

Cholera in India: an analysis of reports, 1997–2006

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Objective To more accurately define the annual incidence of cholera in India, believed to be higher than reported to the World Health Organization (WHO).

Methods We searched the biomedical literature to extract data on the cases of cholera reported in India from 1997 to 2006 and compared the numbers found to those reported annually to WHO over the same period. The latter were obtained from WHO's annual summaries of reported cholera cases and *National health profile 2006*, published by India's Central Bureau of Health Intelligence.

Findings Of India's 35 states or union territories, 21 reported cholera cases during at least one year between 1997 and 2006. The state of West Bengal reported cases during all 10 years, while the state of Maharashtra and the union territory of Delhi reported cases during nine, and Orissa during seven. There were 68 outbreaks in 18 states, and 222 038 cases were detected overall. This figure is about six times higher than the number reported to WHO (37 783) over the same period. The states of Orissa, West Bengal, Andaman and Nicobar Islands, Assam and Chhattisgarh accounted for 91% of all outbreak-related cases.

Conclusion The reporting of cholera cases in India is incomplete and the methods used to keep statistics on cholera incidence are inadequate. Although the data are sparse and heterogeneous, cholera notification in India is highly deficient.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Cholera is an acute diarrhoeal illness caused by toxigenic strains of *Vibrio cholerae* serogroups O1 and O139. Presently, *V. cholerae* O1 belonging to the El Tor biotype is the most common serogroup in India, while the frequency of serogroup O139 has declined considerably over the past few years. When analysed by 5-year periods, the incidence of cholera and the absolute number of deaths from the disease have increased steadily since the beginning of the millennium. Whereas a cumulative total of 838 315 cases had been notified to the World Health Organization (WHO) for the period 2004 to 2008, 676 651 cases were reported from 2000 to 2004. This represents a 24% increase in the number of cases reported with respect to the previous 5-year period (2000–2004).¹ However, the estimated actual burden of cholera is in the vicinity of 3 to 5 million cases and 100 000 to 130 000 deaths per year.²

Cholera is also changing epidemiologically. Multiple antibiotic resistant strains of *V. cholerae* have emerged,^{3,4} along with the El Tor variants that produce the cholera toxin of the classical biotype that has spread into Asia and parts of Africa.^{5–7} The severity of the disease appears to be intensifying,^{8,9} and recent cholera outbreaks in various places, including Zimbabwe,¹⁰ have run a more protracted course.

During a meeting of the WHO Strategic Advisory Group of Experts on immunization that was held in October 2009 in Geneva, Switzerland, cholera control was identified as a priority in areas with endemic cholera, since outbreaks of the disease can disrupt health systems.¹¹ While long-term intervention to improve water and sanitation should be the mainstay of cholera control measures, the group recommended the use of oral cholera vaccines (OCVs) to obtain

a short-term effect for an immediate response. Given the availability of two OCVs (one prequalified and the other pending prequalification by WHO) and new data on their efficacy, field effectiveness, feasibility and acceptance in cholera-affected populations, these vaccines should be used in areas where cholera is endemic, particularly in those at risk of outbreaks, in conjunction with other prevention and control strategies.¹¹

Of the two OCVs, the low-cost bivalent inactivated whole-cell OCV known as Shanchol[®] (Shantha Biotechnics Ltd., Hyderabad, AP, India) is now licensed in India following clinical trials in Viet Nam¹² and in the city of Kolkata.^{13,14} A safe, inexpensive and efficacious cholera vaccine has thus become available in India after almost three decades of non-availability of any cholera vaccine in India. Shanchol[®] traces its lineage to the original bivalent ORC-Vax[®] (VaBiotech, Hanoi, Viet Nam) that was licensed in Viet Nam in 1997. In collaboration with the manufacturer, the International Vaccine Institute (IVI) modified the ORC-Vax[®] by altering the cocktail of immunizing strains, which resulted in an increase in the lypopolysaccharide content.¹⁵ Another live oral attenuated cholera vaccine known as VA1.4, created in India and manufactured by Shantha Biotechnics, Ltd., will shortly undergo phase III field trials in Kolkata.¹⁶

