Residual paralysis cases in an Acute Flaccid Paralysis surveillance system
in China during 2001-2010

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Abstract

Background: China was declared polio-free in 2000 and maintains an acute flaccid paralysis (AFP) surveillance system. Residual paralysis (RP) in children with acute flaccid paralysis can be caused by Sabin-strain poliovirus (PV) and non-polio enteroviruses (NPEV). We characterize residual paralysis in China between 2001 and 2010.

Methods: AFP surveillance data in mainland China during 2001-2010 were analyze to describe epidemiological patterns and virus isolation result in AFP cases aged less than 15 years and with residual paralysis at 60 days. The four groups, AFP cases with RP isolated with PV, AFP cases with RP isolated with NPEV, AFP without RP isolated with PV, and AFP without RP isolated with NPEV, were compared to see epidemiological features in AFP with RP isolated with PV or isolated with NPEV.

Results: Average annual incidences of AFP with residual paralysis in population aged <15 years old ranged between 5.00/100,000. The age distribution for AFP with RP and PV isolates was peaked 2-4 months. Types II and III Sabin-strain poliovirus were the most commonly isolated. A summer season peak in AFP with RP and NEPV isolates suggested the enteroviruses infections were the potential cause of residual paralysis.

Conclusions: Ten years of AFP surveillance data containing the occurrence of RP can serve as a baseline for the period of polio vaccine transition in China, to help detect vaccine safety signals in a timely manner, and to support future studies on NPEV serotypes circulating in China in the post-eradication era.

Keywords: Residual paralysis, Acute Flaccid Paralysis surveillance system, Sabin-poliovirus, Non-Polio Enteroviruses
INTRODUCTION

Residual paralysis in children with acute flaccid paralysis (AFP) is a severe clinical condition that can be caused by infectious and non-infectious factors. Enteroviruses causing residual paralysis include polio viruses and non-polio viruses. Historically, wild poliovirus types I, II, and III were the most common causes of AFP. Approximately 1% of polio infections led to infection of motor neurons and caused irreversible weakness of lower limb and (5-10%) respiratory muscles, resulting in AFP with residual paralysis. Vaccine associated paralytic poliomyelitis (VAPP), caused by Sabin-poliovirus, is a rare adverse event following the administration of OPV, which can also cause persistent paralysis. Non-Polio Enteroviruses (NEPV), including Coxsackie virus, Echovirus, and newly discovered Enteroviruses, are also major causes of AFP, and occasionally resulting in residual paralysis.

In 2000, China was certified polio-free by the World Health Organization. A core strategy for maintaining polio-free status is strong acute flaccid paralysis (AFP) surveillance. In China, AFP surveillance was established in 1991 and has been operating in all provinces since 1993. It has the capability of timely detection and identification of wild polioviruses and polio vaccine derived viruses. This surveillance is a nationwide source of data about the occurrence of residual paralysis, including virus isolation and virus identification. In this study, we analyzed national AFP surveillance data to describe AFP cases with residual paralysis in mainland China during 2001-2010 to provide insight into the epidemiological patterns of AFP cases with residual paralysis and detection of virus.
METHODS

Overview of AFP surveillance in China

AFP surveillance is conducted through reporting and laboratory testing of fecal specimens for all cases of acute flaccid paralysis (AFP) among children <15 years of age. An AFP case is defined as a child < 15 years of age showing acute or sudden onset of flaccid paralysis in one or more limbs, or other suspected poliomyelitis in a person of any age. Detection of AFP cases relies on passive reporting from hospitals, and active surveillance by county-level epidemic preventive stations (EPS; which later became CDC) staff responsible of periodical examination of hospital charts done to know approximately how many percentages of cases would be missed by the passive reporting. When an AFP case is identified and reported to the surveillance system, epidemiological and clinical information is collected at both an initial investigation and 60 days after the onset of paralysis. Two stool specimens are collected within 14 days of onset of paralysis for virological testing in accordance with WHO recommendation. Isolates are reported as negative or positive for poliovirus and/or Non-Polio Enteroviruses (NEPV). According to international performance standards, in order to be considered sensitive, the non-polio AFP rate is required to be at least 1 case per 100,000 population under 15 years of age. This performance indicator was met in 1995, and then began to be surpassed, ranging from 1.8-2.0/100,000 during 2001-2010. The percentages of AFP cases with adequate stool samples (two stools with more than 5g each collected within 14 days after onset, at least 24 hours apart, arriving at the laboratory in good condition and kept cold with
ice) ranged from 88-91%[1] during the same time.

