Measles outbreak investigation, Greater Francistown District, Botswana, 2023

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Utlwanang Modise[1,&], Tshepang Carter Ntsose[1], Gotsileene Monamodi[1], Olerile Mosupiemeng[2], Boitumelo Solomon[1], Boitshwarelo Masunda[1], Onkabetse Wilson[1], Gorata Baraedi[1], Dominique Mayenzanisi[1], Samuel Kolane[3], Nesredin Jami Oumer[4], Uzoma Ogbonna[4]

[1]Botswana Ministry of Health, Greater Francistown District Health Management Team, Francistown, Botswana, [2]Department of Family Medicine, University of Botswana, Gaborone, Botswana, [3]Ministry of Health, Gaborone, Botswana, [4]African Field Epidemiology Network, Field Epidemiology Training Program, Gaborone, Botswana

[&]CORRESPONDING AUTHOR
Utlwanang Modise, Botswana Ministry of Health Francistown, BOTSWANA,
Email: modiseu@gmail.com,
ORCID: https://orcid.org/0009-0008-9728-6020

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ABSTRACT

Introduction: Measles causes significant childhood morbidity and mortality worldwide. Botswana has targeted measles for elimination. On January 7 2023, the Greater Francistown district health management team was informed of a suspected measles outbreak. We investigated the outbreak to verify the diagnosis, describe the epidemiological characteristics of cases and institute control measures. **Methods**: We adapted the World Health Organization case definition for measles. We conducted active case search, interviewed caregivers, patients, community members and reviewed medical records. We collected patient's demographic, clinical, and exposure history. Blood samples obtained from community cases were sent to the National Health Laboratory, Gaborone. We summarized data using summary statistics, frequencies and proportions. **Results**: From week 52, 2022 to week 36, 2023, we identified 25 cases (CFR: 0%): 21 confirmed and 4 probable cases. All 25 (100%) cases presented with a maculopapular rash and fever; one (4%) case was hospitalized. Median age was 7 years (range: 1 – 24 years). Persons aged <10 years accounted for 72% (18/25) cases, 64% (16/25) were males, 72% (18/25) Bazezurus and 52% (13/25) lived in Chadibe. Eight percent (2/25) reported travel to a country with a confirmed measles outbreak. Sixty-four percent (16/25) had not received Measles Containing Vaccine (MCV) dose, 89% (16/18) of these were Bazezurus. The measles vaccination coverage was 98% in Chadibe, and MCV1 coverage amongst Bazezurus was 42%. **Conclusion**: The measles outbreak in Greater Francistown may have resulted from vaccine refusal by a vaccine-hesitant religious group leading to pockets of measles susceptible children.

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Introduction

Measles is caused by a virus of the *paramyxoviridae* family. It is characterized by fever, cough, coryza, conjunctivitis and a maculopapular rash. The median incubation period is approximately 12 (range:7-21) days. Humans and primates are inherently susceptible to the measles virus. It is a vaccine-preventable disease [1-3].

Measles remains a global health threat causing considerable pediatric morbidity and mortality, with 140,000 measles associated deaths reported globally in 2018 [2,4]. In 2021, there was an estimated 9,484,464 (95%CI: 5,681,867 – 14,881,517) cases of measles globally, a decrease from 34,012,63 (95%CI: 27,393,416 – 42,901,683) in 2000. This downward trend was observed in the African region with an estimated 4,430,595 (95%CI: 2,619,358 – 7,030,815) cases in 2021 as compared to 10,965,152(95%CI: 7,134,948 – 14,649,839) in 2000. An estimated 66,229(95%CI: 38,811 – 106,293) deaths were attributed to measles in 2021 in the African region [5].

Despite the progress, there has been a resurgence of measles, with outbreaks frequently reported [3]. In 2021, in two WHO regions, twenty-two disruptive outbreaks of measles were documented, eighteen (82%) of these occurred in the African region [5]. Measles outbreaks may ensue in under-served settings such as those following armed conflicts, social exclusion, geographic inaccessibility, and poverty. Additionally, nosocomial transmission, suboptimal vaccination coverage and vaccine hesitancy leading to an accumulation of measles-susceptible persons are factors known to enable the occurrence of outbreaks. Certain subpopulations such as nomadic, religious, and migrant communities are known to be at increased risk of measles outbreaks [3, 6-9].

