International Journal of Community Medicine and Public Health
Islam SM et al. Int J Community Med Public Health. 2021 Jan;8(1):439-445
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20205734

Review Article

Massive diphtheria outbreak in South Asia: an epidemiological evidence review and lesson learnt

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Received: 19 October 2020
Revised: 11 December 2020
Accepted: 14 December 2020

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ABSTRACT

Vaccination is to be considerd as one of the most well-known economically viable medical procedures to prevent massive diphtheria outbreaks happening in recent times. Under this circumstance, the available data on diphtheria and vaccination coverage of three South Asian countries is warranted. The published English-language literature between January 2007 and January 2019 was retrieved from search results in eight highly resourceful journal databases using the specific terms. A massive diphtheria outbreak was occurred in refugee camps in Cox Bazar, a harbour city in Bangladesh, between November 2017 and March 2019. A total of 8641 diphtheria case-patients were reported including 45 deaths in the refugee camps. Our synthesis data shows that there is a gap of immunity which creates a large scale of potentiality for a new pandemic for adult couples along with children. The DTP3 coverage in India and Myanmar is less than 90% and these two countries had no standard coverage of DTP3 dose. We concluded that the massive outbreak of diphtheria in South Asia normally occurred due to low coverage of vaccination or incomplete vaccination. Crowded living environment, low socio-economic conditions, cultural belief, and importation of microorganisms are considered for massive outbreak of diphtheria outbreaks. Community-based awareness program and vaccinating individuals and some cases revaccination of older age groups are needed to stop further transmission and control the diphtheria outbreaks in South Asia. Further research is required to fully assess the vaccination coverage in the stateless populations in this region.

Keywords: Bangladesh, Diphtheria, Epidemic, India, Migration, Myanmar, Outbreak, Rohingya, Vaccination

INTRODUCTION

Diphtheria is known as an infectious disease in countries with low immunization coverage.[1] It was a leading ground of infancy death before 1923 and the incidence rate quickly declined from subsequent uses of vaccine.[2,3] It being an infectious disease, even with the highest level of vaccination advancement a high rate of diphtheria occurred in 1990 in Russian Federation. The outbreak infected over 157,000 cases and caused 5000 deaths, of which 64-76% was aged 15 years and older.[4,5] Such an outbreak suggests possible future severe outbreaks, in case of a community with expanding population of non-immune and limited immunization of children.[6] Some

environmental conditions favourable for an outbreak are enormous wave of relocation, declining financial conditions, and disturbances of immunization supply chains and programs.[6] However, failure to vaccinate is the problem rather than vaccine failure.[7,8] Low vaccination coverage or incomplete vaccination creates poor levels of immunity and such conditions can introduce a new case especially among migrating populations.[9] Around 22569 diphtheria cases were reported globally in 2019, among them about 60% and 19% cases were from India and Madagascar, respectively.[10] The scope of three doses of diphtheria vaccination was 79% in India 2019, in spite of the fact that the active cases of diphtheria stayed high. The causes of low diphtheria coverage among children and adults including hilly areas, lack of awareness and socio-cultural factors.[11] Diphtheria was also epidemic in Myanmar and Bangladesh, around as 564 and 284 active cases were recorded from 2007-2019, respectively. In diphtheria cases, The Case Fatality Rate (CFR) is 5%-10% while it is 20% amongst the children and 5% among adults >40 years[12]. The diphtheria outbreak started in Bangladesh refugee camps on 3 November 2017 and end in 20 March, 2019. A total of 8,641 diphtheria cases had been reported including 45 deaths, 2,710 classified as probable, and 5,339 classified as suspected cases.[12,13] There was very limited scope of vaccination of Rohingya population as they did not have proper health services in Myanmar. India and Myanmar had diphtheria immunization below 85% and have a chance of local disease, resulting in transmission from imported cases. The numbers of imported cases are high both in Myanmar and India. This scoping review highlights on three countries diphtheria information, vaccination rate, prevention strategies and very recent massive outbreak among Rohingya refugees at Cox Bazar district Bangladesh. Recent diphtheria outbreaks in South-Asia such among Rohingya refugees make a sense to review the available data from three neighbour countries (Bangladesh, Myanmar and India).

Objective of this literature review was to assess rate of vaccination coverage and other factors role in such massive outbreaks among the refugee people.

METHODS

We examined common epidemiological patterns of diphtheria over time in three countries, Bangladesh, Myanmar and India. Our review included three countries diphtheria outbreaks cases (2007-2019) and rate of vaccination and Rohingya outcasts' diphtheria detailed cases of 2017-2019 also included.

To enhance our understanding of the issue in question, available databases were used. We applied realist literature review (RLR) techniques in our appraisal, such as (a) searching for the startling list to consider, (b) Relevance appraisal, and (c) removal of examination of data.