**Materials**

AFP cases, occurring during 2001-2010, aged less than 15 years, whose enterovirus isolation results and reports of 60-days follow up clinical examination were available, were reviewed for this study. For cases with no virus isolated, we only included cases with stools samples that satisfied the “adequate stool” criteria.

We classified AFP cases into four categories depending on results of 60-day follow up examinations and stool isolates identification: (1) AFP with residual paralysis (RP) with isolated Sabin-poliovirus (PV), PV were all Sabin viruses whose sequences differed by <1% (0.6% for serotype 2) from the parent strain, (2) AFP with RP with isolated Non-Polio Enteroviruses (NEPV), (3) AFP without RP but with isolated PV, and (4) AFP without RP but with isolated NPEV. AFP in which both PV and non-polio enterovirus were isolated, were classified in both categories, so the total number of AFP isolated PV and non-polio enterovirus was larger than the number of AFP cases.

**Statistical analysis**

We describe the epidemiological profiles of AFP cases with RP and compare with AFP without RP in the four categories of AFP cases. We calculate incidence rates by year and season, describe demographic characters (gender and age), and describe OPV vaccination history and final diagnosis. The rates of isolation of the three types of Sabin-poliovirus in AFP with/without RP were determined with respect to OPV vaccination history. In order to analyze epidemiological features in AFP cases associated with PV isolation/with NPEV isolations, we use median, interquartile
range, minimum, and maximum values to describe the monthly distribution of AFP with/without RP. We carried out all statistical analysis using SAS version 9.2.

RESULTS

During 2001-2010, 52,644 cases were reported into national AFP surveillance system, among which, 76 AFP cases were 15 years and older; 1,581 did not have 60-day follow-up examination information; 1,609 had negative stool isolation results but did not have qualified stool samples. A total of 4,266 cases were excluded from analysis. Among the remaining 45,721 AFP cases, 17.7% were AFP cases with residual paralysis.

Temporal distribution of AFP with residual paralysis and virus identification

The average annual incidence rates were 5.00/100,000 for AFP with RP, 0.78/100,000 and 0.61/100,000 for AFP with RP from which, respectively, PV and NEPV, were isolated. Table 1 and Figures 1 and 2 show this information on an annual basis. AFP with RP decreased over time, as did the PV isolation rate. NPEV isolation rates did not decrease during this time. The PV isolation rate was higher in AFP with RP (15.7%) than AFP without RP (3.6%). In AFP with RP, the number of case with PV isolates was slightly larger than cases with non-polio enterovirus isolates (1,269: 989). In contrast, the number of cases of AFP without RP and with PV isolates was much smaller than the number of cases with non-polio enterovirus isolates (1,346: 4,327). AFP cases with RP peaked in summer season from May to August, compared with AFP cases without RP which was relatively constant throughout the year. For AFP
with PV isolates, the number of cases increased at the end and beginning of the years (Fig 1-2).

**Demographic, OPV history, final diagnosis of four categories AFP**

AFP cases below 5 years of age accounted for 94.7%, 76.6%, 88.1%, and 81.6% of AFP with RP and PV isolated, AFP with RP and NPEV isolated, AFP without RP with PV isolated, AFP without RP with NPEV isolated, respectively. In AFP with RP and PV isolates, the sharp peak of onset was occurred in children aged 2-4 month old. The age distribution of AFP without RP with PV isolated did not show a peak (Figure 3).

The sex distribution showed that 61.5-67.4% of cases were male in all four categories. In AFP with PV isolated, the number of cases of AFP with RP was similar to that of AFP without RP (1266:1346), <6 month old constituted 23% in AFP with RP, about two times the number of AFP without RP. For AFP with RP and PV isolates, 81.3% had fever before paralysis onset, a percent that was greater than in the other three categories (52.1%-56.3%). Among the three types of PV, type II, followed by type III, had the highest isolation rates of AFP with RP, especially among cases with a zero-dose OPV history (19.0%) (Tables 2 and 3).

