



Research Article

Outbreak of Diphtheria in South Darfur, Sudan

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Abstract

Introduction: A cluster of suspected cases of diphtheria among children occurred in Al-Sunta locality in State of South Darfur, Sudan triggered an investigation to confirm occurrence, assess magnitude of and assist in response to the outbreak. **Methodology:** Village-to-village active case-finding guided with a sensitive case definition and verbal autopsy. Focus Group Discussions (FGDs) with community leaders in 15 villages and nomadic pastoralists that reported cases. **Results:** Out of 97 cases of diphtheria including 12 deaths (Case Fatality Ratio (CFR) = 12.4%). Female: male sex ratio was 1.69. The mean age (N, SD, IQR, was 12.5 (61, 8.6., 7.0-16.0) and 11.0 (36, 6.0-13.5) for females and males respectively; (p>0.05). Most of the cases occurred among ten neighboring villages. There were no cases reported among nomadic pastoralists. Of all cases, 46 (83.6%) were not vaccinated. Only 40 out of 111 school children were vaccinated (36.4%; [95% Confidence Interval (CI): 27.1% - 45.7%]). There were more vaccinated children among older pupils (grade 6-8) as compared to younger children (grade 1-3). Only five of the fifty-two (9.6%; 95% CI: 3.2- 21.0%) nomadic pastoralists who attended an extended FGD among nomads indicated that vaccinating their children against poliomyelitis 3.8% (95% CI: 1.6% -17.6%). Only two (3.8%; 95% CI: 1.6% -17.6%) reported taking their children to one or more of the routine vaccinations at fixed sites. **Conclusions:** The vaccination coverage against childhood Immunizable diseases was very low in affected localities in South Darfur corrected by implementation of a vaccination campaigns and strengthening routine childhood vaccination program.

Keywords: Diphtheria; Outbreak; Sudan; Darfur; Pastoralists; Focus Discussion Group (FDG)

Introduction

Vaccines are the most cost-effective form of medical intervention in the least developed countries, as they contributed in eliminating or significantly decreasing the occurrence of many diseases which can cause disability and death, and led to increased

life expectancy [1-3]. Many childhood diseases have almost been eliminated in many developed countries primarily through the introduction of routine childhood immunization, pediatric care and improved hygiene status [3,4].

Diphtheria was a leading cause of childhood morbidity and mortality in the pre-vaccination era [5]. In the pre-vaccination era, diphtheria was a leading cause of childhood mortality. [4] Diphtheria usually affects preschool and school-age children, and

is generally rare in infants and adults [6]. Globally, diphtheria has been showing a declining trend due to effective childhood vaccination programs [5]. Re-emergence of diphtheria in many countries, India [5, 7-12] Pakistan, Iran and Sudan are among the list of ten countries with the highest prevalence of diphtheria between 2010 and 2017 [13]. Recent diphtheria outbreaks in many countries, including Sudan, demonstrated a shift in the age distribution of cases to older children and adults [6,14].

A village midwife noted occurrence of a cluster of suspected cases of diphtheria in a village in Al Sunta locality in State of South Darfur, Sudan during the International Epidemiologic Week (IW) 43, she notified the State Ministry of Health (SMOH) on 4 November 2019 (IW 44). More suspected cases of diphtheria were reported from Al Sunta, Buram and Merchang localities in South Darfur. Supported by the World health Organization (WHO), the SMOH deployed a Rapid Response Team (RRT) to confirm occurrence, assess magnitude and severity of the outbreak and assist in implementation of appropriate response measures.

Methodology

The Study Area

Al-Sunta locality is located in the south-eastern part of South Darfur State, bordered to the east by East Darfur State and to the north by Geraidha locality, to the south by South Sudan and to the west by Buram locality. The locality lies at the periphery of the State with poor infrastructure. A total of 90,880 people reside in 41 scattered villages in Al Sunta locality. Children less than one year constitute 3,311 (3.64%); and under 5-year old children are about 15,441 (17%). There are sizable numbers of nomadic pastoralists, Internally Displaced Populations (IDPs) and refugees in the locality. There are neither paved roads nor electricity in the locality. There are intermittent telecommunication services. The PHC services are provided by only one health facility that belongs to the health insurance. Vaccination coverage is very low in Al Sunta locality. The Penta 3 coverage was 37%, 75%, and 91% for the years 2016, 2017 and 2018 respectively [15]. Currently, Penta 3 coverage stands at 33% in 2019 [10]. A laboratory confirmed outbreak of diphtheria was reported from Al Salam locality in South Darfur in 2018 (Figure 1).