Searching for the startling list of considers

Initially we are utilizing some keywords to inquiry each record so it resembles articles on diphtheria, immunization coverage and frequency of diphtheria. Our searching areas were limited due to scope of the study and focus on practical database of diphtheria outbreaks cases.

Table 1: Searching summary.

Number of total articles found (2007-2019)							
Searched Database			**Search terms**				
Eight data sources	**Field and access**	**Document type**	**Diphtheria AND Outbreak OR Cluster OR Epidemic OR South Asia**	**Diphtheria AND Outbreak OR Cluster OR Epidemic OR Migration OR South Asia**	**Diphtheria AND Outbreak OR Cluster OR Epidemic OR Migration OR South Asia OR Bangladesh**	**Diphtheria AND Outbreak OR Cluster OR Epidemic OR Migration OR South Asia OR Myanmar**	**Diphtheria AND Outbreak OR Cluster OR Epidemic OR Migration OR South Asia OR India**
Springer Link	All	Journals	86	55	25	9	49
Science Direct	All	Journals	90	46	21	12	39
Wiley Online Library	All	Journals	52	34	11	09	21
Medline (PubMed)	All	Journals	124	**63**	18	11	33
CINAHL	All	Journals	45	23	12	05	23
PsycInfo	All	Journals	32	13	08	02	11
Web of Science (SCI, SSCI, HCI)	All	Journals	34	14	07	02	17
Google Scholar	All	All	891	243	78	42	112
Total			1354	491	180	110	305

The investigation process was executed on 8 journals website (Table 1) utilizing particular watchwords like; diphtheria AND outbreak, OR cluster epidemic OR migration. The investigation found 595 interesting abstracts, which were reviewed by 7 researchers. They resolved their differences regarding the review through discussion.

Relevance appraisal

In this stage, we have chosen relevant papers and excluded others by examining the titles, catchphrases, abstracts, and full substance. Articles that were included in the list had one of the following information: age of the client, and/or immunization status, cases of respiratory diphtheria caused by *C. diphtheria* between the years of 2007-2019 and Rohingya well-being issues.[1-3] Articles were excluded from the list due to; not relevant on abstract review, duplicates with the previous abstract, not fully related to the epidemiology of diphtheria and language barrier.

Data extraction

Data on diphtheria cases (2007-2019) were obtained from world health organization fact sheet considered as a grey literature. Five overview articles have been used to inform the background and methodology. Four investigators evaluated each article, who compiled related information in an Excel database. Again eight published manuscripts were introduced through the reference lists, and 3 grey literature additionally used in reviewed. For India, Bangladesh and Myanmar, DTP3 exposure details from the WHO-UNICEF were compared with occurrence records from the JRF and the case datasets.

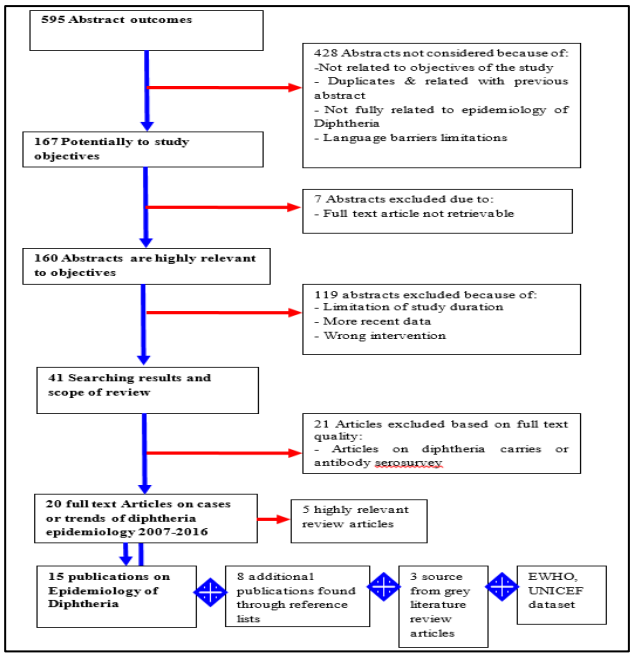

Figure 1: Result of search and selection of studies, and sources for data used in analysis.

RESULTS

Diphtheria epidemiologic trends, 2007-2019

Since1980s diphtheria was coming back, but not in the wave of an epidemic as before the advent of immunization. Incidences of diphtheria declined worldwide due to EPI and public health programs, but it continued as epidemic in few countries: India, Myanmar and Bangladesh. On an average 4621 cases were reported annually in India, 21 in Myanmar, and 43 Bangladesh (Table 2). However, diphtheria cases in Bangladesh diminished slowly, while expanded significantly in India and Myanmar. The big concern is that the numbers of diphtheria cases increased significantly after an outbreak among Rohingya refugees in 2017 (Table 2).