Measles elimination, defined as the lack of measles spread in a defined geographical region for a minimum of 12 months in the presence of a high-quality surveillance system has been targeted by the World Health Organization African Region. In the measles elimination phase, a single measles case signifies the existence of an outbreak requiring prompt investigation and response [10,11]. Australia, Macao, Mongolia, DPR Korea, Japan, Cambodia and Brunei Darussalam are some of the countries and areas that have eliminated measles [12]. Botswana aims to eliminate measles and has adopted the World Health Organization (WHO) recommended strategies [13]. Measles elimination strategies include attaining a 95% vaccination coverage with two doses of a Measles Containing Vaccine (MCV), instituting a high-quality case-based measles surveillance system, establishing high-quality laboratory support to surveillance and having the capacity to respond effectively to outbreaks [6].

A key intervention in achieving the elimination goal is vaccination. Globally, in 2022, the first dose MCV (MCV1) coverage was 83%. As at 2022, one hundred and eighty-eight WHO member states had introduced a measles second dose to the immunization schedule, and the second dose (MCV2) was 74%[14]. In the WHO Afro region in 2022, MCV1 was estimated at 69% and MCV2 at 45% [15].

Botswana has made progress towards its elimination goal; the Botswana national policy is to provide MCV1 at 9 months and MCV2 at 18 months. From 2020, to 2021, the MCV1 coverage ranged from 70% to 74% and the MCV2 coverage ranged from 66% to 70%. In 2022, the MCV1 coverage was 70% and MCV2 was 77 [16], the measles incidence rate was 0.4/1,000,000 population in 2022, a decrease from 408/1,000,000 population in 2010 [13]. In 2023, twenty-one confirmed cases of measles were reported in the Greater Francistown district, surpassing the nine cases reported in Botswana from 2013 to 2022 [17].

On January 7, 2023, the Greater Francistown district health management team (GFDHMT) was informed of a suspected measles outbreak by the Thalogang Health Post. On January 18, 2023, we investigated the suspected outbreak so as to verify the diagnosis, describe the epidemiological characteristics of cases and institute control measures.

Methods

Setting

The outbreak occurred in the Greater Francistown District, a district comprising four subdistricts namely Francistown, Tonota, Northeast and Tutume. The reported cases were limited to Francistown and Tonota subdistricts. Francistown hosts the country's second-largest city in Botswana. The 2022 census estimates the general population of these 2 subdistricts at 171,524, with an under-five population of 11,996 and 3,103 children under 1 year of age. Greater Francistown is in Eastern Botswana, about 400 kilometres (250 miles) northeast of the capital Gaborone and 90 kilometres (56 miles) from

the international border with Zimbabwe. It is inhabited by various ethnic groups such as the Bakalaka, Bangwato, Bakgatla, Barolong, Barotsi and foreign nationals mostly from Zimbabwe. Additionally, inhabitants are adherents of different Christian denominations namely Pentecostal, Roman Catholic, and Bazezuru. Several inhabitants are African traditionalists. The Bazezuru sect does not subscribe to western medicine and frequently rejects vaccines [18].

Study design and population

We conducted a descriptive cross-sectional study targeting all persons who had symptoms suggestive of measles infection in the Francistown and Tonota subdistricts.

Public health response

The GFDHMT engaged the community to increase measles awareness and the importance of vaccination. Furthermore, healthcare facilities were alerted and provided guidelines to identify, treat and isolate cases. A measles vaccination campaign targeting children of 9-59 months was conducted and cases were isolated to reduce transmission.

Outbreak case definition

The outbreak case definition was adapted from the WHO standard case definition for measles. Persons presenting with fever and rash were categorized into suspect, probable and confirmed cases with the following criteria –

Suspect case: any resident of Greater Francistown with a rash and fever and any of these symptoms: cough, coryza (runny nose) or conjunctivitis (red eyes) from January 1, 2023, to August 31, 2023.

