American Journal of Infectious Diseases and Microbiology, 2016, Vol. 4, No. 6, 123-128
Available online at http://pubs.sciepub.com/ajidm/4/6/3

DOI:10.12691/ajidm-4-6-3

Outcomes of Management of Cholera Outbreak among IDPs and Non-IDPs in a Complex Emergency Setting of South Sudan

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Abstract Displaced communities barely have access to safe drinking water and sanitation, therefore the risk of communicable diseases like cholera, acute watery diarrhea, and acute bloody diarrhea increasing exponentially. Since the outbreak of the conflict in 2013 in South Sudan, an estimated 1.87 million people have been displaced and are living in Internally Displace Persons Camps (IDPs). Consequently, outbreaks which include cholera have been reported in 2014 and 2015. We retrospectively analyzed the data from these two outbreaks to compare risks and other characteristics among the IDPs and non-IDPs. It was noted that the risk of cholera was higher among the IDPs compared to non-IDPs. Cholera cases in IDPs were more likely to be children under five years compared to older persons from non-displaced populations. Even though cases of cholera in IDPs were 1.45 times likely to seek care after 48hrs, this was not statistically different from Non-IDPs. Cholera cases in the IDPs were more likely than those in the host communities to have received zero doses of oral cholera vaccine. The burden of cholera cases among sexes, duration of admission of admission and survival rates were not significantly different among IDPs and Non IDPs. In the context of timely response to protect vulnerable populations and coupled with the limitations of the global oral cholera vaccines stockpile management, it is recommended that children less than five years in IDPs should be prioritized for oral cholera vaccination.

Keywords: *Cholera, Internally Displace Persons Camps (IDPs), non-IDPs, Oral Cholera Vaccine, Conflict setting, South Sudan*

Cite This Article: Wamala F. Joseph, Mpairwe M Allan, Boateng Kofi, Maleghemi Sylvester, Ujjiga T. A. Thomas, Mutebi Moses, Lyosi Evans, Rumunu P. John, and Usman Abdulmumini, "Outcomes of Management of Cholera outbreak among IDPs and Non-IDPs in a Complex Emergency Setting of South Sudan." *American Journal of Infectious Diseases and Microbiology*, vol. 4, no. 6 (2016): 123-128. doi: 10.12691/ajidm-4-6-3.

1. Introduction

Cholera is a major global public health problem in developing countries where the risk is highest in congregate populations like slums and displaced populations with poor [1]. Cholera is a major cause of diarrhea disease burden and is estimated to account for 2.9 million cases and 95,000 deaths globally every year [2]. Over half of these cases are reported from countries like South Sudan in sub-Saharan Africa where cholera is a common disease outbreak [3]. Cholera is a severe intestinal infection caused by toxigenic strains of Vibrio cholerae serogroup O1 or O139 with symptoms and signs ranging from asymptomatic carriage to severe diarrhea, vomiting, and profound shock [4] Untreated cholera is fatal in ≈25% of cases, but with aggressive volume and electrolyte replacement, the number of persons who die of cholera is limited to <1% [5].

Cholera remains endemic in South Sudan and is responsible for inflicting a high burden of disease upon vulnerable populations in endemic and epidemic situations. The exact scale of the problem is uncertain because of limitations in existing surveillance systems, differences in reporting procedures, and failure to report cholera cases to WHO [1] and other relevant authorities. Between 2006 and 2016, South Sudan experienced 6 major cholera epidemics in many parts of the country where safe water supply, sanitation, food safety and hygiene situations were inadequate and access to health care services was not available. Since the signing of the comprehensive peace agreement in 2005, there have been seven major cholera outbreaks in South Sudan and typically occurred during the rainy season in states along the big rivers. It is noted that IDPs, refugees and other areas with high concentrations of people have a higher risk of suffering cholera outbreaks [5].

Since the outbreak of the conflict in 2013, an estimated 1.6 million people have been displaced and are leaving in IDPs Camps [6]. Displaced communities barely have access, to safe drinking water and sanitation, the risk of communicable diseases like cholera, acute watery diarrhea, acute bloody diarrhea increase exponentially [7]. Consequently,

three cholera outbreaks have been reported in South Sudan since the onset of the current crisis.

