ORIGINALES

Most polio cases should be confirmed by laboratory in endemic countries

P. Godoy[a], M. Haghgou[b], F. Popovici[a] and N.A. Sadozai[b]

[a]Stop Polio Team. World Health Organization. [b]World Health Organization. Afghanistan.

SUMMARY

Background. The objective of this study was to characterise cases of polio classified as "compatible" by comparing them with cases confirmed by laboratory.

Methods. Since 1997, when an acute flaccid paralysis (AFP) case was detected in Afghanistan it was investigated and two stool samples were collected. To investigate the association between the dependent variable (either compatible polio or laboratory confirmed polio) and the independent variables we calculated the adjusted OR (ORa).

Results. Over the period 1997-1999, 365 AFP cases were detected, of which 59.2% were classified as poliomyelitis (216/365); 44.4% of polio cases (96/216) had wild poliovirus isolated and the rest, 55.6% (120/216) were considered "compatible" with poliomyelitis.

There were differences between "compatible" and polio cases confirmed by laboratory of variables: under 1 year age group (ORa = 0.1; CI 95%: 0.1-0.3), 1 to 2 years old (ORa = 0.2; CI 95%: 0.1-0.5) and 2 to 3 years old (ORa = 0.2; CI 95%: 0.1-0.9); fever at onset of paralysis (ORa = 0.1; CI 95%: 0.1-0.7) and asymmetric paralysis (ORa = 0.6; CI 95%: 0.3-1.2).

Conclusions. This study provides evidence that there are some differences between "compatible" and confirmed cases of polio and suggests that some patients could be misclassify as having poliomyelitis. Furthermore, it shows that most polio cases should be confirmed by laboratory in endemic countries.

KEY WORDS: Poliomyelitis. Poliovirus. Epidemiology.

RESUMEN

Antecedentes. El objetivo del estudio fue caracterizar los casos de polio clasificados como "compatibles" mediante su comparación con los casos confirmados por el laboratorio.

Métodos. En Afganistán desde 1997, en todos los casos de parálisis fláccida aguda (PFA) detectados se recogieron dos muestras de heces y posteriormente fueron investigados.

Para estudiar la asociación entre la variable dependiente (caso de polio compatible o confirmado por el laboratorio) con el resto de las variables independientes se calcularon las *odds ratio* ajustadas (ORa).

Resultados. En el período 1997-1999 se detectaron 365 casos de PFA de los cuales el 59,2% fueron clasificados como casos de poliomielitis (216/365). En el 44,4% de los casos de polio (96/216) se aisló un poliovirus y el resto de casos, 55,6% (120/216), fueron considerados como "compatibles" con poliomielitis. Se observaron diferencias entre los casos de polio "compatibles" con los casos confirmados por el laboratorio para las variables: menores de 1 año (ORa = 0,1; IC del 95% = 0,1-0,3), de 1 a 2 años (ORa = 0,2; IC del 95% = 0,1-0,5) y de 2 a 3 años (ORa = 0,2; IC del 95% = 0,1-0,9); fiebre en el inicio de la parálisis (ORa = 0,1; IC del 95% = 0,1-0,7) y parálisis asimétrica (ORa = 0,6; IC del 95% = 0,3-1,2).

Conclusiones. Este estudio evidencia la existencia de diferencias entre los casos de polio "compatibles" con los confirmados por el laboratorio y sugiere que algunos pacientes podrían estar clasificados erróneamente como casos de poliomielitis. Ello pone de manifiesto que la mayoría de casos deberían ser confirmados por el laboratorio en los países con endemia de polio.

PALABRAS CLAVE: Poliomielitis. Poliovirus. Epidemiología.

Correspondence: P. Godoy. Vall d'Aneu, 45. 25199 Lleida. Spain. E-mail: godoy@slle.scs.es

Introduction

In 1988 the World Health Assembly adopted a resolution for the global eradication of poliomyelitis by the year 2000 and polio eradication initiatives are now operational in all polio endemic countries[1,2]. In a number of countries, however, disease surveillance systems are weak due a variety of factors ranging from a lack of human and financial resources to unrest and war[3,4].