India, which comprises 28 states and 7 union territories, has a total population of 1.15 billion people. Nearly two-thirds of them live in rural areas, where only 28% of households use piped drinking water and 26% of households have access to good sanitation.¹⁷ It is not surprising that cholera continues to be an important public health problem in the country. However, cholera cases are hugely underreported mainly because disease surveillance is limited, laboratory capacity is inadequate, especially at peripheral health-care

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centres, and authorities are reluctant to acknowledge, for fear of societal repercussion, that there has been a breakdown in sanitation and in the supply of safe water. Yet the above-cited reasons for poor case reporting appear to apply to cholera exclusively. Acute diarrhoeal diseases overall are also underreported, but mainly on account of poor reporting by private health-care services. According to *National health profile 2008*, 11 231 039 cases of acute diarrhoea were recorded that year, but only 2 680 were cholera cases and only one death was due to cholera.¹⁸ These were the national figures conveyed to WHO.

As policymakers have pointed out, to decide the scope of control strategies, including vaccination, it is essential to know the age-specific incidence of cholera.¹⁹ Now that a cholera vaccine has been introduced in India, it is important to assess its impact in the country, and that is not possible unless the disease burden can be estimated. With this goal in mind, we searched the biomedical literature to investigate the burden of cholera in India, compare the findings to the “official” figures reported to WHO, and determine how much the burden of cholera is underestimated.

Methods

We searched in PubMed with the key words “India” and “cholera” and identified 1134 publications, 500 of which were included in this review. We also searched with the key words “acute gastroenteritis”, “acute watery diarrhoea” (or “diarrhea”) and “India” but found no additional papers. Using the same keywords, we also searched the following databases: Freemedicaljournals, Medexplorer, Medscape and Medhunt. No additional publications were identified. We included publications in which cases were detected from 1997 to 2006, the specific regions in India where the cases occurred were indicated, and the dates of occurrence were specified. To identify the state or union territory where the cholera cases occurred, we included reports of routine surveillance activities as well as outbreaks. A routine surveillance system was defined as any mechanism existing in a hospital or institute for the purpose of using microbiological techniques to identify

the pathogens responsible for cases of diarrhoea. Thus, all cholera cases identified during routine surveillance were confirmed by bacterial culture. However, during outbreaks not all cases of diarrhoea were confirmed in the laboratory, and the authors used the WHO case definition: any patient with diarrhoea in an area where culture-confirmed cases of infection with *V. cholerae* O1 or O139 were identified during the outbreak.²⁰ An outbreak was defined as the occurrence of more cholera cases than expected during a specific period. Since information on “expected” cases was unavailable in most instances, we relied on the authors’ discretion when reporting these outbreaks.

Since outbreaks may occur during routine surveillance, to avoid duplication of cases we tabulated and counted outbreak cases with special attention to the point in time and geographical location of the cases. When we came upon multiple reports of the same outbreak, we drew on data from the source with more detailed information.

By definition, cholera is endemic when the causative organisms reside in the local environment and the occurrence of the disease in humans is not dependent on the importation of cholera from outside. The mechanism by which cholera becomes endemic depends on the environmental reservoir of cholera. Major outbreaks of cholera usually result from an interplay of factors, such as favourable climate conditions and poor sanitation.¹

We excluded papers in languages other than English or that dealt with laboratory or environmental issues and focused on molecular mechanisms or other aspects of *V. cholerae*. We also excluded studies encompassing several years but without a yearly breakdown of the number of cholera cases.

We supplemented our literature search by looking up reports from the Field Epidemiology Training Program of the National Institute of Epidemiology (Chennai, India)^{21–28} and annual reports published by the National Institute of Cholera and Enteric Diseases (NICED) (Kolkata, India).²⁹ Cholera cases in India are not systematically reported to the NICED. Thus, NICED contains no information on cholera outbreaks that are not reported to the institute. However, NICED is a WHO collaborating centre for research and

