Compatible poliomyelitis cases in India during 2000
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Objective To describe the characteristics of compatible poliomyelitis cases and to assess the programmatic implications of clusters of such cases in India.

Methods We described the characteristics of compatible poliomyelitis cases, identified clusters of compatible cases (two or more in the same district or neighbouring districts within two months), and examined their relationship to wild poliovirus cases.

Findings There were 362 compatible cases in 2000. The incidence of compatible cases was higher in districts with laboratory-confirmed poliomyelitis cases than in districts without laboratory-confirmed cases. Of 580 districts, 96 reported one compatible case and 72 reported two or more compatible cases. Among these 168 districts with at least one compatible case, 123 had internal or cross-border clusters of compatible cases. In 27 districts with clusters of compatible cases, no wild poliovirus was isolated either in the same district or in neighbouring districts. Three of these 27 districts presented laboratory-confirmed poliomyelitis cases during 2001.

Conclusion Most clusters of compatible cases occurred in districts identified as areas with continuing wild poliovirus transmission and where mopping-up vaccination campaigns were carried out. As certification nears, areas with compatible poliomyelitis cases should be investigated and deficiencies in surveillance should be corrected in order to ensure that certification is justified.

Keywords Poliomyelitis/diagnosis/epidemiology; Paralysis/classification/virology; Muscle hypotonia/classification/virology; Poliovirus/isolation and purification; Feces/virology; Cluster analysis; India (source: MeSH, NLM).

Mots clés Poliomyélite antérieure aiguë/diagnostique/épidémiologie; Paralysie/classification/virologie; Hypotone musculaire/classification/virologie; Poliovirus humain/isolement et purification; Fécès/virologie; Sondage en grappes; Inde (source: MeSH, INSERM).

Palabras clave Poliomielitis/diagnóstico/epidemiología; Parálisis/clasificación/virología; Hipotonia muscular/clasificación/virología; Poliovirus/aislamiento y purificación; Heces/virología; Análisis por conglomerados; India (fuente: DeCS, BIREME).


Introduction

In the acute flaccid paralysis (AFP) surveillance system fell from 1126 in 1999 to 265 in 2000 (1), when the WHO-recommended virological classification scheme for AFP cases was adopted (2). AFP cases from whom wild poliovirus is isolated from at least one stool specimen are classified as confirmed poliomyelitis. AFP cases for whom there are not two adequate stool specimens and one stool sample are classified as confirmed poliomyelitis. AFP cases from whom wild poliovirus is isolated from at least virological classification scheme for AFP cases was adopted (2). Of 580 districts, 96 reported one compatible case and 72 reported two or more compatible cases. Among these 168 districts with at least one compatible case, 123 had internal or cross-border clusters of compatible cases. In 27 districts with clusters of compatible cases, no wild poliovirus was isolated either in the same district or in neighbouring districts. Three of these 27 districts presented laboratory-confirmed poliomyelitis cases during 2001.

Conclusion Most clusters of compatible cases occurred in districts identified as areas with continuing wild poliovirus transmission and where mopping-up vaccination campaigns were carried out. As certification nears, areas with compatible poliomyelitis cases should be investigated and deficiencies in surveillance should be corrected in order to ensure that certification is justified.

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Two stool specimens collected at least 24 h apart, both within 14 days of the onset of paralysis and both arriving in the laboratory in good condition ( > 8 g; maintained in the cold chain; no desiccation; no leakage).
consider their occurrence over time and compare their characteristics to those of other AFP cases. Finally, we examine the geographical and temporal clustering of compatible cases and discuss their programmatic importance with respect to the identification of areas of poliovirus transmission.

Methods

Surveillance data

The AFP surveillance system in India collects data on all AFP cases occurring in children aged under 15 years and on any cases where poliomyelitis is suspected, regardless of age (3). Approximately 210 surveillance medical officers are posted throughout the country to oversee a surveillance network involving over 8500 health care institutions and private providers that were reporting weekly at the end of 2000 (4). The surveillance medical officers visit every AFP case, take clinical histories, and perform clinical examinations. Two stool samples should be collected from each reported case within 14 days of the onset of paralysis and sent to WHO-accredited laboratories for poliovirus isolation and intratypic differentiation as Sabin vaccine-like or wild type. At 60 days after the onset of paralysis the surveillance medical officers re-examine all cases in order to verify whether paralysis has persisted. The National Polio Surveillance Project in New Delhi maintains a database on case investigation and laboratory results for all AFP cases.