Figure 1: Map of Al-Sunta locality.

Data collection

A suspected case of diphtheria was defined as any child or young adult who complained of moderate fever, sore throat, unilateral or bilateral swelling of the neck, enlarged tonsils, and or epistaxis and mild exudative pharyngitis during the month prior to the visit of the investigation team. The investigation team ascertained the vaccination history and examined suspected cases and contacts for presence of pseudo-membranes form in the throat. Presence of grey membrane was considered as a clinically confirmed case. Verbal autopsy was taken from parents of the deceased children using case definitions and extra probing questions to confirm or rule out the diagnosis of diphtheria. Parents were asked about questions related to cardiac (chest pain) and neurological manifestations. The investigation team asked about occurrence of similar cases among neighbors or acquaintances. Local names of the disease were used to identify active cases in the community (Dignn daier, Al-Khannag, Abu Hilaig). The active case finding was based on a line listing of the reported suspected cases.

A total of 111 laboratory specimens (52 oropharyngeal and/or nasopharyngeal swabs and 59 5-ml blood samples) were collected from suspected cases, close contacts and recovered cases by trained physicians or a laboratory technician. Ames transport media was used for swabs while clotted blood samples were separated and serum collected. All specimens were kept in ice packs in sample carrier during the field visit. Samples were transported by road to Nyala, Capital City of the State, and were shipped to the National Public Health Laboratory (NPHL) in Khartoum for confirmation of diagnosis. Polymerase Chain Reaction (PCR) was used to differentiate toxigenic and non-toxigenic diphtheria.

The investigation team used structured and open ended questionnaires to guide interviews and Focus Group Discussions (FGDs) to stimulate discussion and allow for probing questions. The key informants included Director General, State Ministry of Health (SMOH), Expanded Program on Immunization (EPI) Director, SMOH, EPI Officer in Buram locality, and Medical Assistants in Buram and Al Sunta localities. The investigators also held series of Focus Discussion Groups (FGDs) with community leaders in fifteen villages that reported suspected cases of diphtheria and associated deaths. The team conducted an expanded FGD with nomadic pastoralists who attended the weekly market in Tajreeba Town. The team asked for regular pathways and season of nomadic pastoralists' movement. Two major schools in the area (boys and girls) were visited to identify additional unreported cases of diphtheria, vaccination history and absenteeism from school. The ad hoc surveys included 111 male schooled children in Tajreeba School in Al Sunta locality.

Interviews and FGDs were videotaped and transcribed.

Parents and healthcare workers were asked to describe in detail the sequence of symptoms and progression of the disease, the medical care and related events. Parents were also asked about the history of vaccination of their children using quick ad hoc survey in Tajreeba market. Community members were asked if vaccinators were visiting their areas. Probing questions were asked regarding the circulating rumors on animal deaths and pesticides sprayed to kill migratory birds in the area.

While visiting the health facilities, the investigators observed and reviewed logbooks at Family Health Units (FHUs) to look into the reports, feedback, and defaulters tracing mechanisms. The team observed functionality of the cold chain systems and potency of the vaccines. Treatment regimens used to manage suspected diphtheria cases were also reviewed. The team visited Nyala Teaching Hospital to assess the capacity and preparedness for case management including presence of an isolation ward. The team assessed the capacity, availability and functionality of State Public Health Laboratory (SPHL) in terms of staff, equipment, reagents, and consumables. The investigators reviewed the recent Simple Spatial Survey Method (S3M) and the EPI data for South Darfur State to assess the immunization coverage.

Results

Confirmation of the outbreak

The index case was a 7-year old girl from Um Baighla village in Al Sunta locality on International epidemiologic Week (IW) 42. She demonstrated symptoms and signs consistent with case definition of a probable case of diphtheria. She had been playing with the son and daughter of a farmer from Um Kitaika; the boy developed similar symptoms on IW 43 and spread the disease in Um Kitaika. All of the three primary cases died.