training on diarrhoeal diseases and is also the National Phage Typing Centre for Cholera in India. It receives, on average, more than 900 strains of *V. cholerae* O1, O139 and non-O1, non-O139 annually from all parts of the country for phage typing, biotyping and serotyping. Additionally, the NICED is periodically called upon by the Indian Council of Medical Research and the Ministry of Health and Family Welfare of the Government of India to investigate outbreaks of cholera occurring in different parts of the country. The results of phage typing and outbreak investigations are described in the NICED’s annual reports, which are available on the NICED web site beginning in 2005.²⁹ Annual summaries of cholera cases in India reported to WHO are provided by the Central Bureau of Health Intelligence through *National health profile*, a yearly publication initiated in 2005. The Central Bureau acknowledges that the database is incomplete, the reason being that private medical and health-care institutions do not always report to their respective government health units. Thus, the data come primarily from the directorates of health and family welfare services of the 35 states and union territories.¹⁸ The WHO’s annual summaries of cholera case reports^{30–39} as well as *National health profile 2006* data were compared with the results of the literature search.

Results

India reported cholera cases and deaths to WHO regularly from 1997 to 2006 (Table 1). Over the 10-year period, the average number of cases reported annually was 3 631. The case fatality rate showed a somewhat decreasing trend (range: 0.57–0.07). The numbers of cholera cases and deaths in *National health profile 2006* were found to be similar to the numbers reported to the WHO.

Of the 35 states or union territories we identified in our search, 21 reported cholera cases in at least one year from 1997 to 2006. However, the 14 states or union territories that reported no cholera cases were not necessarily free of cholera. They may simply have lacked proper surveillance or the laboratory capacity to identify *V. cholerae* O1 or O139.

The state of West Bengal reported cholera cases during all of the 10 years reviewed, while the state of Maharashtra and the union territory of Delhi reported cases during nine of those years, Orissa during seven, and Gujarat, Kerala, Tamil Nadu and Punjab during five.

Fig. 1 shows the distribution of cholera cases from routine surveillance and during cholera outbreaks from 1997 to 2006. Routine surveillance was in place in six institutes located in Kolkata, Nagpur, Chandigarh, Kerala, Vellore and Orissa. The states of Assam, Chhattisgarh, Himachal Pradesh, Madhya Pradesh, Tripura and the union territory of Andaman and Nicobar Islands did not report cholera cases on a regular basis but did report outbreaks over the 10-year period. Some states, however, such as West Bengal, Maharashtra and Orissa and in the union territory of Delhi, reported epidemics during multiple years over 1997–2006. Although the causative agent of the outbreaks before 2004 was not identified, Orissa had four outbreaks from 1999–2003. The number of states affected by cholera outbreaks has varied considerably. Only two states reported outbreaks in 1997, while eight reported them in 2004. On average, seven outbreaks occurred annually throughout the country. Since cholera incidence follows a seasonal pattern, cholera outbreaks did not recur in the same geographical area during the same year.

Table 1. Cholera cases and deaths reported by India to the World Health Organization, 1997–2006^{30–39}

Reporting year	No. of cases	No. of deaths	CFR
1997	2 768	16	0.57
1998	7 151	10	0.14
1999	3 839	6	0.16
2000	3 807	18	0.47
2001	4 081	6	0.15
2002	3 455	10	0.29
2003	2 893	2	0.07
2004	4 695	7	0.15
2005	3 155	6	0.19
2006	1 939	3	0.15
Total	37 783	84	–

CFR, case fatality rate.

Several states reported outbreaks during multiple years in 1997–2006. Table 2 shows the actual figures obtained through our literature search. The states of Andhra Pradesh, Assam, Haryana, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Orissa and West Bengal and the union territories of Andaman and Nicobar Islands, Delhi and Chandigarh had cholera outbreaks during more than 1 year. During the 10-year period studied, the states having the highest number of reported outbreaks were West Bengal, Orissa, Maharashtra and Kerala, which together accounted for 60% of all reported outbreaks. Of the cholera cases that occurred during outbreaks, 91%