In South Sudan, the burden of cholera has increased during the period post-CPA. Cholera is most common in areas that lack clean water sources and sanitation services. Areas like refugee camps and urban slums, where people live in close proximity with little to no access to clean water and sanitation facilities are at a very high risk of experiencing a cholera epidemic. Typical at-risk areas include peri-urban slums where basic infrastructure is not available and camps for internally displaced people where the minimum requirements of clean water and sanitation are not met [8]. The greatest risk occurs in over-populated communities and refugee settings characterized by poor sanitation, unsafe drinking water and increased person to person transmission [9]. Individuals with lower immunity, such as malnourished children or people living with HIV, are at greater risk of death if infected by cholera. Cholera is one of the most dreaded diseases in the world, in some cases leading to death within 24h if left untreated. Without treatment, severe infection has a mortality rate of 30–50% [5].

Although prevention of cholera requires clean water supplies and appropriate sanitation facilities, the implementation of these improvements in low-income countries is often slow. Regions, where such interventions have not yet been put in place, are those at greatest risk of cholera epidemics. Cholera outbreaks are often associated with population displacements, humanitarian emergencies but in addition to the regular public health measures, the use of OCV has greatly enhanced the outcome of the public health interventions and protected vulnerable populations [10]. Outbreaks become endemic when a large proportion of the population is immune or semi-immune to infection. Mass vaccination against cholera is a relatively new strategy that could be used in conjunction with efforts to improved sanitation in certain high-risk populations; however, identification of these populations requires effective disease surveillance [1]. The long-term solution for cholera control lies in economic development and universal access to safe drinking water and adequate sanitation.

Although the management and treatment of Cholera remain straight forward, the lifesaving interventions life replacement of lost fluids can be difficult, to administered where there is a shortage of medical health facilities which is the case in complex humanitarian emergencies and the rapid progression of the disease means that there is only a narrow therapeutic window [11].

Early detection of outbreaks is critical for reducing mortality rate to the recommended below 1% by ensuring access to treatment and controlling the disease. To achieve this, all partners involved should be properly coordinated and those in charge of water and sanitation must be included in the response strategy. The main tools used for the treatment of cholera are:

- proper and timely rehydration in cholera-treatment centers and oral rehydration corners;
- specific training for proper case management, including avoidance of nosocomial infections;
- sufficient prepositioned medical supplies for case management, e.g. diarrhoeal disease kits;
- improved access to water, effective sanitation, proper waste management, and vector control;
- enhanced hygiene and food safety practices; and
- improved communication and public information
- Vaccination of the most vulnerable and at-risk population with 2 doses of OCV.

Following the 2013 crisis in South Sudan, a humanitarian crisis ensued with nearly one million displaced persons. Many lived in congested camps with sub-optimal access to safe water and sanitation facilities. In line with the WHO 2010 position paper on oral cholera vaccines, the Ministry of Health adopted the complementary use of oral cholera vaccines alongside water, sanitation, and hygiene interventions to mitigate the risk of cholera in displaced populations.

The intent of this study was to assess the effectiveness of cholera prevention and response interventions by comparing the magnitude, severity, geographical spread, outbreak detection and response; and clinical management of cholera in IDP and host communities within the context of the 2013 humanitarian crisis.

2. Methods

This was a retrospective study, comparing the outcomes of cases of cholera reported in IDP camps and Non-IDP camps in South Sudan in 2014 and 2015. We examined the risk of the burden of cholera between the two populations based on selected outcomes provided for in the lines list, and further used secondary data of previous outbreaks from 2006 to 2015 to understand trends of cases and case fatalities over time.

Thus, the risk of the burden of cholera cases in IDPs and Non-IDPs stratified by age group, sex, residence outside the capital, survival, non-exposure to the Oral Cholera Vaccines, duration of reporting and duration of admission defined the key variables for our study.