Definition of compatible cases

AFP cases in which wild poliovirus has been isolated from a stool specimen are classified as confirmed poliomyelitis. Those with two adequate stool specimens that are negative for wild poliovirus are classified as non-polio AFP cases (5). AFP cases without adequate stool specimens and with no residual weakness 60 days after the onset of paralysis are discarded as non-polio AFP cases.

As soon as it is apparent that an AFP case will not have two adequate stool specimens, the surveillance medical officer initiates a standard procedure leading to expert review. Whenever possible, nerve conduction velocity tests and electromyography are performed along with a detailed neurological examination at least three weeks after the onset of paralysis. The surveillance medical officer compiles documentation including hospital records, interviews with attending physicians, clinical examination, and epidemiological investigation; a map of the area in question is included, showing the location of all wild poliovirus and compatible and non-polio AFP cases. AFP cases with two adequate stool specimens and without adequate stool specimens and with no residual weakness 60 days after the onset of paralysis are discarded as non-polio AFP cases.

Laboratory procedures

A network of eight WHO-accredited laboratories in India conducts poliovirus isolation studies on AFP stool specimens. One of these laboratories is used for intratypic differentiation of polioviruses as wild or vaccine-derived. Standard procedures are used to isolate viruses from stool suspensions by culture in a rhadomyosarcoma and L20B cell monolayer (6, 7). Serotypes are determined by means of neutralization tests involving the use of high-titre poliovirus equine antisera. Poliovirus isolates are further characterized as Sabin vaccine-like or wild by hybridization with genotypic probes (8), enzyme-linked immunosorbent assay (9), and polymerase chain reaction analyses (10).

Clusters

We defined clusters of compatible cases as two or more compatible cases occurring within two months in the same or in a neighbouring district (11), with clusters being identified by examining the date and district of onset of each compatible case. We determined whether wild poliovirus isolates or additional compatible cases occurred within ±60 days of each compatible case, and whether these cases occurred in the same district or in neighbouring districts.

Results

Compatible poliomyelitis cases

The AFP surveillance system reported 8103 AFP cases. Of these, 93% were investigated within 48 h of notification; 265 were classified as virologically confirmed poliomyelitis, and 6839 were classified as non-polio AFP. The expert panel reviewed the remaining 999 cases in order to arrive at a final classification. Of these, 637 were discarded as non-polio AFP and 362 were classified as compatible with poliomyelitis (Fig. 1).

The median time between the onset of paralysis and the final classification of all 999 cases reviewed by the expert committee was 145 days (range, 19–362 days). Of the
362 compatible cases, 100 were classified as clinically compatible with poliomyelitis, 165 had strong evidence suggesting they were poliomyelitis cases, and 97 had insufficient evidence to be discarded as non-polio AFP.

Table 1 shows the clinical and demographic characteristics of all 8103 AFP cases that were reported and classified during 2000. Compatible cases and confirmed poliovirus cases were on average younger than those discarded as non-polio AFP. Fever was present at the time of onset of paralysis in 79% of confirmed cases and in 68% of compatible cases. Of the confirmed and compatible cases, 83% and 69%, respectively, presented with asymmetric paralysis. It was reported by 30% of confirmed cases that fewer than three doses of oral poliovirus vaccine had been received. Of the 362 compatible cases, follow-up revealed that 247 had residual weakness at 60 days, 112 had died, and 3 were lost to follow-up.