Table 2: Reported diphtheria cases in Bangladesh, Myanmar and India and rest of the world (2007-2019).

Year	Bangladesh	Myanmar	India	Rest of the world
2007	86	5	3812	739
2008	43	3	3977	955
2009	23	19	3529	778
2010	27	4	3434	1138
2011	11	7	4233	1374
2012	16	19	2525	1930
2013	2	38	3133	1507
2014	13	29	6094	1638
2015	6	87	2365	2077
2016	2	136	3280	3579
2017	5	68	5293	3448
2018	36	127	8788	7932
2019	14	22	9622	12911
Total	284	564	60085	40006

WHO, UNICEF, 2020

Level of vaccination in India, Myanmar and Bangladesh (2007-2019)

Approximately 2 to 3 million deaths can be deflected globally by immunization of diphtheria, tetanus, pertusis and measles whereas an extra 1.5 million may be dodged worldwide if vaccination scope moves forward. Worldwide (116.5 million) near about 86% of newborn received DTP3 antibody and by 2019,130 countries had come to at slightest 90% scope of DTP3 antibody. Almost 19.5 million newborn children around the world are losing out on fundamental vaccines.[14] India has the world biggest annual birth cohort, while she has the low immunization coverage in 2019 compared with other South Asian countries. Near about 87% of India's children had received DTP1 and 79% had DTP3 vaccine, while 98% DTP1 and 95% DTP3 were received in Bangladesh, and 91% DPT1 and 86% DTP3 received by Myanmar children (Table 2). The factors related with low vaccination scope in India are gender, age, birth rate, family components, devout components, caste and state-

level factors.[15] It seems generally epidemic returns to a country where, there is a gap of immunity among children and adults because of low coverage of diphtheria vaccine. India, Myanmar and Bangladesh are such countries where the return of diphtheria is widespread through migration, displacement, importation of microorganism, low immunization coverage and poor socioeconomic conditions.

Table 3: Comparison of vaccination coverage (in %) of DTP1 and DTP3 of Bangladesh, Myanmar and India from 2007-2019.

Country	Dose	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Mean coverage
Bangladesh	DTP1	98	99	99	98	99	97	98	99	99	99	99	98	99	98.50
	DTP3	94	96	97	94	96	94	96	97	97	97	97	97	96	95.80
Myanmar	DTP1	89	88	93	93	88	89	90	92	94	94	94	93	94	91.00
	DTP3	86	85	90	90	84	84	75	88	89	90	90	89	91	86.10
India	DTP1	81	81	84	86	89	89	90	90	90	91	91	91	90	87.10
	DTP3	64	70	74	79	82	82	83	85	87	88	88	89	87	79.04

National vaccination schedules, 2007-2019

Entire country population immunity can be changed by continuing vaccination programs at the local and national scales. Children have a high level of diphtheria resistance which is the result of childhood vaccination and booster doses play a vital role in this context. We observed that the mean average DPT coverage of Bangladesh was about 95%, followed by Myanmar 86% and India 79% while the total diphtheria cases were 284, 564, and 60085 respectively (Table 4).

Table 4: Vaccination plans and DTP3 coverage for the studies of three countries detailing the foremost cases of diphtheria in 2007-2019.

Country	Reported diphtheria cases (2007-2019)	Vaccination schedule	Age at last booster dose	Mean DTP3 coverage (2007-2019)
India	60085	3 dose + 2	5	79%
Myanmar	564	3 dose	-	86%
Bangladesh	284	3 dose+2	5	95%

Diphtheria outbreak among Rohingya refugees in Bangladesh, 2017-2019

About 1.7 million Rohingya people are living by scattered in 10 countries globally with indefinable worst situations as stateless people in Bangladesh. Cox's Bazar district about 1 million documented refugees settled in 15 densely camps without good health and hygiene services.[16-18] The majorities (58%) of the refugees are <18 years and most of them are women.[19,20] The diphtheria outbreak started on November 3, 2017 and ended on March 20, 2019. A total of 8641 diphtheria case-patients were reported including 45 deaths. In addition, 2710 were classified as probable and 5339 as suspected cases in refugee camps.[21,22] Our synthesis data shows that about 67% of cases of diphtheria-patients were less than 15 years and 13% less than 5 years and about 56% were females. Densely populated camps, fleeting settlements, unsafe water, and health condition, lack of proper sanitation, and poor health services are the reasons for spreading diphtheria. Insusceptibility crevices in adult couples with expanding numbers of vulnerable children make the possibility for modern serious scourge. It is difficult to give the diphtheria vaccine among Rogingya people; all should take this vaccine.