Confirmed case: suspect-case that tested positive for measles IgM antibody on enzyme linked immunosorbent assay using sera or tested positive to measles antigen from throat swabs.

Probable case: suspect case whose biological specimen was not collected but had an epidemiologic link to a confirmed case.

Data collection

Data was collected from the onset of the investigation January 18, 2023 to August 31, 2023. To collect data relevant to the outbreak, we adapted the integrated disease surveillance and response measles case investigation form. The case investigation form captured data on age, sex, religion, place of residence, date of onset of symptoms, travel history, hospitalization history, immunization history. We conducted active surveillance to identify unreported cases of measles, this strategy included a house-to-house search and a review of health facility records. Records review and house-to-house search were conducted from the January 18, 2023 to the February 1, 2023. Snowballing was employed during the house-to-house search. Data was obtained from all detected suspected cases during active case search through face-to-face interviews from caregivers of children or case and patients that fit the outbreak case definition. The child vaccination card when available was checked to confirm the reported vaccination status of the cases. Furthermore, we abstracted data of suspected cases identified during record review from hospital records and documented the district routine immunization coverage records. Between February 2, 20223 and August 31, 2023, data was updated from records as new cases kept on coming. All data was entered into a line list.

Specimen collection

An informed verbal consent was obtained from suspected cases prior to specimen collection. Blood samples were collected from all suspected cases identified during active surveillance in the communities within the first few days of the rash onset for optimal detection of the virus's RNA and sent to Itekeng Clinic laboratory in Greater Francistown. At Itekeng Clinic laboratory, the blood samples were centrifuged to separate the serum from red cells. The serum and throat swab samples were sent to the National Health Laboratory, Gaborone for testing. Samples were not obtained from all suspected cases identified through a review of hospital records because either their symptoms had subsided, or they were no longer reachable.

Laboratory testing

Real Time Polymerase Chain Reaction RT-PCR (rRT-PCR) testing was done on the blood samples for detection of measles RNA antigen. Firstly, we conducted RNA extraction to isolate viral RNA from the other cellular components using reagents and equipment to break open cells and release RNA that was then purified for use in PCR. We subsequently used reverse transcriptase to convert the viral RNA into complementary DNA (cDNA), this step was essential as PCR amplifies DNA, not RNA. Specific primers targeting the measles virus genome, commonly the measles nucleocapsid or hemagglutinin genes were added to the cDNA. The cDNA was then amplified using PCR cycles that

involved denaturation, annealing, and extension. This amplification enabled the detection of the measles virus cDNA if present in the sample. The presence of the measles virus was confirmed by detecting a specific DNA fragment using fluorescent probes method in quantitative PCR. The presence of the measles virus cDNA in the sample confirmed an active infection.

Data analysis

We calculated summary statistics, frequencies, and proportions using Microsoft Excel. We described the data in time, person, and place. We calculated measles Attack Rate (AR) by age and sex and summarized the timeline of the outbreak as an epidemic curve. The AR was calculated using the formula cases/population at risk/100,000 population) and the case fatality rate (CFR) as deaths/cases. We computed the vaccination coverage as number of persons who received vaccination/number of eligible persons x 100% for MCV1 and MCV2.

Ethical consideration

This outbreak investigation was carried out as part of the statutory functions of the GFDHMT and consequently excused from institutional ethical review. Participants were treated with respect and willingly participated in the investigation with no payment or coercion. The data was stored in a password-protected computer and analyzed and reported in formats that did not reveal the identity of the participants. Permission to take photographs was obtained from caregivers of children and participants above 16 years.

Results

We identified 239 suspected cases with onset of symptoms occurring from week 52, 2022 to week 36, 2023, and samples were collected from 107 suspected cases detected during a house-to-house search. Blood samples could not be obtained from 55% (132/239) of suspected cases. These 132 suspected cases were those identified through a review of health facility records and were either unreachable or no longer symptomatic precluding blood sample collection.