Two stool specimens were collected from 206 (57%) of the compatible cases, one stool specimen was collected from 35 (10%), and no specimens were obtained from 121 (33%) such cases. Among the 250 compatible cases who did not die, two stool specimens were collected from 195 (78%) and none were collected from the others. For the 35 compatible cases from whom only one stool specimen was collected, the median interval from the onset of paralysis to stool collection was 4 days (range, 1–28 days); 31 (80%) of the stools were in good condition; non-polio enterovirus was isolated from 5 (14%) stools. Of the 206 compatible cases for which two stools were collected, the median interval from the onset of paralysis to stool collection was 27 days (range, 4–88 days) and the median interval between the collection of the first and second specimens was 1 day (range, 1–9 days). The condition of 99% of the first and second stools was good. Only 7 of the first stools were collected within 14 days of the onset of paralysis. In one case both stools were collected within 14 days of the onset of paralysis but they did not arrive at the laboratory in good condition. Non-polio enterovirus was isolated from 36 and 33 of the first and second stool specimens, respectively (18% and 16%); in 29 cases (14%), non-polio enterovirus was isolated from both specimens.

The compatible cases occurred in 15 states; 43% were in Uttar Pradesh and 24% were in Bihar (Fig. 2). In contrast, Uttar Pradesh and Bihar accounted for 68% and 19%, respectively, of all wild poliovirus cases. Higher proportions of AFP cases in Uttar Pradesh and Bihar (16% and 13%, respectively) were referred for expert review than in the rest of the country (11%). In Uttar Pradesh, one-third of the cases occurred in the districts of Ghaziabad (14%), Muzaffarnagar (8%), Meerut (7%), and Badaun (7%). In Bihar, Darbhanga district had 11% of the cases, followed by Hazaribagh, Purnia, and Samastipur districts (8% each). Laboratory-confirmed poliomyelitis cases presented a clear seasonal trend, the majority being detected

Table 1. Characteristics of classified acute flaccid paralysis (AFP) cases, India, 2000

<table>
<thead>
<tr>
<th>Variable</th>
<th>Compatible cases after expert review (n = 362)</th>
<th>Wild poliovirus isolated (n = 265)</th>
<th>Non-polio AFP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Discarded after expert review (n = 637)</td>
<td>No expert review (n = 6839)</td>
<td></td>
</tr>
<tr>
<td>Mean age ± SD (months)</td>
<td>25 ± 20</td>
<td>23 ± 20</td>
<td>61 ± 43</td>
</tr>
<tr>
<td>Median age (months)</td>
<td>18 (1–167)a</td>
<td>18 (2–144)</td>
<td>49 (1–202)</td>
</tr>
<tr>
<td>% aged &lt; 5 years</td>
<td>96</td>
<td>96</td>
<td>59</td>
</tr>
<tr>
<td>Died (%)</td>
<td>31</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>Fever (%)</td>
<td>68</td>
<td>79</td>
<td>55</td>
</tr>
<tr>
<td>Asymmetry (%)</td>
<td>69</td>
<td>83</td>
<td>48</td>
</tr>
<tr>
<td>Mean OPV doses ± SD</td>
<td>6 ± 4</td>
<td>5 ± 4</td>
<td>7 ± 5</td>
</tr>
<tr>
<td>Median OPV doses</td>
<td>6 (0–20)</td>
<td>4 (0–17)</td>
<td>7 (0–25)</td>
</tr>
<tr>
<td>&lt;3 OPV doses (%)</td>
<td>20</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>Median interval (days) to stool 1</td>
<td>24 (1–88)</td>
<td>6 (0–33)</td>
<td>19 (0–88)</td>
</tr>
<tr>
<td>No. of stools collected</td>
<td>33</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>1 (%)</td>
<td>10</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>2 (%)</td>
<td>57</td>
<td>98</td>
<td>69</td>
</tr>
<tr>
<td>2 adequate stool specimensb</td>
<td>0</td>
<td>88</td>
<td>0</td>
</tr>
<tr>
<td>NPEVd isolated in at least one stool</td>
<td>19</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>State</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uttar Pradesh (%)</td>
<td>43</td>
<td>68</td>
<td>22</td>
</tr>
<tr>
<td>Bihar (%)</td>
<td>24</td>
<td>19</td>
<td>16</td>
</tr>
</tbody>
</table>

a Figures in parentheses are the range.

b Defined as both collected within 14 days of paralysis onset and both arriving at the lab in good condition. By definition, compatible cases do not have 2 adequate stool specimens.

c 559 of 6839 discarded without expert review did not have 2 adequate stool specimens. All of these 559 cases were followed up at 60 days after paralysis onset and none had residual weakness at follow-up.

d NPEV = non-polio enterovirus.
between July and January. There was no clear seasonal trend for compatible cases (Fig. 3).