Afghanistan, a country in the Eastern Mediterranean Region (EMR) with an ongoing civil war, is one of five countries (Afghanistan, Egypt, Iraq, Pakistan, Somalia and Sudan) that have reported cases with indigenous strains of wild poliovirus since 1996[4,5]. Although no national disease surveillance system was previously in place in Afghanistan, in 1997 acute flaccid paralysis (AFP) surveillance was introduced at major health facilities in regional capitals and the system was extended in 1999[4,6].

As a result of the initiative to eradicate polio, paralytic poliomyelitis has became rare, however physicians may not be familiar with the disease or may confuse poliomyelitis with other causes of AFP[7,8]. The diagnosis of paralytic poliomyelitis is based on: *a)* clinical course; *b)* virological testing, and *c)* residual neurological deficit 60 days after the onset of symptoms. Without a positive laboratory result case classification must be based on clinical symptoms and a panel of independent experts must determine whether a case meets the case definition[8]. At the end of a polio eradication initiative the decision making, including deciding when to stop immunization[9,10], has to be based on surveillance results. The objective of this study was to characterise cases of polio classified as "compatible" and to compare them with laboratory confirmed cases.

Methods

Cases were detected by a surveillance system based on sentinel sites (generally hospital health centres), which had been set up in Afghanistan in September 1997. After demostrating its utility the system was extended in 1999. Local staff were trained in AFP surveillance procedures to enable them to conduct regular active surveillance visits to health centres and to identify and investigate AFP cases.

When an AFP case was detected it had to be investigated within 48 h, and a standard case investigation form was completed and two stool samples were collected with an interval of 24-48 h between samples.

Cases of AFP in children under 15 years old and paralysing illnesses in people of all ages were regarded as probable cases of poliomyelitis. After full investigation, "probable" polio cases were reclassified as either "confirmed", "compatible" or "discarded". An AFP case was confirmed if poliovirus was isolated in a specimen from the patient. Cases of AFP associated with inadequate specimens, residual paralysis or death and those that were not followed up were classified as "compatible". "Discarded" cases were properly investigated, including the collection of adequate stool samples, but either another cause of paralysis was identified or laboratory tests did not detect wild poliovirus. An adequate stool sample was defined as two specimens collected from a patient, with an interval of at least 24 hours between specimens and with collection within 14 days of onset of paralysis. Each specimen had to have an adequate volume (8-10 g) and to arrive at the laboratory in "good" condition (no desiccation, no leakage and adequately documented).

The variables in this study were: classification of AFP cases (polio and non-polio AFP), cases of poliomyelitis (either compatible or virologically confirmed), date of onset of paralysis, date of report, date of investigation, age, gender, residence, symptoms (fever, flaccid paralysis, asymmetric paralysis, residual paralysis at 60 days, flaccid paralysis at 60 days), date of stool samples, doses of oral polio vaccine (OPV) (two categories: one or more and none or unknown).

We calculated the standard indicators of AFP surveillance: annual AFP non-polio rate per 10^5 population under 15 years of age (target ≥ 1); reported cases investigated with two adequate stool samples collected within 14 days of the onset of paralysis (target ≥ 80%); reported AFP cases with stool samples arriving at the laboratory within three days (target ≥ 80%); reported AFP cases with a follow-up examination at least 60 days after the onset of paralysis (target ≥ 80%).

To investigate the association between the dependent variable (compatible polio or laboratory confirmed polio) and the independent variables (age group, gender, symptoms, vaccination status) we used odds ratio (OR) with a confidence interval (CI) of 95%. We calculated the adjusted OR (ORa) using a non-conditional model of multivariate logistic regression in order to determine the independent effect of each variable and its contribution to the compatible or confirmed polio case.

The stool samples were analysed at the virology laboratory of Pakistan's National Institute of Health, in Islamabad. First, attempts were made to recover poliovirus from the samples and to characterise isolated viruses as wild type or vaccine related. Once serotype had been demonstrated intratypic differentiation was considered. Finally, the strains were sent to CDC for genomic sequencing of the poliovirus.

Results

During the period 1997-1999, 365 AFP cases were reported, of which 59.2% were classified as cases of poliomyelitis (216/365) and 40.8% were discarded (149/365).