As of 04 March 2020, a total of 97 probable cases of diphtheria were reported by the disease surveillance system: 36 males (43.6%) and 31 girls (56.4%); the female: male sex ratio was 1.3. The diagnosis of diphtheria was clinically and laboratory confirmed. Toxigenic *Corynebacterium diphtheria* was identified by culture and Polymerase Chain Reaction (PCR) from one out of six pharyngeal swabs collected by the RRT. Most of the cases occurred among fifteen neighboring villages around Al Sunta locality, mainly Um Kitaika village and Tajreeba town.

In two of the households visited, they reported three cases and two deaths from same house. There were no cases reported among nomadic pastoralists in the locality. Of all cases, 90 (92.8%) were not vaccinated. The mean age (N, SD, IQR, was 12.5 (61, 8.6., 7.0-16.0) and 11.0 (36, 6.0-13.5) for females and males respectively; the difference was not statistically significant two-tailed p value=0.3608. Twelve cases died (Case Fatality Ratio (CFR) = 12.4%).

Most of the cases occurred among neighboring villages around Al Sunta locality. there were three cases and two deaths from same house. There were no cases reported among nomadic pastoralists. Most of the suspected cases were not vaccinated (No data were available).

Figure 2 shows the epidemic curves of the diphtheria outbreak in South Darfur, 2019. The outbreak spread serially from one village to another. More cases occurred in a large village, Um Kitaika and a small town I the locality, Tajreeba.

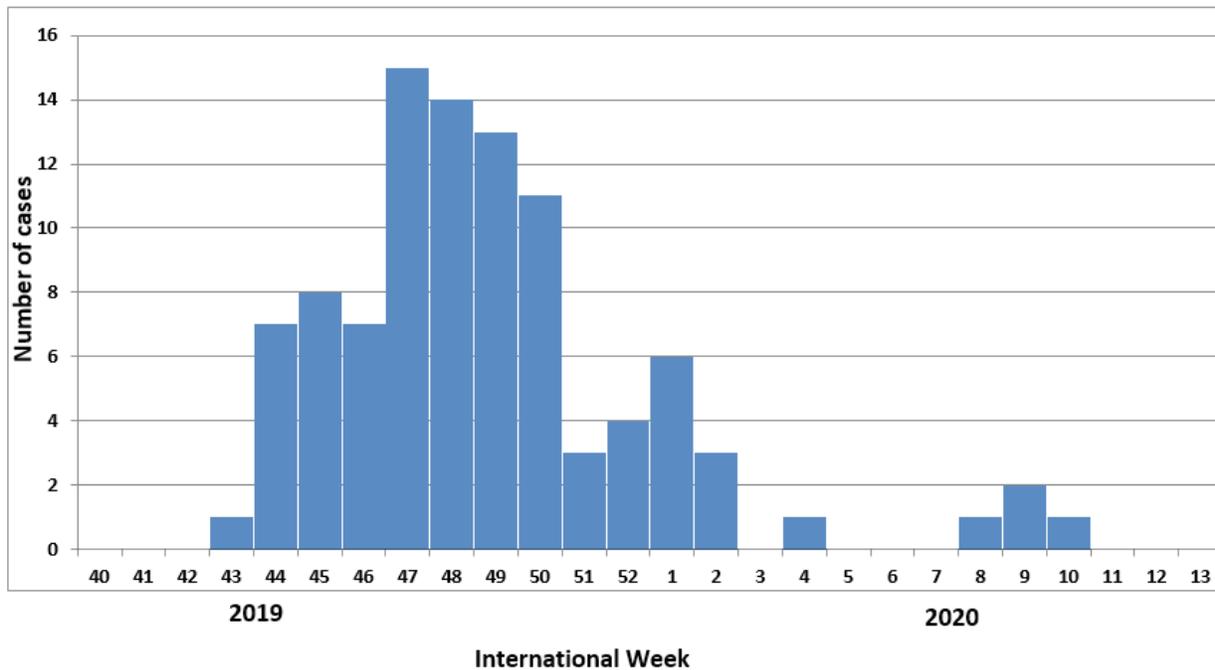


Figure 2: The epidemic curves of the diphtheria outbreak in South Darfur, 2019-2020.