There were certain differences between the cases classified as non-polio AFP after expert review and the non-polio AFP cases that did not undergo expert review. Those that were discarded after expert review were generally older (median age, 49 months) and presented less frequently with asymmetric paralysis (48% versus 59%). Both categories of non-polio AFP cases were similar with respect to the presence of fever at the onset of paralysis and geographical distribution. The 112 compatible cases that died and the 250 that did not die were similar with respect to age, presence of fever, and number of doses of oral poliovirus vaccine received.

Table 2 shows the characteristics of all compatible cases by category (strong evidence/clinical poliomyelitis/insufficient evidence to discard). Cases with strong evidence were generally more likely than others to have asymmetric paralysis and had a longer interval between the onset of paralysis and the collection of the first stool specimen. Cases for which there was insufficient evidence to discard were older than the others (median age, 26 months versus 17 months and 18 months for the “strong evidence” and “clinical poliomyelitis” categories, respectively) and 65% had fever at the onset of paralysis. No stool specimens were collected from 57% of the cases in the “insufficient evidence to discard” category, and 77% of the cases in this category died before 60-day follow-up could be completed.

Clusters of compatible cases
At least one laboratory-confirmed poliomyelitis case was detected in 89 of 580 districts. In these 89 districts the incidence of compatible cases was 2 per million population aged under 15 years, whereas it was only 0.5 in all other districts (Table 3). Uttar Pradesh had the highest incidences of both laboratory-confirmed and compatible cases in comparison with Bihar and the rest of the country.
Of the 580 districts, 168 reported at least one compatible case during 2000 and 72 reported two or more such cases. Clusters of compatible cases, i.e. two or more within two months in a district or a neighbouring district, affected 123 districts (Fig. 4). Of the 123 districts with clusters, 96 had wild poliovirus isolated in the same district or a neighbouring district and were thus included in mopping-up activities. During 2000, isolated clusters of compatible cases occurred in 27 districts that were not selected for mopping-up because no wild poliovirus was identified in the areas concerned. In 3 of these 27 districts, wild poliovirus was isolated in 2001.

Discussion

The large number of compatible poliomyelitis cases reported during 2000 in India offered a unique opportunity to characterize this subgroup of AFP cases, which is becoming more important as eradication progresses. Understanding the patterns of occurrence of compatible cases can help to pinpoint weaknesses in the AFP surveillance system and indicate what corrective measures should be taken.

Of the 362 compatible cases, 68% were assessed 60 days after the onset of paralysis and found to be affected by residual weakness. These cases were classified as compatible because of inadequate stool collection, the main factor in which was a long interval between the onset of paralysis and case notification. Additional factors contributing to delayed stool collection should be identified so that this component of the surveillance system can be improved. In order to reduce the number of compatible cases it is necessary to minimize the time between the onset of paralysis and case notification and investigation.

Weak links at this level may include delays in case presentation to the reporting network and delays between the notification and the investigation of reported cases. The second most common factor leading to the classification of AFP cases as compatible with poliomyelitis was the death of patients for whom two adequate stool specimens had not been obtained. The only clinical difference between the compatible cases who died and those who did not die was that fewer of the former had asymmetric paralysis.