The rate of non-polio AFP in children under 15 years increased from 0.1 in 1997 to 0.8 in 1999, and the number of patients subjected to a follow-up examination met or almost met the target for this indicator. Nevertheless, fewer than 60% of the patients provided two specimens within 14 days of the onset of paralysis and fewer than 20% of specimens arrived at the laboratory within 3 days of collection.

Over the whole period 216 polio cases were detected. The most frequent clinical symptoms were: fever (92.6%), flaccid paralysis (86.7%), residual paralysis at 60 days (82.9%) and asymmetric paralysis (66.6%) (table 1). Most cases appeared in the under 2 years age group, and, although 42.5% (92/216) had been vaccinated with at least one dose of OPV, only 16.7% had received three doses (36/216). Out of the total number of polio cases, 96 (44.4%) had wild poliovirus isolated from a stool specimen while the other 55.6% (120/216), were considered as "compatible" with poliomyelitis. The percentage of virologically confirmed cases of polio by region ranged from 0.0% in Ghazni to 65.2% in Herat (table 2). This

TABLE 1

Distribution of polio cases diagnosed on clinical basis or by laboratory, according to different variables

Variable	Clinical diagnosis n (%)	Lab diagnosis n (%)	OR	95% CI
Age (years)				
> 1	26 (21.7)	45 (46.9)	0.1	0.1-0.3
1-2	46 (38.3)	37 (38.9)	0.2	0.1-0.5
2-3	16 (13.3)	9 (9.4)	0.3	0.1-0.9
3+	32 (26.7)	5 (5.2)	Reference	
Gender				
Female	51 (42.9)	44 (45.8)	0.9	0.5-1.5
Male	68 (57.1)	52 (54.2)	Reference	
At least one dose OPV				
Yes	51 (42.5)	41 (42.7)	1.3	0.7-2.1
No	69 (57.5)	55 (57.3)	Reference	
Fever				
Yes	160 (88.3)	94 (97.9)	0.2	0.1-0.7
No	14 (11.7)	2 (2.1)	Reference	
Flaccid paralysis				
Yes	61 (83.6)	56 (90.3)	0.5	0.2-1.5
No	12 (16.4)	6 (9.7)	Reference	
Asymmetric paralysis				
Yes	71 (49.7)	72 (75.8)	0.5	0.3-0.9
No	48 (40.2)	23 (24.2)	Reference	
Residual paralysis				
Yes	101 (84.2)	74 (81.3)	1.2	0.6-2.5
No	19 (15.8)	17 (18.7)	Reference	

OR: odds ratio; CI: confidence interval.

TABLE 2

Polio cases, by region and laboratory confirmation, Afghanistan 1997-1999

Region	Diagnosis		Total
	Laboratory, n (%)	Clinical, n (%)	
Faizabad	2 (28.6)	5 (71.4)	7
Ghazni	0 (0.0)	13 (100.0)	13
Herat	30 (65.2)	16 (34.8)	46
Jalalabad	16 (43.2)	21 (56.8)	37
Kabul	2 (9.5)	19 (90.5)	21
Kandahar	31 (49.2)	32 (50.8)	63
Kunduz	14 (63.6)	8 (36.4)	22
Mazar	1 (14.3)	6 (85.7)	7
Total	96 (44.4)	120 (55.6)	216

$\chi^2 = 35.99$; p = 0.00000730.

revealed important geographical differences in AFP surveillance systems within Afghanistan.

Differences between "compatible" cases and polio cases confirmed by laboratory remained constant or increased in the multivariate analysis of variables: under 1 year age group (ORa = 0.1; CI 95%: 0.1-0.2), 1 to 2 years old (ORa = 0.1; CI 95%: 0.1-0.5) and and 2 to 3 years old (ORa = 0.2; CI 95%: 0.1-0.9); fever at the onset of paralysis (ORa = 0.1; CI 95%: 0.1-0.7) but decreased in the case of asymmetric paralyisis (ORa = 0.6; CI 95%: 0.3-1.2) (table 3).

From 96 virologically confirmed cases, we isolated 63 type 1 wild poliovirus (65.6%), 2 (2.1%) type 2 poliovirus (2.1%) and 29 cases of type 3 (30.2%). However, wild poliovirus type 2 was not isolated after 1997.