South Sudan Cholera Outbreak Management Mechanism

The MoH leads a coordination team, the Emergency Preparedness and Response that ensures that all partners for Surveillance, Case Management, Social Mobilization, WASH, and Logistics are engaged in cholera outbreak. The MoH has the Integrated Diseases Surveillance and Response system since 2006 that is implemented with technical guidance from WHO. The IDSR system provides a weekly review of trends of all outbreaks including cholera since 2009. The team is guided by relevant technical protocols on surveillance and response. There also exist contingency plans for cholera outbreaks detection and response including strengthened capacity for Early Warning Systems and Laboratory Diagnosis.

Case Definition: We used the MoH and WHO definitions with a suspected case of cholera as a patient aged five (5) years or more presenting with severe dehydration or a death from acute watery diarrhea. As per the guidelines after a laboratory confirms a case of cholera, the case definition of a suspected case changes by lowering the age of the affected person to 2 years or more, with acute watery diarrhea, with or without vomiting. A confirmed cholera case is a suspected case in which Vibrio cholerae O1 or O139 has been isolated from the stool sample of the patient.

Case Detection and Investigation: The alert threshold for cholera in South Sudan is one suspect case, and once

surpassed, an immediate investigation warranted within 48-72 hours of the report.

Laboratory Confirmation: The stool sample was used to conduct on-the-site rapid cholera testing using Crystal VC (Span Diagnostics Ltd., India). For each stool sample collected, a stool swab preserved in Carry Blair was secured and transported to the National Public Health Laboratory in Juba for microbiological culturing under standard conditions. A sample of positive isolates and negative samples were shipped to the Central Public Health Laboratory in Kampala, Uganda for quality control testing and microbial sensitivity testing. For each of the new areas reporting suspect cholera cases, at least 10 stool samples were collected in a stool container to facilitate laboratory confirmation.

Data Handling: Information on patients was collected by clinicians involved in the management of the patients using standard medical format and tools, with initial portion consisting of demographic data, then presenting signs and symptoms, followed by an observation and physical examination and concluded with diagnosis and treatment. Records on previous immunization with OCV were also collected. The forms are then submitted to the recorder and or the laboratory technician. All suspect cases that met the case definition were entered into a cholera line at the end of the day 23.59hrs the line list is transferred to the electronic line list by data clerks, while the initial form is filed with a treatment sheet generated. The data is cross-checked for errors before and after entering it into the spreadsheets.

Data analysis: Cholera case based data was entered into the Microsoft excel. Where possible, responses were coded to minimize data entry errors. Data cleaning and validation of entries was done daily. The data set was exported into IBM SPPS Statistics version 21 to perform bivariate analysis to identify predictors effective response in displaced population as compared to host communities. Subsequently, multivariate analysis was performed using stepwise binary logistic regression in SPSS. To do this, all the factors that had a p-value of 0.25 or less in bivariate analysis were entered into the model one at a time with only significant ($p<0.05$) variables being left in the final model. However, potential confounders like sex, age, and residence were left in the final model regardless of the p-value. We used Arc GIS to map cholera cases by the residence to identify cholera transmission hotspots.

3. Results

The historical records showed that cholera cases from 2006 to 2015 peaked in 2009 with 48,035 cases but declined to 1818 cases in 2015. Cholera outbreaks were not reported from 2010 – 2013. The case fatality rates for the same period (2006 – 2015) showed a declining trend from 2.9% in 2006 to 0.13% in 2009 but a sharp increase to 2.9% in 2014 (see Table 1).

In the 2014 – 2015 outbreaks a total of 8,208 cases were reported of which 85.9% were in the Non-IDP population and the rest, 14.1% of the IDP population. In the Non-IDP population, of the 7,051 cases reported, over 90% of cases were reported in Central Equatoria, (53.9%) and Eastern Equatoria, (42.2%). Out of the total of 1156 cases in the IDP population 20.2% and 79.8% were recorded in Central Equatoria and Upper Nile respectively. Thus, no cases in displaced populations were reported from Eastern and Western Equatoria and Jonglei states.

The Case fatality from the 2014 – 2015 outbreaks was high in the non-IDP population, 2.33% as compared to the IDP population 1.90%. Upper Nile recorded the highest case fatality rates in both Non-IDP and IDP populations, 3.28% vs 1.95% respectively. No fatalities were recorded in Western Equatoria as shown in Table 2 below.