Distribution of compatible poliomyelitis cases in India

Our analysis showed a comparatively high incidence of compatible poliomyelitis cases in districts that reported laboratory-confirmed cases. This analysis does not account for other factors at the district level, such as poor stool collection rates or active AFP detection when wild poliovirus is found, which directly contribute to the rate of compatible cases. Analysis of geographical and temporal clustering of compatible cases in India in 2000 revealed that 24% of districts with clusters of compatibles did not identify laboratory-confirmed cases and did not have a neighbouring district with laboratory-confirmed cases. Most clusters of compatibles

Table 2. Characteristics of compatible cases, India, 2000, by category of compatibility

<table>
<thead>
<tr>
<th>Variable</th>
<th>Strong evidence (n = 165)</th>
<th>Clinically polio (n = 100)</th>
<th>Insufficient evidence to discard (n = 97)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD (months)</td>
<td>24 ± 23</td>
<td>22 ± 14</td>
<td>30 ± 19</td>
</tr>
<tr>
<td>Median age (months)</td>
<td>17 (1–167)</td>
<td>18 (2–81)</td>
<td>26 (1–94)</td>
</tr>
<tr>
<td>Died (%)</td>
<td>0.6</td>
<td>36</td>
<td>77</td>
</tr>
<tr>
<td>Fever (%)</td>
<td>73</td>
<td>69</td>
<td>65</td>
</tr>
<tr>
<td>Asymmetry (%)</td>
<td>87</td>
<td>70</td>
<td>47</td>
</tr>
<tr>
<td>Mean OPV doses ± SD</td>
<td>6 ± 4</td>
<td>5 ± 3</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>Median OPV doses</td>
<td>6 (0–20)</td>
<td>5 (0–13)</td>
<td>6 (0–15)</td>
</tr>
<tr>
<td>&lt;3 OPV doses (%)</td>
<td>19</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Median interval to stool (days)</td>
<td>27 (14–88)</td>
<td>23.5 (1–67)</td>
<td>20 (1–68)</td>
</tr>
<tr>
<td>No. of stools collected 0 (%)</td>
<td>23</td>
<td>28</td>
<td>57</td>
</tr>
<tr>
<td>1 (%)</td>
<td>77</td>
<td>56</td>
<td>24</td>
</tr>
<tr>
<td>2 (%)</td>
<td>0</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>NPEVb isolated in at least one stool</td>
<td>18</td>
<td>22</td>
<td>14</td>
</tr>
</tbody>
</table>

a Figures in parentheses are the range.

b NPEV = non-polio enterovirus.
occurred in districts where wild poliovirus isolates were obtained or where there was at least one wild poliovirus isolate in a neighbouring district during the year. In other words, clusters of compatibles occurred in districts that would otherwise have been identified as areas with ongoing wild poliovirus transmission and would have been included in mopping-up vaccination campaigns. A limitation of our analysis is that the size of a district — both its geographical area and population — affects the likelihood of finding clusters of compatibles. The numbers of compatible cases and clusters are likely to be higher in districts with comparatively large populations than in those with smaller populations. This should be taken into consideration when our analysis is being compared with analyses made in other countries.

The only other published analysis of clusters of compatible AFP cases was conducted in China. A more specific definition of compatibles was used, requiring, in addition to our criteria, that the AFP cases had fever at the onset of paralysis and that fewer than three doses of oral poliovirus vaccine were administered. During 1997, a total of 57 of these high-risk cases occurred and four clusters were identified in five counties. Areas with clusters of high-risk AFP cases corresponded to areas where wild poliovirus had last been reported and where poor implementation of poliomyelitis eradication strategies had been recognized. In contrast to the situation in India in 2000, there were no wild poliovirus cases in China at the time of this cluster analysis. The authors concluded that areas with clusters should be investigated and that surveillance indicators should be assessed, to reveal and correct surveillance inadequacies or pockets of low immunization coverage.

**AFP cases and the Indian classification system**

Most countries now use the virological classification system for AFP cases. Only in India are compatible cases subdivided into three categories on the basis of expert review. Evidence of anterior horn cell disease is likely to increase the specificity of the diagnosis. Unfortunately, such evidence is difficult to obtain from cases that die or are lost to follow-up. In India, electrophysiological evidence was used, when available, in order to subdivide compatible cases. This was an additional measure that did not affect the classification of cases as compatible or not.