TABLE 3

Factors associated with compatible polio cases, Afghanistan 1997-1999

Variable	OR crude	OR adjusted*	95% CI
Age (years)			
> 1	0.1	0.1	0.1-0.3
1-2	0.2	0.1	0.1-0.6
2-3	0.3	0.2	0.1-0.9
+3	Reference		
Fever			
Yes	0.2	0.1	0.1-0.7
No	Reference		
Asymmetric paralysis			
Yes	0.5	0.6	0.3-1.2
No	Reference		

*OR adjusted, odds ratio adjusted for the rest of variables in the table; CI: confidence interval.

Discussion

Surveillance of cases of AFP is critical for guiding programmed activities and also for working towards an eventual polio free situation. AFP surveillance also helps to monitor the quality of surveillance in the absence of cases of poliomyelitis. In the final stages of eradication, it would otherwise be impossible to decide whether apparent poliomyelitis cases represented a reliable result or were simply due to deficiencies in surveillance techniques[7,8].

Although coverage surveys conducted in Afghanistan in 1998 suggested that routine vaccination was applied to fewer than 30% of children, National Immunization Days (NID) were conducted nation-wide in 1997, 1998 and 1999, and there were two additional rounds in 1999[4]. Thus, the observed increase in recorded polio cases from 1997 to 1999 could mainly be attributed to improvements in AFP surveillance. As reporting becomes more complete, a higher percentage of polio cases will be identified and reported, even though the real number of cases will probably have decreased substantially[4].

The recorded non-polio rate per 10^5 children under 15 years of age increased from 0.1 in 1997 to 0.8 in 1999. Furthermore, the rate to year 2000 has recently been reported as 1.20[4]. However, the indicators relating to laboratory performance are far from the recommended goals[5] and they deserve particular attention particularly as this compromises the ability of the system to detect wild poliovirus.

The clinical symptoms observed in this study confirm the results of other publications[11,12]. The wide regional disparities in the percentage of compatible cases indicate that there are large geographic differences in surveillance performance and suggests that certain regions (Kabul, Ghazni, Mazar) need special intervention programmes.

Cases of compatible polio were less likely in children under 3 years of age and were not generally associated with fever before the onset of paralysis. Other studies found that, compared with the "gold standard" of virologically confirmed poliomyelitis, the clinical case definition had a sensitivity of 64% and a specificity of 82%, and both were related to the age of patients (under 6 years), to fever at the onset of paralysis and to rapid progression to the maximum extent of paralysis. Other studies reported similar findings and coincided in less sensitivity (false negative results) than specificity (false positive results)[7,11,12].

This study shows that there are important differences between clinical and confirmed polio cases and suggests that some patients

could be misclassified as having poliomyelitis (false positive). As these differences are related to variables such as age and region, the specific data considered when decision making (age group in NID, areas which deserve mopping-up, outbreak immunisation response) could lead to wrong decisions being taken in the final stages of polio eradication.

It is recommended that indicators related to laboratory performance should be improved in the short term. This is the only way to increase the percentage of polio cases confirmed by laboratory (currently 44.4%). Furthermore, some cases are classified as "discarded" as they present two negative stool samples taken within 14 days of the onset of paralysis, although we know that some specimens take more than three days to reach the laboratory and could really be polio cases. This misclassification (false negative) is especially relevant in endemic countries because it could lead to an overestimation of non-polio AFP rates and to an undervaluation of endemic polio. Nevertheless, as Afghanistan has a poor communications system, this goal could be difficult to achieve without additional resources[4-6].

The relative percentages of the different types of poliovirus isolated were similar to those observed in other areas. Type 1 was the most frequent and also the last type to disappear from endemic areas. Type 3 poliovirus is the second in frequency and also disappears before type 1[13,14]. Type 2 was only isolated in 1997 and may now have been eliminated from Afghanistan[15,16]. Virological surveillance should continue in order to confirm this elimination and to monitor reduction in poliovirus biodiversity and in the number of independent chains of transmission[16].

As Afghanistan is one of the last areas in the world with endemic polio, special attention is needed in order to reduce the number of compatible polio cases[17]. However, cultural questions, the lack of adequate means of transport and a weak surveillance system call for special intervention and additional resources[17].

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