Parents of suspected diphtheria cases and deceased children stated that their children had high grade fever, sore throat, dysphagia (difficulty in swallowing), neck swelling, protrusion of the tongue and some children suffered from difficulty in breathing. The symptoms got worse on the third day following onset of the disease. Later, some patients complained of discharge from the mouth and epistaxis. Verbal autopsy from parents of the deceased children reported that children were suffering from severe chest pain just before death. There were no neurological symptoms observed or reported. The health care workers mentioned that the tonsils were excessively enlarged among few of the cases, almost touching each other. They reported observation of grey membrane behind the tonsils in some of the cases.

Low immunization coverage

The cold chain system in Al Sunta was not functioning for more than three years. Vaccines were kept in refrigerators in nearby shops along with soft drinks. The vaccinator stated that he reported the case to EPI department repeatedly with no response. The investigators found out the Vaccine Vial Monitor (VVM) reading of the vaccines stored in the private refrigerator was almost stage 3. In Rammis village, Al-Sunta locality, a cold chain system was installed in the Family Health Unit (FHU) in May 2019. There were no means of transportation to conduct outreach vaccination services. More defaulters were registered in Al Sunta and Buram localities (Figure 3).

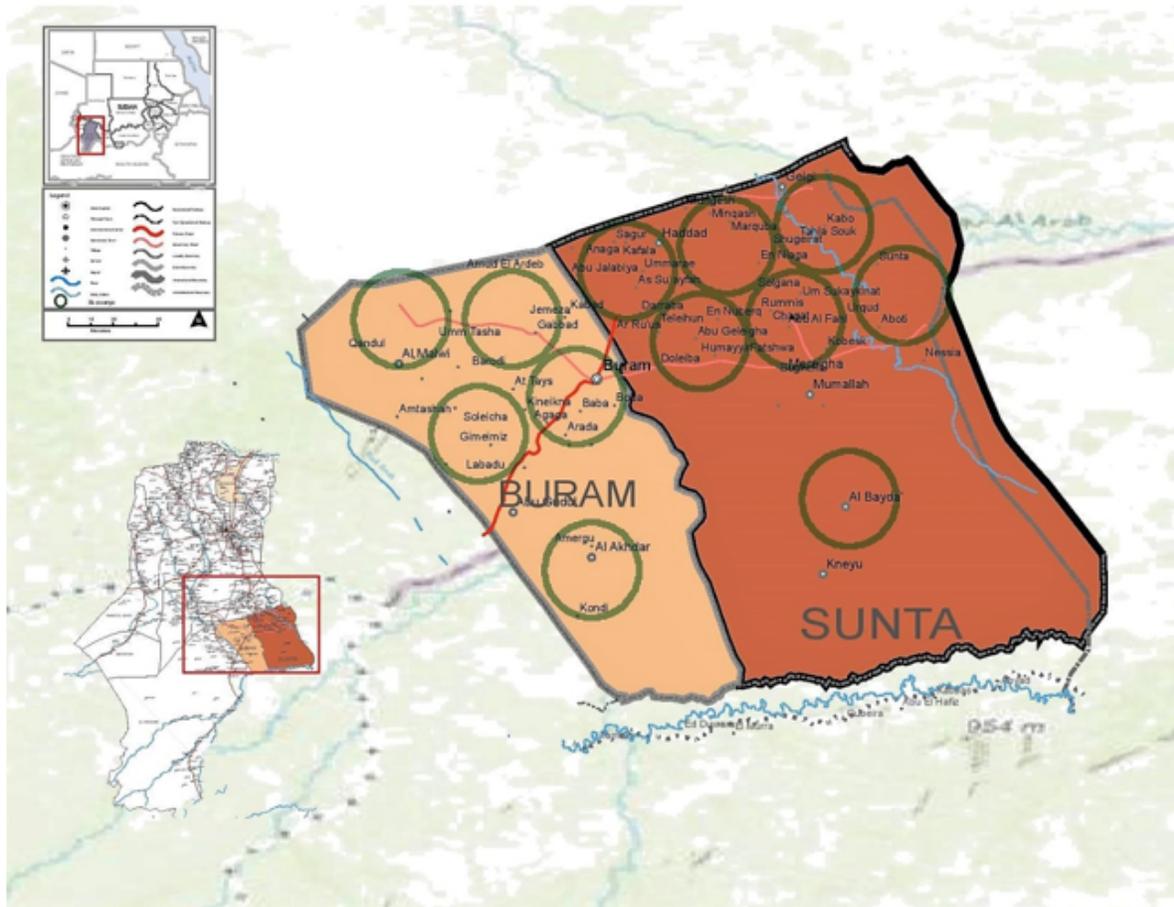


Figure 3: Proposed sites for vaccination posts in Al Sunta and Buram localities.

