Cohort Study

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Demographical, clinical, and complication differences between vaccinated and unvaccinated hospitalized children with measles in mogadishu somalia: a hospital-based retrospective cohort study

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Background: Measles is endemic in Somalia; recurrent outbreaks are reported annually. Under-five children are the most affected due to low immunization coverage, vitamin A deficiency, and malnutrition. The study aims to evaluate the demographical, clinical, and complication variations between vaccinated and unvaccinated hospitalized children with measles in the study hospital.

Method: A hospital-based retrospective cohort study was implemented between 10 October and 10 November 2022 by reviewing case record files following a well-structured checklist of admitted clinical features, demographic characteristics, history of measles immunization, and measles complication status. Descriptive statistics were used by presenting frequency and percentage for categorical and the mean score for continuous variables. χ^2 and Fisher's exact test at $P = 0.05$ were used to identify the proportions differences between vaccinated and unvaccinated cases.

Result: A total of 93 hospitalized measles children participated in the study. Over half were boys, the mean age in months was 20.9 (SD ± 7.28), and over two-thirds of the mothers/caregivers did not have formal education. Almost 9.7% of hospitalized measles children had one dose of the measles-containing vaccine, while none had two doses. The vaccinated cases had fewer ill with fewer complications than the unvaccinated cases. Fever, cough, rash, and Koplik's spots were clinical features associated with measles immunization status.

Conclusion: Around one in ten hospitalized children had one dose of the measles vaccine. Vaccinated cases had fewer illnesses with few complications than unvaccinated cases. The paper highly emphasizes providing booster doses, improving vaccine logistics and storage, and following immunization schedules. In addition, conducting further multicentral high sample-size studies is highly required to identify whether vaccine inadequacy was due to host-related or vaccine-related factors.

Keywords: measles outbreak, measles-containing vaccine (MCV1), somalia, unvaccinated, vaccinated, vaccination failure and inadequacy

Background

Measles is an infectious disease caused by the Morbillivirus of the Paramyxoviridae family; it can transmit droplets from an infected person through coughs or sneezes[1]. The most contagious period is 3–5 days after the rash. It may extend due to the blood, urine, nasopharyngeal mucosa, and mouth virus presence, and the contagious period is high due to the virus's replication in the upper respiratory tract[2]. Measles outbreaks are cyclical epidemics that appear mainly between the late winter and early spring and are highly related to crowded and low vaccine coverage[3]. In addition, several studies have reported that a high birth rate is an outbreak's supporting factor[4]. The incubation period is between four days before the rash and four days after, estimated to be 10–14 days[5]. The level of viremia is related to the period of coughing, coryza. It may increase viral transmission,

HIGHLIGHTS

- 9.7% of the hospitalized cases due to the measles infection had one dose of the measles-containing vaccine.
- Rash, cough, Koplik's spots, and fever are clinical characteristics statistically associated with immunization status.
- This paper highly recommended providing booster doses, improving vaccine logistics and storage, and following immunization schedules.

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and an unbroken transmission chain leads to sustaining the virus in humans since it is undetectable in animal reservoirs[6,7].

The most common measles complications are otitis, encephalitis, pneumonia, and secondary bacterial infections[8–13]. Measles infection is not considered a pediatric disease. It occurs at any age since several studies reported that those older than 20 years had a greater risk of measles infection with complications, particularly unvaccinated people living in endemic areas with vaccination coverage of less than 95%[14]. In addition, several regions had vaccination strategies that focused the adult population on ensuring each adult received at least two doses of measles-containing vaccine (MCV1)[15].

Low measles vaccination coverage leads to recurrent measles outbreaks[16]. Fewer measles cases were reported after the national vaccination program in Romania[17,18]. The commonest measles clinical features were high fever, cough, coryza, conjunctivitis, and kolpik spots with or without a maculopapular rash. Patients' complication status, severity, and hospitalization depend on patient factors such as vitamin A deficiency and nutritional and immunization status[19,20]. Insufficient immunization or vaccination failure was the most changing factor against measles eradication. Over 70 000 measles cases were reported[21]. Most cohorts that reported vaccination failure still recommended vaccine uptake, reasoning that vaccinated cases had mild illnesses with fewer complications than unvaccinated cases. Additionally, vaccination uptake reduces the number of cases and disease contagious[18].