Twenty-one of the 107 suspected community cases (positivity rate: 20%) were confirmed to be cases of measles, and an additional four cases identified during health facility records review were classified as probable cases. The first case had onset of symptoms in week 52, 2022, cases peaked in week 4, 2023, and the last case was detected on August 19, 2023 (week 33, 2023). Outbreak investigation activities were suspended from week 8 to week 20,2023, as there was a prioritized polio outbreak response following the detection of a circulating vaccine-derived poliovirus type 2 (cVDPV2) on environmental sampling that the district human and logistic resources were redirected to. As a result of the temporary discontinuation of outbreak investigation activities, suspected cases were not detected during the period covering the polio outbreak response, (Figure 1).

Clinical features

All 25 (100%) cases presented with a maculopapular rash and fever, while 18 (72%) presented with cough, (Figure 2). There were zero deaths (CFR: 0%) and one hospitalization.

Sociodemographic characteristics

The median age of cases was 7 years (range: 1 – 24 years). Persons aged 10 years or less accounted for 72% (18/25) of cases. The AR was highest (58/100,000 persons) in the age group of 1 – 5 years. Sixty-four percent (16/25) were males with a 2:1 male:female ratio, the AR was 25/100,000 persons for males and 13/100,000 persons in females. Seventy-five percent (18/25) of cases were from the Bazezuru sect, the AR amongst the Bazezuru sect was 429/1,000 persons and 108/1,000 persons for the rest of the community. Fifty-two percent (13/25) of cases lived in Chadibe village where the AR was highest (242/100,000 persons). Eight percent (2/25) reported travel to a neighboring country with a measles outbreak, these two cases were the first cases and were Bazezurus (Table 1).

Vaccination coverage

Sixty-four percent (16/25) cases had not received a dose of MCV, all these 16 cases were Bazeuru sect and accounted for 89% (16/18) of all the cases in the sect. In 2022, the MCV1 coverage was 98% in Chadibe, 86% in Shashemooke, 68% in Tatisiding, 82% in Francistown, and 38% in Mandunyane. The MCV1 coverage amongst persons of the Bazezuru sect was 42%. The measles vaccination coverage was 66% and 67% for MCV1 and MCV2 respectively in the district, (Table 1).

Public health response

The DHMT conducted a measles vaccination catchup from February 1, 2023, to March 31, 2023, in Chadibe village which was the epicenter of the measles outbreak targeting 107 children (42 Bazezurus). One hundred and one children were reached of which 33 (33%) Bazezuru children received the vaccine

Discussion

This paper describes the investigation of a confirmed measles outbreak in Greater Francistown district, Botswana in 2023. To the best of our knowledge, this is the first documented investigation of a vaccine-preventable disease in a faith-based unvaccinated group in Botswana.

Findings from this investigation confirmed a measles outbreak in Greater Francistown with Chadibe as the epicenter accounting for more than 50% of all reported cases and the highest attack rate. An attack rate of 242 per 100,000 is significantly higher than expected in a country in the measles elimination phase and with a strong routine immunization program. In Botswana, where measles vaccination coverage has historically been high for the first dose of MCV [19] such a high rate suggests either pockets of unvaccinated individuals or potential vaccine program failure in Chadibe. Several contributing factors may explain how Chadibe became the epicenter including suboptimal vaccination coverage, poor access to health services, disruptions in vaccine supply or cold chain systems and delayed detection and response [5]. Compared to previous outbreaks in Botswana, this attack rate is high. For instance, the 2009 measles outbreak in Botswana reported national attack rates far below 100/100,000, and even localized hotspots did not reach such levels [20]. However, in other Southern African countries, such as Zimbabwe and Namibia, localized outbreaks with attack rates exceeding 200/100,000 have been observed in areas with substantial immunity gaps [6].

This finding highlights the critical need for community-based surveillance, especially in areas where national averages may mask local hotspots. Strengthening community-based surveillance, ensuring high-quality immunization outreach, and conducting post-campaign coverage surveys are essential to prevent future outbreaks.