DISCUSSION

The former Russian Federation, Latin American and Caribbean flare-up highlighted diphtheria's dreariness, mortality, the significance of persistent reconnaissance and homogenous vaccination coverage.[23] It is suggested that at the age of 2, 4 and 6 months are appropriate for the primary doses of Diphtheria which is a routine immunization schedule in Myanmar. The range of DPT for <1 years was 70% to 90% between 2007 and 2019 in Myanmar but this coverage was very low for Rakhine and Shah state (65%-79%) and as a result entire population of these state vaccination coverage was very poor. We observed (2007-2019) DPT3 coverage was <90% for India and <95% for Myanmar.[24] The Rohingya refugees were forced migrated from Rakhine state and most of them were not vaccinated. Many seroepidemiological studies suggested immunity gaps may exit in the older age people or young adult, either due to weak immunity or incomplete vaccination.[25-27] In our study we found that in Europe and most part of former Russian federation has experienced massive diphtheria outbreaks due to poor vaccination rates among the entire population.[28] Rohingya refugees are living muddy hills areas without good access to water, sanitation and hygiene and majority (84%) do not have good knowledge concerning WASH. Majority of suspected cases patients were Rohingya population who are living unhealthy environment and they have poor hygiene practices.[29] Evidence shows that globally about 2.5 million deaths can be stopped through full doses of vaccination and effective public health interventions.[30] Globally 1 person is uprooted every 2 seconds and at the moment about 3.9 million stateless people appear in 78

countries worldwide and among them 75% belong to minorities' groups.[31] The health risks for stateless/refugee people are multifaceted and undoubtedly and they are face significant barriers to access healthcare especially for getting vaccine.

This review stresses the migrated people and their socio-demographic conditions are associated with massive outbreaks and as a result diphtheria remains endemic in developing countries and displaced people.[32] There are no past records about vaccination of Rohingya people and research on vaccination coverage of refugees is subsequently justified. In the period (2007-2017) the number of cases of diphtheria was very low in Bangladesh and DPT3 doses rate was above 98% whereas the numbers of cases were higher for India and Myanmar and DTP3 doses below 90%. Evidence shows that three or more doses effectiveness was 96%-98% if the vaccination coverage was 95% and above.[33,34] The interesting fact is that the numbers of cases of diphtheria becomes doubled for three countries if we compared the cases for the period of 3 years before outbreaks (2014-2016) and after outbreaks (2017-2019) among the Rohinga refugees in Bangladesh at Cox Bazar district. This finding indicates that imported diphtheria cases still a big concern to control the diphtheria in this region. Another concern is that we observed high discrimination in vaccination coverage among minorities community in Myanmar and India and some cases incomplete vaccination rates is high due to lack of community-based awareness program. Our finding show that the coverage of vaccination <1 year age children was 70-79% in Rakhine state whereas remaining part of Myanmar vaccination coverage was 90% for the same age children. Our reviews affirm a routine booster dose at school leaving age for both Myanmar and India, and Bangladesh may be a model for two countries. We had identified some critical areas that have to address by public health practitioners as well as policy makers to further control the outbreak in the entire population in this reasons. Firstly we need to develop surveillance system for early warning the cases; second we need improve the knowledge of refugees about WASH, third massive awareness campaign on infectious disease.

Research highlights

Our scoping review highlights the recent diphtheria outbreaks and its associated factors among Rohingya refugees. Geographically Bangladesh, Myanmar, and India are inter-connected by broader and displaced Rohingya refugee is a big concern for these countries. Around 90% of displaced Rohingya refugees are living in Cox Bazar Bangladesh and this seaport area under threat of further diphtheria outbreak. Our paper describes the importance of vaccination coverage and other socio-economic factors roles to control such an infectious disease outbreak in south Asian countries.

The limitation of this study is that there is not much available data on diphtheria and its vaccination coverage from Myanmar and we only review documents three countries due to the constraints of our resources. Further research is required to fully assess the vaccination coverage in the stateless populations in this region.

CONCLUSION

Our review indicates imported diphtheria cases and stateless people are the main way of transmission of such infectious disease in south Asia. Low vaccination coverage, high rate of incomplete vaccination and discrimination against minorities' community are the contributing agent for high number of diphtheria cases in this region. An immunity gap exist in older age groups and we suggest for revaccination of older age group. Three booster doses of diphtheria-containing vaccine should be administered at childhood and completed by adolescence and 95% of DTP3 doses coverage must be ensured. Further research can be conducted for fully assessing the vaccination coverage in the stateless populations in this region.

ACKNOWLEDGEMENTS

We would like to acknowledge Professor Abul Hasnat Golam Quddus (MPH, PhD USA), Honorary Director Dr. Ahmadur Rahman Research Centre, University of Chittagong, Bangladesh for his comments on the very initial version.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Islam SM, Chowdhury SM, Mahfuz A, Das BC, Reza M, Mahbuba K, et al. Massive diphtheria outbreak in South Asia: an epidemiological evidence review and lesson learnt. Int J Community Med Public Health 2021;8:439-45.