The Somali diaspora has been vital in most measles outbreaks in western countries for the last decade. Almost 18 measles cases were reported in Norway majority were Somali community[22]. In Minnesota US, an unvaccinated US-born Somali child was infected after visiting Kenya in 2011, leading to over 20 measles cases in Minnesota[23]. Consequently, in 2017 the most extensive US measles outbreak occurred in Minnesota; 75 cases were reported, over 90% were unvaccinated, and more than 80% were from the Somali community in Minnesota. In addition, measles vaccination coverage in US-born Somali children was 42% at that time[24]. Somali diaspora parents in Minnesota and Norway had voiced concerns about the measles vaccine causing autism, and subsequent discussions showed that unvaccinated status is highly associated with false vaccine beliefs[24–27]. Health literacy and poor prevention practices were reported in Somali women's life in Norway[28,29].

In Somalia, measles is endemic new cases are reported every year. In 2022, 3509 measles cases were documented between the first of January and the end of March 2022 in the 18 regions of the country. Two hundred forty-nine samples were collected and tested 57% became positive for measles-IgM, and 81% were under-five years children. In addition, 23 039 cases were documented in 2017 in every county region and are considered the highest Somali measles outbreak in the last decade. Moreover, 2596 cases were reported in 2020, which is high even though 7494 cases were reported in 2021. WHO and UNICEF estimated that the national first dose of measles immunization coverage is 46%, while the second dose was established in November 2021[20]. Low national measles vaccination coverage, vaccination failure, a high incidence of vitamin A deficiency, and malnutrition among under-five children exacerbate the situation[20].

In addition, response activities are ongoing, including surveillance and contact tracing, vaccination, laboratory investigation, case management, and training healthcare workers; at the same time, outbreaks occur, and new cases are received annually, including vaccinated and unvaccinated children. Based on these facts and previous recurrent outbreaks in Somalia and the Somali diaspora in western countries, the study aims to examine the demographical, clinical, and complication differences between previously vaccinated and unvaccinated hospitalized children with measles in the study hospital.

Method

Study design

A hospital-based retrospective cohort was conducted between 10 October and 10 November 2022 to evaluate the demographical, clinical, and complication variations between previously vaccinated and unvaccinated hospitalized children with measles virus infection during the last measles outbreak from 1 January to 30 March 2022[20].

Study setting and population

The Banadir Hospital is located in Mogadishu Somalia, which is the capital and highest populated city in the country. The study hospital is a public, teaching, and referral hospital administered by the Ministry of Health in the Federal Republic of Somalia. Established in 1977, it provides medical services to over three million population. The study population was all hospitalized children with measles admitted or referred to the study hospital during the last measles outbreak between 1 January to 30 March 2022.

Sampling procedure

All measles admitted or referral children's case record files in the study hospital met the study criteria and were included after excluding incomplete case record files. To ensure this sample is enough a statistical power recommended by Kim et all[30] called 'post hoc power analysis' was used rather than sample-size calculation due to the study being a retrospective study and the primary outcome being a binary variable (vaccinated and unvaccinated). The power analysis was 1-beta (power of the test) at 80% set as the power of analysis with alpha $=0.05$ used. A workflow diagram is provided to know how participants were recruited (Fig. 1).