A key finding from the measles outbreak investigation was that the Bazezurus accounted for approximately 75% of all reported cases and experienced an attack rate nearly four times higher than that of non-Bazezurus. This indicates that the Bazezuru population was disproportionately affected and represents a high-risk group within the broader population. The true number of cases is likely to be higher as the Bazezurus are known to refuse vaccines and not seek medical diagnosis and treatment [18]. This elevated burden is likely linked to their religious beliefs. These findings suggest that unless interventions targeting this community are implemented, the Botswana measles elimination goal will not be met.

The observation of sustained measles transmission despite a high measles vaccination coverage could be attributed to pockets of measles susceptible children among the Bazezurus enabling spread of the measles virus. It is established that 95% vaccine coverage is required for herd immunity [21], however, our findings show that sustained transmission is possible where vaccine refusal exists even in the presence of high vaccine coverage. Documented reports of disease outbreaks among the Bazezurus are scarce, this could be due to the inability of the disease surveillance system to detect outbreaks within this group as they do not seek health care services [18].

Findings of religious groups being disproportionately affected by vaccine-preventable diseases like measles are well-documented both in Africa and internationally. Our findings are similar to what was observed in a measles outbreak investigation in Zimbabwe that determined that vaccine refusal by a religious sect was a risk factor for measles infection [22, 23]. In Nigeria, outbreaks have been associated with religious communities opposing immunization due to rumours of infertility and conspiracy, particularly in the north of the country [24]. In the Netherlands, measles outbreaks have repeatedly occurred among members of the Reformed Orthodox Protestant community, a group known for vaccine refusal based on religious beliefs. In 2013, 2,600 cases were reported in these communities [25]. In the United States, vaccine refusal was associated with an outbreak as cases of measles were majorly among deliberately unvaccinated persons [26]. However, this finding is dissimilar to that observed in a measles outbreak that occurred in a highly vaccinated population [27] where secondary vaccine failure was adduced as a factor enabling the outbreak. Our findings also contrasted with that reported in an outbreak of measles that occurred following a Tsunami in India. In this setting, the measles vaccination coverage was

high, however, a one dosage vaccination strategy was found to have limitations in providing herd immunity to forestall an outbreak [28].
The findings from the Bazezuru community point to a need for a culturally sensitive health education campaign that respects religious values while emphasizing the benefits and safety of immunization.
The attack rate was highest in the 1-5 years' age group, this indicates a suboptimal vaccination coverage over several years leading to an accumulation of a measles susceptible population. This is also compatible with the acquisition of measles immunity by adult members due to a previous measles infection. Though the risk of disease was highest in the 1 – 5-year age group, the majority of the cases were found within the 1 – 10-year age group in our study. These findings are similar to results of measles outbreak investigations in Nigeria and Ethiopia [29-31] and in contrast to observations in India where persons aged 18 – 20 years were most at risk of the disease [32].

Study limitation

The findings from this outbreak are subject to a limitation. Blood specimen for laboratory testing were only collected from suspected cases detected during house-to-house search and not from those detected during a review of health facility records. These suspected cases might not be representative of all cases.

Conclusion

The investigation confirmed a measles outbreak in the Greater Francistown District, Botswana. The measles outbreak likely resulted from persistent vaccine refusals by a religious group resulting in a population of measles susceptible children.

Recommendation

We recommended a district-wide immunization catch-up campaign targeted at the Bazezuru to attain herd immunity and prevent future outbreaks. The community including the Bazezurus should be sensitized on the importance of immunization. Efforts should be made to evaluate strategies for creating vaccine demand in Greater Francistown, Botswana.

What is already known about the topic

- Measles is a highly-transmissible acute infection caused by a paramyxovirus, and characterized by fever, conjunctivitis, generalized maculopapular skin rash, and respiratory symptoms.
- Management of measles involves symptom management including fever, rash, conjunctivitis and coryza.