Community members in Um Kitaika village complained that the Community Health Worker (CHW) occasionally refuse to vaccinate their children because they were older than one year or they were brought for vaccination on the wrong days where vaccination was not scheduled or after working hours. The vaccination post functions twice a week. The communities were not fully aware of the vaccination schedule. The vaccinators reported that there was no regular visit and follow up to the routine and vaccination campaigns to the areas. Some community leaders attributed under-utilization of the health facility in Al Sunta to some tribal feuds.

All interviewed groups, including nomadic pastoralists, were aware about the benefits of vaccination of children. Community members repeatedly said that they have been awaiting arrival of the vaccination team as broadcasted by the local radio (Nyala Radio). None of the interviewed groups or parents raised issues that question the benefits of vaccination or expressed distrust, including belief in conspiracy, or concerns about the risk of adverse effects of vaccines.

The ad hoc surveys conducted among 111 boys school in Tajreeba, Al Sunta locality, revealed that only 40 (36.4%) [95% Confidence Interval (CI): 27.1% - 45.7%] reported to have been vaccinated; similar results, 4 out of 10 (40%) were reported among girls school. There were more vaccinated children among older age groups (grade 6-8) as compared to younger children (grade 1-3). Only five of the fifty-two (9.6%; 95% CI: 3.2- 21.0%) nomadic pastoralists who attended the extended FGD reported vaccinating their children against polio, while only two (3.8%; 95% CI: 1.6% -17.6%) reported vaccinating their children against measles during vaccination campaign, and only two (3.8%; 95% CI: 1.6% -17.6%) reported taking their children to one or more of the routine vaccinations at fixed sites.

Limited preparedness measures

There were no trained RRTs in Al Sunta and Buram localities. There were no pre-positioned medicines and vaccines before the rainy season to serve population in remote areas and nomadic pastoralists. There were no health facilities along the pathways of nomadic pastoralists including lack of Point of Entry (PoE) for surveillance. There are no official ground crossings PoE, infrastructure at borders, and joint activities related to surveillance, information-sharing, risk assessment and response across borders.

Capacity of the State Public Health Laboratory

The SPHL has sophisticated equipment including two PCR machines. There were no reagents, consumables and supplies to conduct PCR and other diagnostic tests at the State level. There was no transport media for sample collection and shipment. The staff members were not fully trained on various diagnostic testing methods and transportation of specimens.

Limited access to health services

There were only two health facilities providing medical care in the area. There were no community based prevention and treatment services. The capacity of health workers was limited in diagnosing and treating diphtheria cases. There was no isolation center prepared for case management in all health facilities visited except the referral hospital in Nyala. There was rampant use of traditional healers and sell of drugs in the market as commodities.

Discussion

Low immunization coverage

The epidemic curve of the outbreak revealed that the diphtheria outbreak was going on unnoticed for about five months. It is only when concurrent clusters of cases with associated deaths occurred in more villages that the outbreak was noticed by village midwife in Tajreeba FHU in Al Sunta locality. The IQR of age of diphtheria cases of this outbreak investigation indicated susceptibility of school children to diphtheria. This could be explained by low coverage of diphtheria vaccine in the outbreak area about a decade before the outbreak during the armed conflict in Darfur when the basic health services were not accessible, including routine immunization of children. The armed conflict has not only disrupted the routine childhood immunization programmes but also further widened the disparities and pre-existing inequalities in access to basic health services. Similar findings were reported from Yemen [16]. According to Sudan Multiple Indicator Cluster Survey [17], 63.9% of the children received the third dose of Pentavalent (DPT+HepB+Hib); and the percentage of children who had all the recommended vaccinations by their first birthday was low (42.8%). In South Darfur vaccinations by age 12 months, Sudan was 58.9% [17]. The national disease surveillance system