It is difficult to assess the meaning of the three categories of compatible cases used in the Indian classification system. The probability of the expert committee classifying a case as strongly or clinically compatible may be increased if it has certain clinical characteristics or if it occurs in a district with known wild poliovirus circulation. For example, the finding that asymmetric paralysis and fever tend to occur more frequently in strongly compatible cases than in the other categories of compatible cases may simply reflect the tendency of the expert committee to classify cases with these characteristics as clinically compatible; if there are also supporting electrophysiological data the cases will be classified as strongly compatible. While it is reassuring that the subcategories correspond to what is expected, the programmatic implications of this scheme are unclear. It is important to note that India’s unique subclassification of compatible cases does not follow WHO standard policy and does not make any contribution to the goal of eradication.

**Limitations of our analysis**

Our analysis does not consider whether clusters of compatible cases occurred in districts before wild poliovirus was detected. During 2000, wild poliovirus transmission occurred primarily in focal areas in the northern states. There was considerable overlapping between the dates of onset and the locations of compatible and wild poliomyelitis cases, particularly in Uttar Pradesh.
Résumé

Cas compatibles avec un diagnostic de poliomyélite observés en Inde pendant l’an 2000

Objectif Décrire les caractéristiques des cas compatibles avec un diagnostic de poliomyélite et évaluer les conséquences programmatisques de la présence d’agrégats de tels cas en Inde.

Méthodes Nous avons identifié des agrégats de cas compatibles avec un diagnostic de poliomyélite (deux ou plusieurs cas dans le même district ou dans des districts voisins sur une période de deux mois) et examiné leur relation avec les cas dus au poliovirus sauvage.

Résultats En 2000, 362 cas compatibles ont été dénombrés. L’incidence de ces cas était plus élevée dans les districts comprenant des cas de poliomyélite confirmés au laboratoire. Sur 580 districts, 96 ont rapporté un cas compatible et 72 deux ou plusieurs cas. Des agrégats de cas compatibles ont été observés soit à l’intérieur du district soit sur la zone frontalière dans 123 des 168 districts ayant rapporté au moins un cas compatible. Dans 27 des districts possédant des agrégats de cas, aucun poliovirus sauvage n’a été isolé, non plus que dans les districts voisins. Trois de ces 27 districts ont connu des cas de poliomyélite confirmés au laboratoire en 2001.

Conclusion La plupart des agrégats de cas compatibles avec un diagnostic de poliomyélite ont été observés dans des districts où la transmission du poliovirus sauvage se poursuit et où des campagnes de vaccination par ratissage sont en cours. Comme le moment de la certification approche, les zones possédant des cas compatibles avec un diagnostic de poliomyélite devront faire l’objet d’investigations et tout défaut de surveillance devra être corrigé afin d’assurer que la certification est justifiée.
Poliomielitis en la India: casos compatibles surgidos durante 2000

Objetivo

Describir las características de los casos de aparente poliomielitis y evaluar las implicaciones programáticas de los agrupamientos de esos casos en la India.

Métodos

Identificamos agrupamientos de casos compatibles con el diagnóstico de poliomielitis (dos o más en el mismo distrito o en distritos vecinos en un plazo de dos meses) y su relación con los casos debidos al poliovirus salvaje.

Resultados

En 2000 se registraron 362 casos compatibles. La incidencia de casos compatibles fue mayor en los distritos con casos de poliomielitis confirmados en laboratorio. De 580 distritos, 96 notificaron un caso compatible y 72 notificaron dos o más casos compatibles. Entre esos 168 distritos donde hubo al menos un caso compatible, 123 presentaban agrupamientos internos o transfronterizos de casos compatibles. No se aislaron poliovirus salvajes en 27 de los distritos donde se hallaron agrupamientos, ni en ninguno de los distritos vecinos. Tres de esos 27 distritos presentaron casos de poliomielitis confirmados en laboratorio durante 2001.

Conclusión

La mayoría de los agrupamientos de casos compatibles se dieron en distritos donde seguía habiendo transmisión del poliovirus salvaje y donde se estaban llevando a cabo campañas de vacunación de barrido. A medida que se aproxima la fecha de certificación, habría que investigar las zonas con casos de aparente poliomielitis, y corregir los fallos de la vigilancia detectados a fin de asegurar que la certificación esté justificada.

References