What this study adds

- Measles outbreaks may occur in communities with a high measles vaccine coverage

Competing Interest

The authors declare no competing interests

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Authors´ contributions

UM, TN, GM, OM and UO took part in the conceptualization of the outbreak investigation, protocol write up and conception of the manuscript idea and it's write up; UM, GB, DM, BM and BS contributed to the data collection, compilation and conception of the manuscript idea and it's write up; UM, GM, OM, SK, NJO and UO did compilation, conception of the manuscript idea and final review of manuscript for substantial intellectual content. All authors read and approved the final manuscript.

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Tables & Figures

Table 1: Distribution of sociodemographic characteristics of cases by attack rate and vaccination coverage, Greater Francistown, 2022 – 2023

Characteristics	Number of cases n (%)	Population	Attack rate/100 000	MCV1 coverage (%)	MCV2 coverage (%)	Number of Measles Vaccine Doses Received			
						0	1	2	Total
Overall	25	131,662	19	66	67	16	2	7	25
Age group (years)									
1 – 5	9 (36)	15,404	58			5	1	3	9
6 – 15	15 (60)	28,044	53			10	1	4	15
16 and above	1 (4)	88,214	1			1	0	0	1
Sex									
Male	16 (64)	62,979	25			9	1	6	16
Female	9 (36)	68,683	13			7	1	1	9
Village									
Chadibe	13 (52)	5,371	242	98	99	11	1	1	13
Mandunyane	7 (28)	4,584	152	38	53	4	1	2	7
Francistown	3 (12)	121,707	2	65	66	1	0	2	3
Totals						16	2	7	25