reported concurrent occurrence of sporadic cases of diphtheria in XXX states in the Sudan [18]. The spread of diphtheria among the neighbouring villages the Al-Sunta locality is probably due to crowding of children in a few villages, and the free and continuous movement and mixing of children in the inter-related villages that led to increase in the pool of susceptible children. Diphtheria cases were found to be frequent among school-going children and adolescents in some Indian states [5]. Alternatively, re-emergence of diphtheria cases could be due declining immunity acquired by vaccination or naturally. In countries with sporadic cases, 32% of case-patients were unvaccinated and 66% were >15 years of age, consistent with waning vaccine immunity [19].

Emergence of outbreak of diphtheria should not be surprising because of very low vaccination coverage in the areas as evidenced during the assessment mission. The occurrence of clusters of diphtheria cases in a well-defined geographical area has always been indicative of pitfalls in immunization program. The results of the assessments that used different methods (ad hoc surveys) were consistent with S3M and SMOH data. According to the 2019, S3M report, the vaccination coverage with the third dose of pentavalent vaccine (Penta 3) for children under 12 months of age in Al Sunta and Buram localities was around 33%. The relatively higher coverage in Mershang locality (59%) could explain the limited spread of diphtheria in that particular area. A cross-sectional community-based study was undertaken in Nyala locality, south Darfur State, including urban, rural and IDP population in proportional representation, found that the vaccination coverage of children in their second year of life was low compared to the national coverage [20].

The ongoing outbreaks of diphtheria in Sudan in 2019, especially in South Darfur, classify the burden of diphtheria as high as the population immunity is also low and the implementation of the EPI program in the State of South Darfur was facing many challenges that include, but not limited to, lack of appropriate means of transportation, adaptability to the local context, interruptions in the cold chain system and supervision to the CHWs; especially for nomadic pastoralists. The nomadic pastoralists attributed not vaccinating their children at fixed post to the rigidity of the CHWs, which resulted in missed opportunities. Missed Opportunities for Vaccination (MOVs) occur when persons eligible for vaccination visit a health facility and do not get the vaccines they need. The investigation showed that the vaccines were exposed to heat and their potency could have been compromised. With such level of vaccine quality, even with 100% coverage, one cannot elicit a desired immunity against the disease.

The age-pattern of the children vaccinated identified by the investigation team from the ad hoc surveys at schools showed relatively lower vaccination coverage among the younger children.

This observation, in addition to the poor vaccination coverage among pre-school children, suggest that routine vaccination of children has been low at least for the last ten or more years.

Case-Fatality Ratio (CFR)

The emergence of the outbreak of diphtheria and the associated high CFR could be attributed to low coverage of children with routine vaccination, delayed diagnosis, and unavailability of DAT at the health facilities where cases were treated. During an outbreak of diphtheria in Khartoum, Sudan, in 1988, only 19.1% of patients admitted to hospital were under 5 years of age. This is considerably less than the proportion of such patients seen during a similar outbreak in Khartoum in 1978 (49.5%) and also less than the proportion (55.2%) of under-5-year-olds reported for all inpatients with diphtheria in the Sudan during 1979-86 [16,21]. Cluster surveys carried out between 1981 and 1989 demonstrate that vaccination coverage was much higher for under-5-year-olds (about 65% for the third dose of diphtheria-pertussis-tetanus vaccine (DPT3) than for children of school age (less than 20% for DPT3) at the time of the 1988 outbreak [12]. These results indicate that improved vaccination coverage led to the shift in the age distribution of diphtheria patients seen during the 1988 outbreak [12].

Nomadic Pastoralists

The FGD with nomadic pastoralists attested that the immunization coverage is very low in Al Sunta locality. The nomadic pastoralists are mobile, hard to reach; and remain marginalized from rural development plans and interventions [22]. In South Darfur, the nomadic pastoralists share the rudimentary health services structure provided to the rural communities. Skipped, delayed or missed vaccination doses result in under vaccination, continuous accumulation of susceptible children, which in turn would make children vulnerable to outbreaks of preventable childhood diseases [23]. Hence it is necessary to consider alternative strategies to ensure their access to routine vaccinations. It is plausible that the operational costs for vaccination program for nomadic pastoralists would be more expensive as compare with similar programs for the sedentary agricultural population [24]. Children from nomadic pastoralists might not receive all the recommended doses of vaccines at age-appropriate times due to limited access to immunization services [14]. Sudan is not an exception.