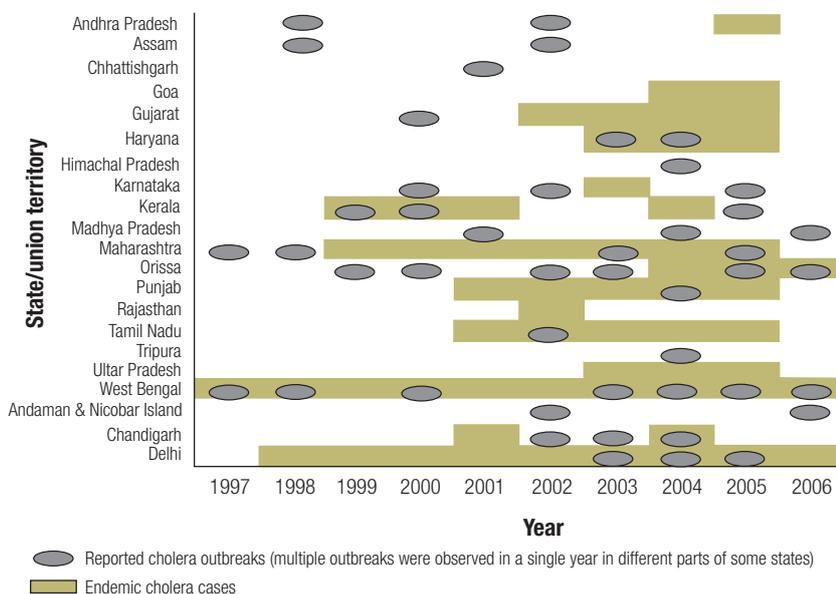
were identified in the states or union territories of Orissa, West Bengal, Andaman and Nicobar Islands, Assam and Chhattisgarh. The number of affected individuals ranged from a low of 4 in Himachal Pradesh to a high of 102 778 in Orissa. In the 10-year period, 823 deaths were reported, and the overall case fatality rate was 0.37%.

Discussion

Our analysis shows that cholera occurs over a wider geographic area in India than was previously recognized. The annual number of cholera cases reported to WHO by the government was several times lower than the numbers we obtained. The reporting of cholera in India is therefore incomplete and the methods used to keep cholera statistics are inadequate. Although the data are sparse and heterogeneous, notification of cholera cases in India is extremely deficient. When we compared the numbers of cases that occurred during outbreaks alone, according to our search, to the number officially reported to WHO, we found that only one-sixth of the cases were reported. This does not necessarily mean, however, that cholera is not present in those areas. Reporting bias or poor laboratory facilities for diagnosis could well account for the lack of reported cases. Furthermore, the reporting of cholera cases is not standardized at either the national or the international level.

Our study has several limitations. Because we used the NICED’s annual reports to broaden our search, the cholera surveillance performed by the

Fig. 1. Distribution of cholera cases and outbreaks in India, 1997–2006



institute resulted in our having a more detailed picture of the epidemiologic distribution of cholera cases in the state of West Bengal, where the NICED is located. Other Indian states may also have experienced outbreaks every year but may have lacked investigators interested in studying and reporting them because they are not novel and therefore unlikely to result in a publication. Clearly, laboratory capacity to isolate the bacterial pathogen was not uniform throughout the country, and this may have influenced the case distribution. Many of the states and union territories did not detect any outbreaks, despite having the same risk factors as those states that did detect outbreaks. For example, in Assam, large numbers of diarrhoeal episodes occurred in 2000 and 2001 but no laboratory investigation was performed, despite the fact that the clinical profile strongly resembled the profile observed during the laboratory-confirmed cholera outbreak of 2002.⁴⁰

A second limitation is that for some outbreaks,^{41–43} information was available only for the confirmed cases and not for all clinical cases, which means that even if the outbreak was identified, the number of individuals affected was often underestimated.^{44,45} Lastly, there were significant delays in the publication and reporting of outbreaks and cholera cases. While most reports were published after two years, some were published three to four years after the initial reporting.^{46–49} We ended our review in 2006 to increase the chances of capturing all the reports published during the 10-year study period.

The annual numbers of cholera cases and deaths reported to WHO were very conservative, yet they illustrate temporal trends in cholera incidence in India and provide at least some insights. The decreasing trend in the case fatality rates may be the result of the widespread use and effectiveness of oral rehydrating solutions and of improved cholera case management. However, the fact that the number of cholera cases reported to WHO was about the same in 2006 as in 1997 suggests that large segments of the population continue to have little or no access to clean water and sanitation.