As seen from Figure 1, cholera cases started in late April 2014, four months into the humanitarian crisis that started in December 2013. The index case, a 28-year-old male resident of Juba 3 IDP camp was detected on 29 April 2014 and the outbreak declared on 15 May 2014. Just like the 2014 cholera outbreak, the initial cases during the 2015 cholera outbreak were detected in Juba 3 IDP camp on 26 May 2015.

Table 1. Trends of Cholera outbreaks in South Sudan

Year	Cholera		
	Cases n	Death n	CFR (%)
2006	19,277	588	2.9
2007	22,412	411	1.8
2008	27,017	154	0.57
2009	48,035	60	0.13
2014	6,421	167	2.6
2015	1818	41	2.2

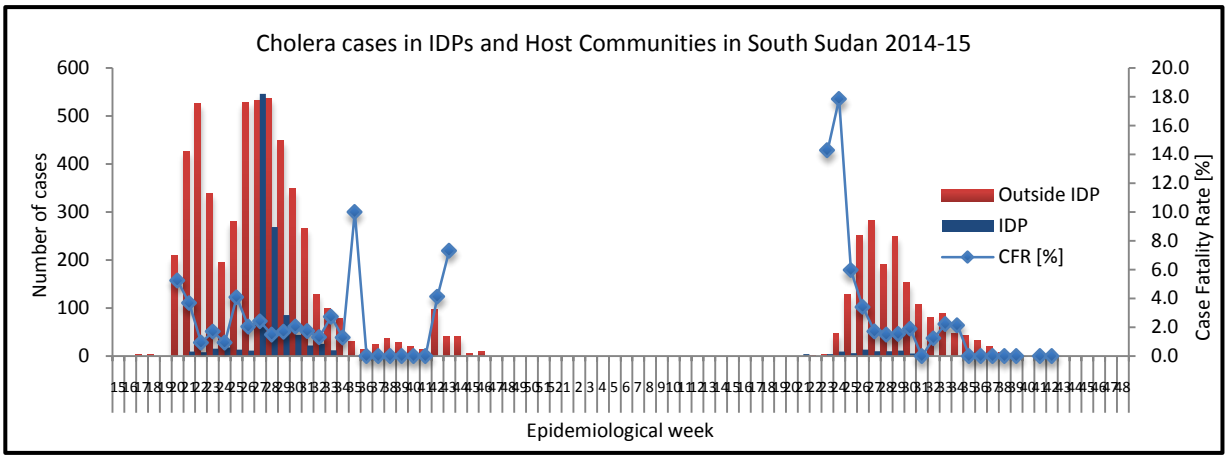

Figure 1. Cholera epidemic curve by settlement in South Sudan, 2014-15

Table 2. Cholera case distribution by residence, 2014-2015

State	Cholera cases in 2014-15			CFR [%] 2014-15	
	non-IDP # (%)	IDP # (%)	Total # (%)	non-IDP	IDP
Central Equatoria State	3806 *(53.9)*	234*(20.2)*	4040*(49.2)*	2.36	1.71
Eastern Equatoria State	2979*(42.2)*	0 (0.0)	2979 *(36.3))*	2.32	0
Jonglei State	140*(1.9)*	0 (0.0)	140 *(1.7)*	0.41	0
Upper Nile State	122*(1.7)*	922*(79.8)*	1044 *(12.7)*	3.28	1.95
Western Equatoria State	3*(0.4)*	0(0.0)	3 *(0.01)*	0	0
National	7051*(85.9)*	1156*(14.1)*	8208 (100.0)	2.33	1.90

In the Non-IDP population in 2014, three major transmission peaks were seen in epi weeks 22, 28 and 42 with 509, 372, 49 cases respectively and a corresponding case fatality rates of 3.1%, 2.7%, and 8%. These peaks coincided with peak transmission in Torit, Lopa/Lafon and Ikotos, all Eastern Equatoria state. In contrast to the IDP population in the same year, one transmission peak was observed in ep week 27 that peak coincided with peak transmission in Wau Shiluk, an IDP camp in Malakal County in Upper Nile state where 516 cases including 16 deaths (CFR 3%) were reported.