Study variables and data quality

Well-structured checklist variables based on previous literature[31] were used as a research tool that consisted of the child and mother or caregivers' sociodemographic characteristics, admitted clinical features, history of measles immunization, and measles complication status. The tool reliability was pretested before the actual study and necessary changes were made to maximize data reliability. A senior pediatrician diagnosis measles based on admitted clinical features, medical history, history of measles exposure, and laboratory investigation. The study's dependent variable was measles immunization status; those who received one dose or more of the MCV1 were recognized as vaccinated cases, while those who had not received even one dose of MCV1 were recognized as unvaccinated[31]. The independent variables were the child, mother, or caregiver's demographic characteristics (sex and age of the child, mother or caregiver's education level, child's place of birth, and monthly family income), admitted clinical

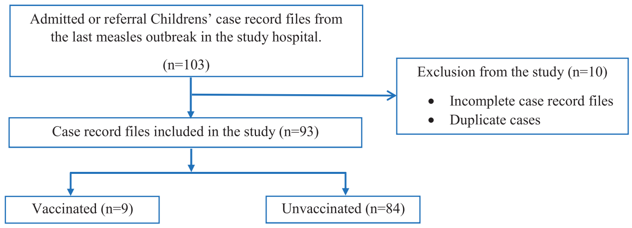

Figure 1. A workflow diagram.

features (fever, cough, coryza, conjunctivitis, rash, and Koplik's spots), and complication status. Those who developed bronchopneumonia, excessive diarrhea with or without dehydration, purulent conjunctivitis, severe mouth ulcer, otitis media, laryngotracheobronchitis, and acute encephalomyelitis in the hospital or before recognized measles complicated cases, while those do not develop any of them are considered uncomplicated cases[32].

Data collection procedure

Data were collected from the case record files through the well-structured checklist between 10 October to 10 November 2022. All complete case record files of the children admitted or referred to the study hospital due to the measles infection during the last measles outbreak between 1 January to 30 March 2022 were included after excluding incomplete cases.

Data analysis

Data were cleaned, coded, entered, and kept on the spreadsheet, then imported into the SPSS version 20 (SPSS) for analysis. Descriptive analysis, including frequency, and percentages, was used for categorical characteristics and the mean score with SD for continuous variables (age in months). T1-beta (power of the test) at 80% set as the power of analysis and χ^2 used for full cells filled or Fisher exact test for cells that expect less than 5 frequencies in 20% of the total cell to identify the proportions differences between vaccinated and unvaccinated hospitalized cases with measles virus infection. This work report aligns with the strengthening the reporting of cohort, cross-sectional and case-control studies in surgery (STROCSS) criteria[33] and registered researchregistry.com with UIN research-registry 8711 https://www.researchregistry.com/register-now#user-researchregistry/researchregistry8711.

Results

Sociodemographic characteristics

A total of 93 measles-hospitalized children participated in the study, mean age in months was 20.9 (SD ± 7.28), over half were boys, 59.1% were born in a hospital, over two-thirds of the mothers or caregivers does not have formal education, and over 48% had monthly family income less than 100 USD (Table 1).

Clinical features of the patients

An 84 (90.3%) of hospitalized measles children does not previously receive at least one dose of MCV1, while 9 (9.7%) received one dose, and none of them had two doses or more. In addition, 95.7% had a high fever, 93.5% had a cough, 67.7% had a rash, 58.1% had coryza, 40.9% had conjunctivitis, and 30.1% had Koplik's spots. Over half (55.9%) had complications associated with measles (Table 2).

Demographic and clinical characteristics associated with measles immunization status were monthly family income ($P = 0.004$), fever ($P = 0.005$), cough ($P = 0.001$), rash ($P = 0.002$), and Koplik's spots ($P = 0.038$) (Table 3).

Table 1

Socio-demographic characteristics

Characteristics	Frequency (*n*)	Percentage (%) *n* = 93
Age in months		
Mean (SD)	Mean = 20.97 (SD ± 7.28)	
Sex		
Boys	54	58.1
Girls	39	41.9
Education of mother or caregiver		
Illiterate	65	69.9
Primary school	24	25.8
≥ Secondary	4	4.3
Place of childbirth		
Home	38	40.9
Hospital	55	59.1
Monthly family income (USD)		
≤ 100	45	48.4
101–200 USD	44	47.3
> 200 USD	4	4.3

Discussion

This study reported that 9.7% of hospitalized measles children become infected since they previously received one dose of