Health services delivery modalities

The investigation revealed that the village midwives and CHWs play an important role in surveillance and case management of diphtheria; especially among nomadic pastoralists. Thus, their involvement in vaccination programs would be indispensable in strengthening the health care delivery system, increasing and

maintaining acceptable coverage levels and reducing missed opportunities for vaccination. In a country plagued by internal conflict and where one in ten people belong to a nomadic pastoralist's tribe, ensuring all children receive life-saving vaccines can be a challenge.

Engagement of village midwives and CHWs could resolve the challenge in attracting qualified health personnel to serve nomadic pastoralists [25]. Moreover, the involvement of CHWs and village midwives would help overcome access and logistical challenges in providing health services particularly in conflict-affected and hard to reach areas [26,27]. The community leaders could help in identifying appropriate candidate to be trained as CHWs or midwives.

It is likely that the coverage of children with routine vaccination program is significantly lower in the population living at long distances from the two fixed FHUs. Similarly, it is unlikely that there would be age or sex difference in the distribution of cases during outbreaks of vaccine preventable diseases.

Therefore, there is dire need to revise the systems for delivery of health services, identify new creative strategies, develop and implement locally appropriate preparedness plans that deal with childhood diseases. Such revisions are critical to attain the third (3.2) Sustainable Development Goals (SDGs) which aims to end preventable deaths of newborns and children under 5 years of age that by 2030.

Point of entries and cross border collaborations

The nomadic pastoralists cross borders freely at almost well-defined periods along certain pathways every year. The borders between Sudan and neighboring countries are porous. Ministers of Health in countries bordering Sudan; namely, Chad, Egypt, Ethiopia, Libya, South Sudan and Sudan on 22 November 2018 in Khartoum, Sudan have signed a declaration committing themselves to strengthening preparedness and response to public health threats and events across borders in an effort to further the implementation of the International Health Regulations (IHR 2005) and enhance global health security.

Conclusion and Recommendations

The outbreak investigation made some recommendations that hinge on three major pillars of interventions: increased immunization coverage of the target population, enhanced prompt clinical and laboratory diagnosis and appropriate management of diphtheria cases, and intensified rapid identification of close contacts to prevent secondary cases. Multiple strategies to strengthen diphtheria surveillance of public and private health institutions for improved disease control are needed. Immediate actions included implement massive vaccination campaigns in the

affected areas targeting children below 15 years. Children aged 6 weeks to 6 years were vaccinated with pentavalent vaccine and older children aged 6 to 15 years with combined Diphtheria Tetanus (DT) vaccine. The immunization campaign was repeated after a month to provide at least 2 doses of the vaccines. Physicians, medical assistants, nurses and community health workers were trained on diagnosis and treatment of cases and close contacts as per the national guidelines and protocols. There was a scale up of active surveillance to ensure timely detection and reporting of suspected cases throughout the State, including establishing a Community Based Surveillance (CBS) especially among nomadic pastoralists. The investigation highlighted the dire need to improve preparedness Strengthen immunization coverage through

- Increasing the number of fixed vaccination sites and equip them with functional solar-operated and regularly maintained cold chain systems,
- Implementing regular mobile vaccination program to augment the routine immunization activities targeting mobile communities (nomadic pastoralists), internally displaced populations (IDP), refugees and communities in hard-to-reach and remote areas.
- Scaling up State-wide vaccination campaign to further increase the EPI coverage whenever deemed necessary. Campaign should not be used as a substitute strategy for vaccination as it is not cost-effective and sustainable model.
- Initiating community level health service deliveries that are proven to be effective in detecting and responding to common childhood illnesses such as Integrated Management of Childhood Illnesses (ICCM) and Community Based-Surveillance (CBS).
- Strengthen the capacity of the State Public Health Laboratory (SPHL) by training on sample collection and shipment and providing reagents, transport medium, and consumables.

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