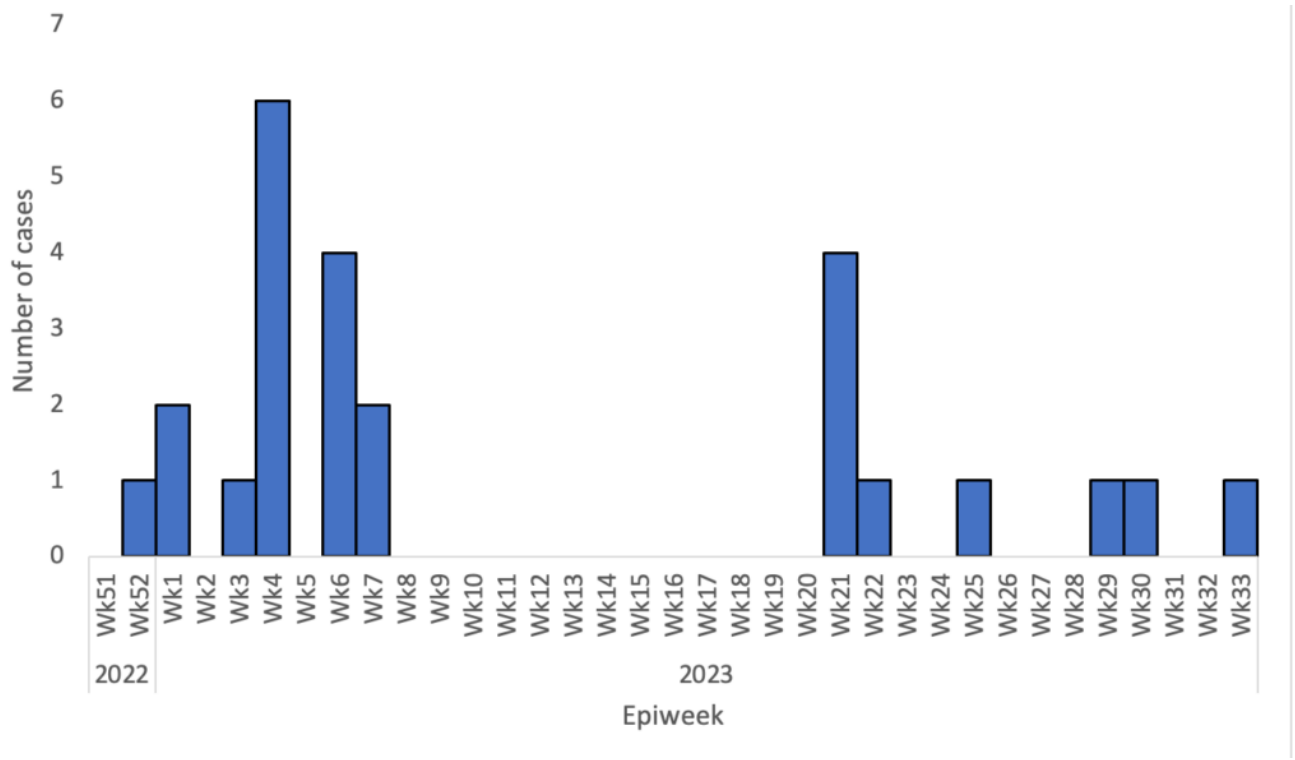

Figure 1: Distribution of measles cases by time, Greater Francistown District, 2022- 2023

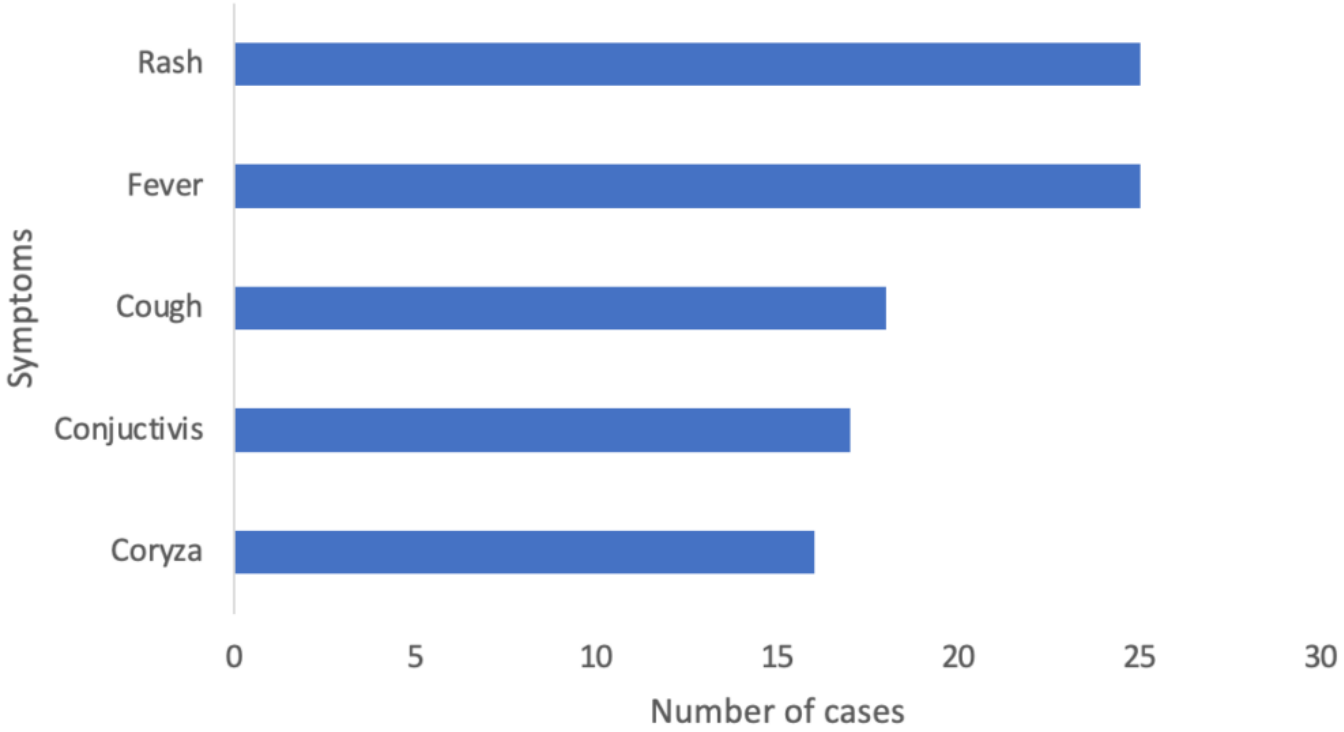

Figure 2: Frequency of measles cases, Greater Francistown District, 2022-2023