The outbreak in 2015 had three peaks in epi weeks 27, 29 and 39 recording corresponding cases of 282, 249 and 89 and respective case fatalities of 1.8%, 1.6%, and 2.2%. The peaks coincided with increased transmission in Juba and Kojo-Keji counties in Central Equatoria, Bor in Jonglei states. Among the IDPs, the transmission levels were low reaching the highest peak of 13 cases in week 26 before declining to zero cases by week.

As seen from Table 3, the incidence of cholera among children under 5years was 198.05/10000 in IDP as against 18.58/10000 in non-IDPs; a similar trend was observed among children five years and above in both IDPs (62.67/10000) and non-IDP (17.96/10000).

Children less than 5years in the IDP were had more than 3 times excess burden of cholera cases as compared to counterparts in the Non-IDP camps (OR 3.03, C.I. (1.54 – 5.96) p<0.01).

The burden of cholera cases per sex in IDP and Non-IDP populations was not statistically significant (OR 0.83; C.I. (0.46, 1.48; p=0.52).

Unadjusted odds analysis showed that IDPs living outside Juba county compared to Non-IDP outside Juba had 4 times fold of cholera cases (OR 4.17; C.I. [3.57, 4.83]; p<0.001).

Table 3. Case distribution by age and gender in South Sudan, 2014-2015

Variable		number of cases		cases per 10,000	
		non-IDP (%)	IDP (%)	non-IDP	IDP
Age	<5 years	1439	489	18.58	198.05
	≥5 years	5565	619	17.96	62.67
Sex	Female	3314	545	17.83	91.97
	Male	3725	557	18.50	86.76

Table 4. Bivariate and multivariate analyses of factors associated with cholera in IDPs, 2014-15

Variable	IDP n=1156 (%)	Non-IDP n=7051 (%)	Unadjusted OR bivariate analysis (95% CI)	Adjusted OR multivariate analysis (95% CI)
Age <5 years	489 (42.3)	1440 (20.4)	3.054 (2.68-3.49)	3.03 (1.54-5.96)
≥5 years	619 (53.5)	5566 (78.9)	p<0.0001	p<0.01
Sex Male	557 (48.2)	3730 (52.9)	0.91 (0.8-1.03)	0.83 (0.46-1.48)
Female	545 (47.1)	3314 (47.0)	p=0.14	p=0.521
Residence Other County	922 (79.8)	3431 (48.7)	4.17 (3.57-4.83)	NS
Juba County	234 (20.2)	3617 (51.3)	p<0.0001	
Survival Alive	1134 (98.1)	6887 (97.7)	1.23 (0.78-1.93)	
Died	22 (1.9)	164 (2.3)	p=0.37	
Delay seeking care ≥ 2days	21 (1.8)	342 (4.9)	1.45 (0.92-2.29)	
< 2days	268 (23.2)	6321 (89.6)	p=0.112	
OCV doses None	139 (12)	11 (0.2)	0.012 (0.006-0.022)	0.005 (0.002-0.013)
1-3	997 (86.2)	6640 (94.2)	p<0.0001	p<0.0001
Cholera culture Positive	16 (1.4)	57 (0.8)	2.93 (1.13-7.60)	
Negative	7 (0.6)	73 (1.0)	p=0.027	
Admission duration ≥ 4days	139 (12)	386 (5.5)	1.014 (0.82-1.25)	
< 4days	795 (68.8)	2238 (31.7)	p=0.90	
Severity of Illness				
Mild-Moderate	704 (60.9)	3455 (49.0)	2.59 (2.23-3.00)	
Severe	262 (22.7)	3324 (47.1)	p<0.0001	
Year				
2014	1080 (93.4)	5309 (75.3)	4.66 (3.67-5.92)	7.87 (2.44-9.71)
2015	76 (6.6)	1742 (24.7)	p<0.0001	p<0.0001

OR refers to Odds Ratio; **CI** refers to Confidence Interval; please note that missing values were excluded.