Approximately one third of AFP cases with RP had diagnoses as “other,” which was the most common diagnostic category. Among these cases, PV was isolated in 39.3% and NPEV was isolated in 29.0%. Another 15.8% and 8.8% had no final diagnosis information for PV and NPEV isolates respectively. GBS constituted the second largest diagnostic category (Table 3).
DISCUSSION

In this study, we found that the average annual incidence of AFP with residual paralysis (RP) among children aged <15 years was 5.00/100,000 during the years 2001 to 2010. The incidences of AFP with RP in which PV or NPEV was isolated were approximately 15% and 12% of incidence of AFP with RP. The PV isolation rate was greater in cases of AFP with RP than cases of AFP without RP. Children aged 2-4 month old comprised the peak age of AFP with RP and PV isolation. AFP without RP from which PV was isolated can be regarded as Sabin poliovirus infection, meaning intestinal infection with Sabin strains without polio like symptoms. AFP with RP that had PV isolated, may be vaccine associated paralytic poliomyelitis (VAPP). The larger proportion of type II and type III PV isolates is consistent with VAPP\[2, 3\].

In China, recommendation for national diagnosis criteria of VAPP\[4\] had been issued, which including recipient VAPP and contact VAPP. Recipient VAPP is currently defined as any suspect AFP case with onset of fever at an interval of 4-35 days and paralysis at an interval of 6-40 days following receipt of OPV and the presence of neurological sequelae compatible with poliomyelitis 60 days following paralysis onset and isolation of vaccine-related poliovirus from the stools. Contact VAPP is defined as direct contact with recipient VAPP at an interval of 35 days following the receipt of OPV, onset of paralysis at an interval of 6-60 days following contact, and the presence of neurological sequelae compatible with poliomyelitis 60 days following paralysis onset and isolation of vaccine-related poliovirus from the stools. However, the criteria has not been enforced strictly. Different provinces use different diagnosis criteria and,
what’s more, some provinces are reluctant to identify VAPP cases and have a tendency to exclude VAPP cases because of the entanglement and compensation related with VAPP. Currently, VAPP cases information was collected by Adverse Events Following Immunization (AEFI) system which was established in 2009. However, AEFI system just collected VAPP case information among OPV recipients, so VAPP case information among OPV recipients’ direct contacts would be missing. Due to reluctance to judge VAPP case and limitation of VAPP surveillance, the actual incidence of VAPP is underestimated in China now. The occurrence of AFP with residual paralysis and PV isolates can be used as the baseline, especially the upper limits of VAPP occurrence in China in the context of OPV nationwide usage.

The summer season peak of RP from which NPEV was isolated is consistent with studies outside of China[5, 6]. The different age distributions of RP with PV isolated and RP with NPEV isolated may be explained by the different risk age group and paralytic pathogenicity in PV and NEPVs.

The decreasing trend of case number of AFP with PV during 2001-2010 is similar to the decrease usage of OPV in supplementary immunization activities (SIA) during these years (unpublished data). For AFP with PV isolates, the increase at the end and beginning of years may be related to the subnational SIAs implemented in many provinces at that time.

On January 2013, the WHO Executive Board endorsed “The Polio Eradication and
Endgame Strategic Plan 2013-2018,” aiming to end all polio disease (wild and vaccine-related)[7]. This plan requires member countries to introduce at least one dose of affordable IPV into the routine immunization schedule followed by replacement of trivalent OPV with bOPV in all OPV-using countries. The strategic plan sets the stage for eventually ending OPV use in 2019-2020. China plans to introduce at least 1 dose of IPV in the routine vaccination schedule in 2015 following an IPV phased introduction in selected provinces in 2014. This introduction of IPV will be followed by a switch to bOPV in 2017, and to all-IPV in 2018.

The replacement of tOPV with bOPV and IPV introduction will impact the dynamics of population immunity, the circulation patterns of Sabin poliovirus in communities and the proportion of VAPP caused by different serotypes of Sabin poliovirus. Inactivated vaccine does not carry the extremely rare risk of VAPP, but it may leave the newly vaccinated population susceptible to gastrointestinal infection with polioviruses and the risk of circulation of the wild-type virus[8]. The introduction of insufficient levels of IPV at the time of type2 OPV cessation may leave countries vulnerable to the emergence of cVDPV2s. Past occurrence and even outbreaks of VDPV in China demonstrated immunity gaps in some areas and populations. Continued surveillance of cases of acute flaccid paralysis to detect polioviruses is essential until poliovirus is completely eradicated.