Table 2

Characteristics of clinical features

Characteristics	Frequency (*n*)	Percentage (%) *n* = 93
Fever		
Yes	89	95.7
No	4	4.3
Cough		
Yes	87	93.5
No	6	6.5
Coryza		
Yes	54	58.1
No	39	41.9
Conjunctivitis		
Yes	38	40.9
No	55	59.1
Rash		
Yes	63	67.7
No	30	32.3
Koplik's spots		
Yes	28	30.1
No	65	69.9
Measles complication		
Complicated	41	41.1
Uncomplicated	52	55.9

Table 3

Demographical, clinical, and complication comparison between vaccinated and unvaccinated measles cases

	MCV Immunization status			
Characteristics	Vaccinated (%)	Unvaccinated (%)	χ^2	*P*
Age in months				
9–20 months	2 (4.0)	48 (96.0)	3.988†	0.460†
21–37 months	7 (16.3)	36 (83.7)		
Sex				
Boys	4 (7.4)	50 (92.6)	0.759†	0.384†
Girls	5 (12.8)	34 (87.2)		
Mother or caregiver's education				
Illiterate	8 (12.3)	57 (87.7)	1.777†	0.411†
Primary school	1 (4.2)	23 (95.8)		
≥ Secondary	0 (0.0)	4 (100.0)		
Place of childbirth				
Home	2 (5.3)	36 (94.7)	1.432†	0.231†
Hospital	7 (12.7)	48 (87.3)		
Monthly family income (USD)				
≤100	0 (0.0)	45 (100.0)	11.180‡	0.004*
101–200 USD	9 (20.5)	35 (79.5)		
> 200 USD	0 (0.0)	4 (100.0)		
Fever				
Yes	7 (7.9)	82 (92.1)	7.775†	0.005*
No	2 (50.0)	2 (50.0)		
Cough				
Yes	6 (6.9)	81 (93.1)	11.930†	0.001*
No	3 (50.0)	3 (50.0)		
Coryza				
Yes	6 (11.1)	48 (89.9)	0.303†	0.582†
No	3 (7.7)	36 (92.3)		
Conjunctivitis				
Yes	4 (10.5)	34 (89.5)	0.053†	0.818†
No	5 (9.1)	50 (90.9)		
Rash				
Yes	2 (3.2)	61 (96.8)	9.448†	0.002*
No	7 (23.3)	23 (76.7)		
Koplik's spots				
Yes	0 (0.0)	28 (100.0)	4.292†	0.038*
No	9 (13.8)	56 (86.2)		
Measles complication				
Complicated	2 (4.9)	39 (95.1)	1.932†	0.165†
Uncomplicated	7 (13.5)	45 (86.5)		

*P value less than 0.05.
† χ^2 test.
‡Fisher's exact test.

MCV1. Their immune system does not have enough responses against the measles virus infection. Measles vaccination was recognized as an effective preventive method. Also, previous literature reported vaccine inadequacy in different geographical locations, but it was almost 1%, which is rare. Primary and secondary vaccination failures make people susceptible to infection, particularly in measles-endemic areas. Similar studies reported a high vaccination failure in those who took the vaccine long-term ago[34,35]. Furthermore, another study reported a nonresponsiveness or primary vaccination failure effect in around 1–10% of vaccinated healthy individuals. However, its clinical consequences, immunological background, and whether the failure is antigen-specific or a common phenomenon are generally unknown[36].

One more study reported that in primary vaccination failure, the host had an IgM immunological response, while in secondary vaccination failure, the host had immunological memory for the measles virus[37,38]. Insufficient measles immunization and vaccine failure are major factors against measles outbreak eradication, and improving vaccine logistics and storage is highly needed[21]. A study suggests a booster dose for all children who received the first dose of the measles vaccine before one year of age under an immunization skin test[21]. Moreover, secondary vaccination failure was the most expected[34], and vaccine inadequacies were mostly from incomplete attenuation, incorrect immunization schedules, poor vaccine logistics, and a cold chain. Also, some remarkable host factors, such as host-health status, age, genetic factors, vitamin A deficiency, malnutrition among under-five children, and others are more challenging to define and largely unexplained or unknown[36,39].