A total of 68 outbreaks occurred in 18 states and union territories and the

Table 2. Distribution of identified cholera outbreaks in India in 1997–2006 and population of the states affected by cholera in 2006

State/union territory	Population ^a (× 10 ³)	No. of outbreaks	Affected individuals	No. of deaths
Andhra Pradesh	80 712	2	3 618	–
Assam	1 169	2	11 069	266
Chhattisgarh	22 594	1	7 715	46
Gujarat	54 979	1	809	–
Haryana	23 314	2	207	–
Himachal Pradesh	6 455	1	4	–
Karnataka	56 258	3	360	–
Kerala	33 265	6	1 463	–
Madhya Pradesh	66 390	3	220	20
Maharashtra	104 804	6	1 077	–
Orissa	38 887	13	102 778	86
Punjab	26 059	1	19	–
Tamil Nadu	65 135	1	213	2
Tripura	3 407	1	6 261	43
West Bengal	85 216	16	60 458	353
Andaman and Nicobar Island	419	2	20 478	6
Chandigarh	1 103	3	430	1
Delhi	16 021	4	4 859	–
Total		68	222 038	823

^a Projected population in 2006.¹⁸

overall number of cases was 222 038, a figure several times higher than the one reported to WHO (37 783) over the same time period. Furthermore, the numbers reported to WHO include both cases from endemic areas as well as from outbreaks, while the non-outbreak-related cases of cholera occurring repeatedly in endemic areas were not among the cases belonging to the 68 outbreaks included in this review. According to data from population-based diarrhoea surveillance in an endemic area of Kolkata, the incidence of cholera was 2.2 cases per 1000 person-years.⁵⁰ If this data were extrapolated to all endemic areas in the country, the total number of cases would far exceed the numbers quoted above. Our findings confirm that cholera is an under-recognized problem in India.

Our 10-year period analysis indicates that cholera affects areas outside the traditional Gangetic and Brahmaputra deltaic regions of India. An increasing trend was noted in the number of outbreaks, particularly from 2002 to 2005, as well as in the number of individuals affected during each outbreak. That the new El Tor variant strain that produces classical cholera toxin may

have caused these increases cannot be ruled out.

As is true for other diseases spread by the faecal-oral route, an adequate supply of potable water, improved sanitation and the promotion of good hygienic practices, especially in developing countries like India, remain the mainstay for preventing both endemic and epidemic cholera. Improved surveillance of the disease will be useful in assessing the cholera burden in the country and in planning interventions appropriately. Acknowledging that cholera is a significant public health threat in south-eastern Asia will allow policy-makers to target control interventions in high-risk areas. Vaccines, as discussed earlier, may be another preventive strategy that is more feasible in cholera-endemic countries. They may be used in addition to other traditional cholera control strategies, along with improved access to safe water and adequate sanitation. ■

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Résumé**Analyse des rapports sur le choléra en Inde pour la période 1997-2006**

Objectif Déterminer plus précisément l'incidence annuelle du choléra en Inde, que l'on soupçonne d'être plus élevée que le chiffre notifié à l'Organisation mondiale de la Santé (OMS).

Méthodes Nous avons analysé la littérature biomédicale pour en extraire des données sur les cas de choléra signalés en Inde de 1997 à 2006 et comparé les chiffres trouvés à ceux notifiés chaque année à l'OMS sur la même période. Ces derniers ont été tirés des récapitulatifs annuels de l'OMS des cas de choléra et du document *National Health Profile 2006*, publié par le Bureau central indien de l'intelligence sanitaire.

Résultats Parmi les 35 Etats et territoires de l'Union indienne, 21 ont notifié des cas de choléra pendant au moins une des années de la période 1997-2006. L'État du Bengale occidental a notifié des cas sur l'ensemble de ces dix années, tandis que

l'État du Maharastra et le territoire de New Delhi ont rapporté des cas pendant neuf d'entre elles et l'État de l'Orissa pendant sept d'entre elles. Il s'est produit 68 flambées épidémiques de choléra dans 18 Etats et 222 038 cas ont été détectés globalement. Ce chiffre est environ six fois plus élevé que le nombre de cas notifié à l'OMS sur la même période (soit 37 783). Les Etats de l'Orissa et du Bengale occidental, les Iles Andaman et Nicobar, l'Assam et le Chhattisgarh ont totalisé 91 % des cas liés à des flambées.