China’s national AEFI reporting system was established in 2006 and requires VAPP to
be reported to the national level. Previously the AFP surveillance system did not
collect enough clinical information to diagnose VAPP[9], and AFP surveillance did
not make a differential diagnosis of VAPP. To increase the timeliness of AFP
surveillance after the outbreak of type I wild polio virus in Xinjiang province in year
2011[10], China included AFP case reporting into a nationwide real-time web-based
“China Information System for Disease Control and Prevention”. We recommend that
AFP surveillance cases from which a PV is isolated feed into the vaccine safety
system, linking the two systems together to improve the sensitivity to find VAPP. This
10 years surveillance data on RP occurrence can be used as baseline for period of
bOPV and IPV usage in routine immunization system, to take advantage of the
real-time direct reporting system to timely detect abnormal signals of AFP, RP, and
isolation of Sabin-strain poliovirus.

NPEV can cause a broad spectrum of clinical conditions, most of which are mild,
asymptomatic, or subclinical. However, NPEV infection can also result in serious or
even fatal outcomes such as persistent flaccid paralysis[11]. Acute flaccid paralysis
due to wild poliovirus infection is rapidly decreasing due to the tremendous efforts
made by polio eradication initiative. It is becoming increasingly important to know
the burden of AFP and RP due to non-polio causes. In the past, there were several
studies that found at least 20 NPEV serotypes associated with AFP [12, 13]. Studies of
outbreaks of VDPVs in polio-free countries found that VDPVs were recombination
between PV with circulating NPEVs. In order to achieve global eradication of
poliomyelitis, it is also important to concurrently understand the circulation pattern of NPEVs. Our study found 12.2% cases with RP isolated NPEV, smaller than a study in Pakistan, which found 39%. [14] The difference may be explained by different sensitivity of AFP surveillance systems.

Current laboratory procedures used in AFP surveillance can only identify a limited number of NPEVs [15]. Although NPEV detection is only a “partial-outcome” of AFP surveillance, a significant number of AFP cases with RP from which NPEVs was isolated, along with the epidemiological features of NPEV demonstrated in this study made future studies necessary to be based on serological identification of isolated viruses. This will help understand pattern of circulation and clinical residual paralysis occurrence rate associated with each serotype which may help establish specific control measure.

Limitation: Our study has several limitations. First, the isolated enteroviruses from AFP with RP may coincidental infections, transiently localized in the gastrointestinal tract and shed in stools. Little is known about the casual relation contribution of PV or NPEV to overall AFP and residual paralysis. Second, studies have already found that some AFP cases, especially those caused by NPEV, can recover after several months or years. This raises the possibility of misclassification in the follow-up examination existed in this study. We recommend that future studies use a longer follow-up period to correctly classify the outcomes as RP or not.
CONCLUSION

This study was an overview in China of residual paralysis cases with PV/NPEV isolation from AFP surveillance system. This study provides 10 years of data on RP occurrence that can be used as baseline prior to the time of IPV introduction and bOPV usage in the routine immunization system. Data generated from this study can help future studies on NPEV serotypes circulating in China and to formulate more effective strategies in the post eradication era. A better knowledge of the transmission and the implications of NPEV infections in diseases may also support future studies of NPEV molecular epidemiology.

Competing interests
The authors declare that they have no competing interests.

Fundings:
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Authors’ Contributions:
Authors Ning Wen, Chun-Xiang Fan, Lei Cao, Wei Xia, Huiming Luo, Hua-Qing Wang were responsible for national AFP surveillance and data quality control. Qiru Su, HaiBo Wang performed all statistical analysis. Qiru Su, Ning Wen, Li Li wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.
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References

Figure 1. Monthly distribution of paralysis onset in AFP cases with/without residual paralysis during 2001-2010

Median, interquartile range, the minimum and maximum value were used to describe monthly distribution.
Figure 2. Yearly and monthly distribution of paralysis onset in AFP case with/without residual paralysis and with PV/NPEV isolates during 2001-2010 (Abbreviations: PV, Sabin-poliovirus; NPEV: Non-Polio Enterovirus)
Fig. 3. Age distribution of <5 year old AFP cases with/without residual paralysis and with PV/NPEV isolates during 2001-2010

(Abbreviations: PV, Sabin-poliovirus; NPEV: Non-Polio Enterovirus)
### Table 1. AFP with/without residual paralysis and with PV/NPEV isolated, by year