This study reported that unvaccinated hospitalized cases are clinically severe compared to vaccinated cases. The most expected clinical features for vaccinated cases were fever, cough, and coryza, while conjunctivitis, rash, and Koplik's spots are not expected for vaccinated cases. In addition, fever, cough, rash, and Koplik's spots are associated with measles immunization status. Similar studies conducted in California and west Africa were in line[39,40]. Vaccinated children at a very young age experienced mild measles clinical symptoms with less ill and less contagious[39,40]. Early in life, vaccinated children showed subclinical infection and sustained epidemics[34,39]. A systematic review reported that those vaccinated had an immune response if exposed to natural measles, and those with documented secondary vaccine failures always had mild clinical conditions[20].

This study reported that measles complications are common in unvaccinated cases with mild to moderate clinical symptoms compared to those vaccinated. The measles vaccine may not protect enough against infection, but it can reduce the severity and complications possibility. A study done in Nigeria supported and reported that measles infection is more severe in unvaccinated children, particularly females, with no severity difference in age[41]. This study suggests considering the protective roles of other antibodies and cell-mediated immune response when measuring vaccine efficacy, particularly in measles-endemic areas with recurrent measles outbreaks[39].

Less contagious were reported for vaccinated cases but, whether it is related to good public health practice or immunization status is still unclear. Finally, this study revealed Rash and Koplik's spots could appear without cough and fever, particularly in previous vaccinated cases, so the study highly recommended measles diagnosis based on measles PCR test results by collecting throat or nasopharyngeal swab specimens instead of diagnosed by clinical features to avoid misdiagnoses. Finally, full vaccination coverage was an effective prevention method against infectious disease outbreaks. Numerous studies recommended vaccination uptake[42–44].

Conclusion

Around one-ten of hospitalized children had one dose of the MCV1; vaccinated cases had fewer illnesses with few complications than unvaccinated. The Somali community suffers recurrent measles outbreaks, and vaccine inadequacy had a vital role. The outbreak control programs and policymakers must focus on improving vaccine logistics, storage, following immunization schedules, and recognizing outbreaks earlier. In addition, the measles diagnosis must be based on test results rather than clinical ones to reduce misdiagnosis. The paper highly recommends improving vaccination uptake, providing booster doses, and conducting further multicentral high sample-size studies to identify whether vaccine inadequacy was due to host-related or vaccine-related factors. Finally, surveillance, contact tracing, vaccination, laboratory investigation, case management, and healthcare workers' training must continue.

Strength and limitation

More data about the measles outbreak is needed in Somalia, especially in Mogadishu, the capital and highest populated city, prevailing insecurity limits investigation efforts. This is the first study in Somalia reporting vaccine inadequacy and comparing vaccinated and unvaccinated hospitalized measles cases that will become a significant guideline for outbreak control programs and policymakers. In addition, the paper provides policy recommendations and emphasizes conducting further studies. A small sample-size with few vaccinated cases was recognized studies limitation.

Ethical approval

Ethical approval was obtained from the Banadir hospital review board (*IRB Ref no: 2022/10/BH0062*) and all data were presented without reflecting personal information to ensure confidentiality and the study was implemented according to the rules and regulations of the World Medical Association's declaration of Helsinki for human experiments.

Consent

Writing informed consent was waived because data was acquired retrospectively by reviewing the patient's medical record and case record form.

Source of Funding

Not applicable.

Author's Contribution

All authors had research ideas, develop the study design, and review previous literature. Khalif and Najib developed a data collection plan, analyzed data, and write a first draft of the manuscript. Ikran designed the study tool. Omar formulates a timeframe and collected data. All authors read and approved the final manuscript.

Conflicts of interest disclosure

All authors declare that they do not have any conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Not applicable.
2. Unique Identifying number or registration ID: Not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): Not applicable.

Data availability statement

All datasets generated and analyzed during the current study are included in this article.

Provenance and peer review

Not commissioned, externally peer reviewed.

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