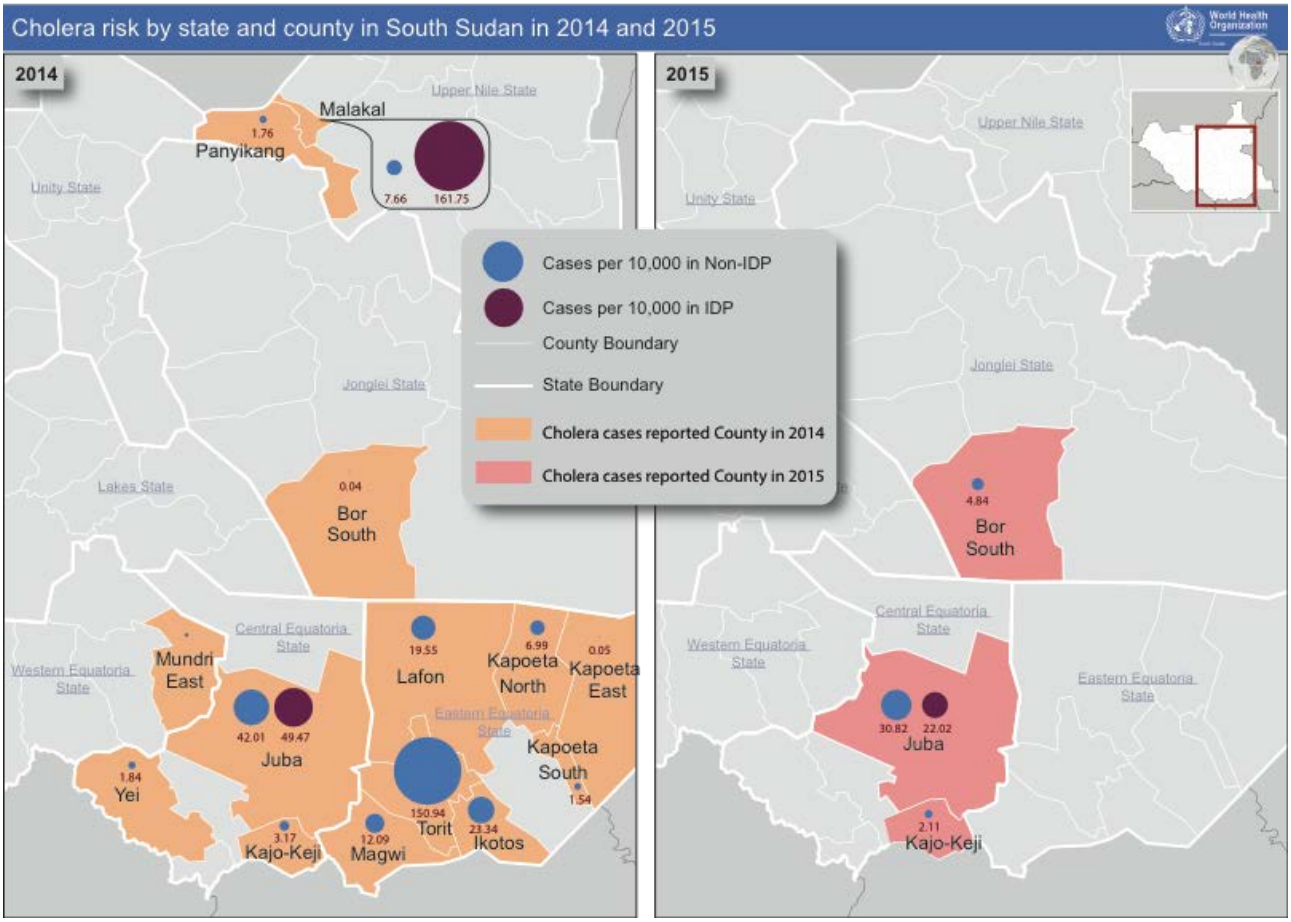

Figure 2. Cholera risk by state and county in 2014 and 2015

Even though cases of cholera in IDPs were 1.45 times likely to seek care after 48hrs, this was no statistical difference between those in Non-IDPs (OR=1.45; C.I. [0.92- 2.29]; p=0.11). Duration of admission of cases both in IDPs and Non-IDPs were also unequivocal (OR=0.01, C.I. [0.82 – 1.25] p0.90).

Outcome of care also showed no statistically significant difference (OR 1.23, C.I. [0.78 – 1.93] p0.37) between survival rates among IDP and Non - IDPs (see Table 4).