Conclusion La notification des cas de choléra en Inde est incomplète et les méthodes servant à la tenue des statistiques sur l'incidence de cette maladie sont inadéquates. Malgré la rareté et l'hétérogénéité des données, on peut affirmer que la notification du choléra est fortement déficiente en Inde.

Resumen**Análisis de la notificación del cólera en la India durante 1997-2006**

Objetivo Definir con más precisión la incidencia anual de cólera en la India, considerada superior a la que se notifica a la Organización Mundial de la Salud (OMS).

Métodos Hicimos búsquedas en las publicaciones médicas para extraer datos sobre los casos de cólera notificados en la India entre 1997 y 2006 y comparamos las cifras obtenidas con las notificadas anualmente a la OMS en el mismo periodo. Estas últimas se obtuvieron a partir de los resúmenes anuales de la OMS sobre los casos de cólera notificados y del *National Health Profile 2006*, publicado por la Oficina Central de Información Sanitaria de la India.

Resultados De 35 estados o territorios de la unión de la India, 21 notificaron casos de cólera durante un año al menos entre 1997 y 2006. El estado de Bengala Occidental notificó casos cada

uno de esos diez años, mientras que el estado de Maharashtra y el territorio de la unión de Delhi notificaron casos nueve años, y Orissa siete. Hubo 68 brotes en 18 estados, y en total se detectaron 222 038 casos. Esta cifra es unas seis veces mayor que la notificada a la OMS (37 783) en el mismo periodo. Los estados de Orissa, Bengala Occidental, Islas Andaman y Nicobar, Assam y Chhattisgarh concentraron el 91% de todos los casos asociados a brotes.

Conclusión La notificación de los casos de cólera en la India es incompleta, y los métodos empleados para mantener las estadísticas sobre la incidencia de la enfermedad son insuficientes. Aunque los datos son escasos y heterogéneos, puede afirmarse que la notificación de los casos de cólera en la India es claramente insatisfactoria.

ملخص**الكوليرا في الهند: تحليل بلاغات الأعوام 2006-1997**

الغرض: التحديد الدقيق لمعدل الوقوع السنوي للكوليرا في الهند، والمعتقد أنه أعلى مما يجري الإبلاغ عنه إلى منظمة الصحة العالمية.

الطريقة: تفقد الباحثون النشريات الطبية لاستخلاص البيانات المتعلقة بحالات الكوليرا في الهند في الأعوام 1997 حتى 2006، وقارنوا الأعداد المكتشفة بالأعداد المبلغ عنها سنوياً لمنظمة الصحة العالمية في نفس الفترة. وجمعت المعلومات الأخيرة من الموجز السنوي لمنظمة الصحة العالمية لحالات الكوليرا المبلغ عنها والمرتمس الصحي الوطني لعام 2006، والذي نشره المكتب المركزي الهندي للاستخبارات الصحية.

الموجودات: من بين 35 ولاية هندية أو مقاطعة اتحادية، أبلغت 21 ولاية منهم عن اكتشاف حالات كوليرا في سنة واحدة على الأقل خلال الأعوام 1997 حتى 2006. وأبلغت ولاية غرب البنغال عن وجود حالات الكوليرا طوال

العشر سنوات، بينما أبلغت ولاية ماهاراشتا والولاية الاتحادية لدلهي عن وجود الحالات طوال تسع سنوات، وأبلغت ولاية أوريسا عن وجود الحالات طوال سبع سنوات. ووقعت 68 فاشية في 18 ولاية، وبلغ إجمالي الحالات المكتشفة 222038 حالة. وهذا الرقم يساوي ستة أضعاف الرقم المبلغ عنه لمنظمة الصحة العالمية في نفس الفترة (وهو 37783 حالة). وشكلت ولايات أوريسا، وغرب البنغال، وأندامان، وجزر نيكوبار، وآسام، وتشهاتيسغار 91% من جميع الحالات المتعلقة بالفاشيات.

الاستنتاج: بعد التبليغ عن حالات الكوليرا غير مكتمل في الهند، وتعد الطرق المستخدمة لحفظ الإحصائيات الخاصة بمعدلات الوقوع غير كافية. وبالرغم من أن ضآلة البيانات وتباينها، فإن التبليغ عن الكوليرا في الهند يعاني من العجز الشديد.

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