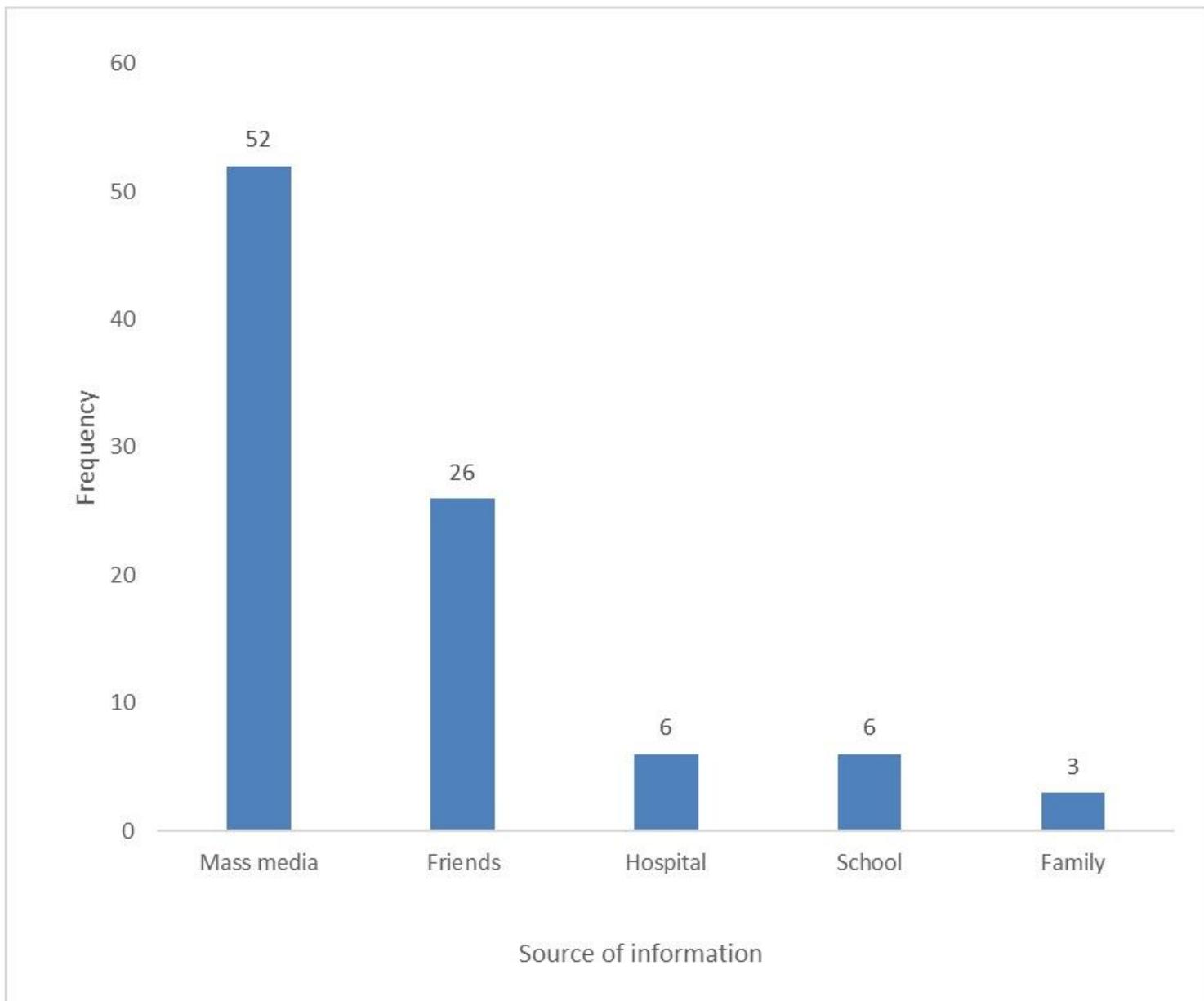
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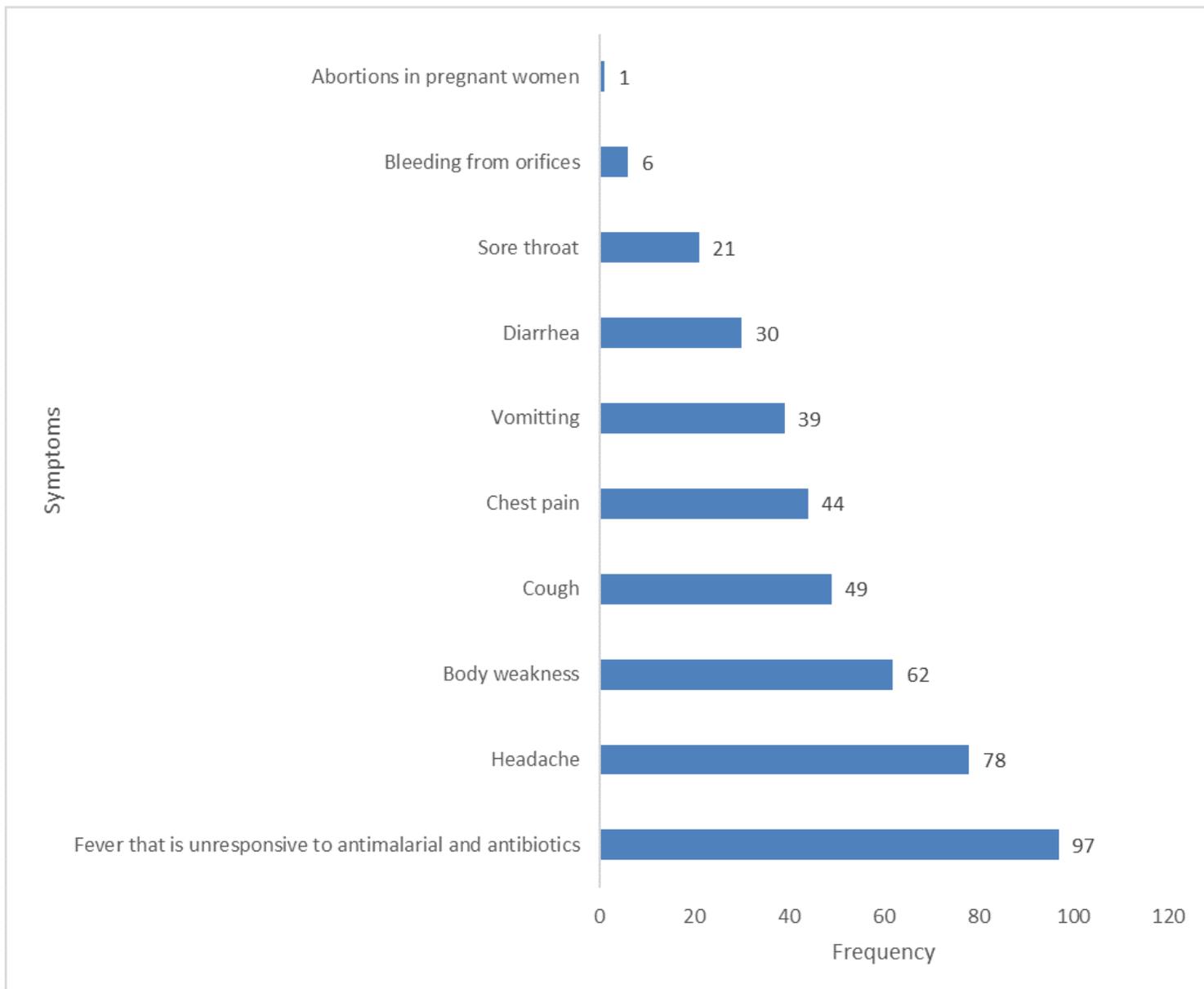
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## Figures



**Figure 1**

Sources of information on Lassa Fever among respondents



**Figure 2**

Symptoms of Lassa fever infection among respondents