Cases of cholera in IDP population that did not receive the OCV vaccine were significantly protected (OR = 0.012 C.I. [0.0 – 0.02] p<0.001) compared to those in Non-IDPs who did not receive the vaccine. Thus, the herd immunity by OCV ensured that 99% of cases in non-vaccinated in IDP were protected as compared to Non-IDPs.

4. Discussions

Two years after gaining independence, South Sudan was plunged into conflict. By November 2015, the total population displaced was estimated at 2.3 million, of which 1.66 million are internally displaced. With access to safe water estimated at less than 70% and the use of improved latrines at 7% prior to the onset of the crisis [12], humanitarian actors had an immense challenge providing optimal living conditions to displaced populations. This trend of events increased the risk of disease outbreaks, especially in displaced populations. Hence with barely four months into the crisis, cholera was confirmed and has continued to recur during the two years of the crisis.

Historical records showed that cholera cases in South Sudan were reported from 2006 to 2009, however, there were no reports of cholera during the independence years from 2010 to 2013. Our findings are consistent the published literature that greatest risk of cholera occurs in over-populated communities and refugee settings characterized by poor sanitation, unsafe drinking water and increased person to person transmission (6). For the two years 2014 and 2015, the risk of cholera was higher in the IDPs when compared to the non-IDP populations, especially outside Juba where IDPs had 4 times risk of cholera compared to non-IDPs. This highlights the unmet need for adequate access to safe water and sanitation in IDP camps/settlements.

Despite the higher risk of cholera among the IDPs, both displaced and non-displaced populations are vulnerable to cholera in South Sudan. The 2014 and 2015 outbreaks affected both IDPs and non-IDPs populations with the 2014 outbreak affecting 15 counties and 2 IDP camps compared to the smaller outbreak in 2015 which affected three counties and only one IDP camp. The vulnerability of both population groups is especially apparent in Juba in both 2014 and 2015 outbreaks. This is not surprising since an earlier publication on risk factors for sustained cholera transmission, Juba county, South Sudan, 2014 [13] found the risk factors for the 2014 outbreak to include eating outside the home. Since the IDPs in Juba usually move to the town during the day, eating and drinking from

the same sources, they could both be equally exposed to cholera.

Though both the 2014 and 2015 outbreaks were first detected among the IDPs, the retrospective discovery of missed cases in the host communities indicated that the epidemic may have started outside the IDP camps, but missed. This confirms the higher sensitivity of surveillance system observed in the IDPs compared that of the health facilities outside the IDPs camps [14]. Once the outbreak was established, there were no differences in the times spent seeking care by both IDPs and non-IDPs as well as the duration of admission. This could be related to the response activities which are similar in both settings coordinated by the EPR committees.

The risk of cholera in emergency setting is known to affect more children less than five years, however, the risk in IDP camps is scanty. Moreover, prioritization of critical interventions such as vaccination, in the face of management of oral cholera stockpiles for efficiency is not well documented. We found that children less than 5 years among the IDPs had more than 3 times excess burden of cholera cases as compared to counterparts in the Non-IDP camps (OR 3.03, C.I. (1.54 – 5.96) $p<0.01$). This could be related to overcrowding, where children in camps had fewer facilities for hygiene, mix more closely with adults and other children compared to those outside the camps. The child care outside the IDP camps could also be better. The higher burden of cholera amongst the children in IDP camps is also an indicator for their prioritization in cholera vaccination.

Host communities had higher CFRs from cholera compared to IDP populations; however, differences survival rates between the two were not significant.

IDP population that did not receive the OCV vaccine were significantly protected compared to those in Non-IDPs who did not receive the vaccine. Thus, the herd immunity by OCV ensured that 99% of cases in non-vaccinated in IDP were protected as compared to Non-IDPs.

5. Conclusions

Cholera cases in IDPs were more likely to be children under five years compared to those from non-displaced populations. Cholera cases in the IDPs were more likely to have received zero doses of OCV when compared to non-IDPs.

In the context of timely response to protect vulnerable populations and coupled with the limitations of the global oral cholera vaccines stockpile management, children less than five years in IDPs should be prioritized for oral cholera vaccination.

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