<table>
<thead>
<tr>
<th>Year</th>
<th>AFP cases with residual paralysis</th>
<th>AFP cases without residual paralysis</th>
<th>Total AFP cases</th>
<th>The number of new cases born (1/100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (% of AFP cases)</td>
<td>Identification of isolates (isolation rate %)</td>
<td>N (% of AFP cases)</td>
<td>Identification of isolates (isolation rate %)</td>
</tr>
<tr>
<td></td>
<td>PV</td>
<td>NPEV</td>
<td>PV</td>
<td>NPEV</td>
</tr>
<tr>
<td>2001</td>
<td>1017 (21.5)</td>
<td>182 (17.9)</td>
<td>94 (9.2)</td>
<td>3718 (78.5)</td>
</tr>
<tr>
<td>2002</td>
<td>999 (21.0)</td>
<td>218 (21.8)</td>
<td>97 (9.7)</td>
<td>3761 (79.0)</td>
</tr>
<tr>
<td>2003</td>
<td>918 (20.8)</td>
<td>153 (16.7)</td>
<td>101 (11.0)</td>
<td>3498 (79.2)</td>
</tr>
<tr>
<td>2004</td>
<td>831 (18.5)</td>
<td>143 (17.2)</td>
<td>95 (11.4)</td>
<td>3672 (81.5)</td>
</tr>
<tr>
<td>2005</td>
<td>832 (17.7)</td>
<td>146 (17.5)</td>
<td>93 (11.2)</td>
<td>3863 (82.3)</td>
</tr>
<tr>
<td>2006</td>
<td>782 (16.0)</td>
<td>113 (14.5)</td>
<td>101 (12.9)</td>
<td>4097 (84.0)</td>
</tr>
<tr>
<td>2007</td>
<td>666 (15.6)</td>
<td>84 (12.6)</td>
<td>69 (10.4)</td>
<td>3613 (84.4)</td>
</tr>
<tr>
<td>2008</td>
<td>718 (16.1)</td>
<td>86 (12.0)</td>
<td>101 (14.1)</td>
<td>3735 (83.9)</td>
</tr>
<tr>
<td>2009</td>
<td>621 (14.2)</td>
<td>80 (12.9)</td>
<td>94 (15.1)</td>
<td>3750 (85.8)</td>
</tr>
<tr>
<td>2010</td>
<td>701 (15.1)</td>
<td>64 (9.1)</td>
<td>144 (20.5)</td>
<td>3929 (84.9)</td>
</tr>
<tr>
<td>Total</td>
<td>8085 (17.7)</td>
<td>1269 (15.7)</td>
<td>989 (12.2)</td>
<td>37636 (82.3)</td>
</tr>
</tbody>
</table>

<15 yrs national population numbers were used as denominator to calculate the incidence rates

Abbreviations: AFP, acute flaccid paralysis; PV, Sabin-poliovirus; NPEV: Non-Polio Enterovirus.
Table 2. Three types of Sabin-strain poliovirus isolates in AFP case with/without residual paralysis and with different OPV history during 2001-2010

<table>
<thead>
<tr>
<th>OPV history</th>
<th>No. Cases (isolation rate %) of serotypes</th>
<th>Residual paralysis</th>
<th>Non-residual paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>III</td>
</tr>
<tr>
<td>0 dose</td>
<td>34(2.8)</td>
<td>230(19.0)</td>
<td>95(7.9)</td>
</tr>
<tr>
<td>1 dose</td>
<td>89(5.4)</td>
<td>236(14.3)</td>
<td>172(10.4)</td>
</tr>
<tr>
<td>2 doses</td>
<td>46(2.6)</td>
<td>79(4.4)</td>
<td>70(3.9)</td>
</tr>
<tr>
<td>≥3 doses</td>
<td>100(0.3)</td>
<td>183(0.5)</td>
<td>137(0.4)</td>
</tr>
<tr>
<td>Unknown1</td>
<td>13(0.4)</td>
<td>44(1.3)</td>
<td>29(0.9)</td>
</tr>
<tr>
<td>Vacancy2</td>
<td>-(0.0)</td>
<td>6(1.4)</td>
<td>2(0.5)</td>
</tr>
</tbody>
</table>

1 Unknown: based on investigation, the case’s OPV history was unknown.

2 Vacancy: the information of OPV history was not filled.
Table 3. Demographic features of AFP case with/without residual paralysis and with PV/NPEV isolates during 2001-2010

<table>
<thead>
<tr>
<th>Gender</th>
<th>PV (No. %)</th>
<th>NPEV (No. %)</th>
<th>PV (No. %)</th>
<th>NPEV (No. %)</th>
<th>PV (No. %)</th>
<th>NPEV (No. %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>855(67.4)</td>
<td>608(61.5)</td>
<td>892(66.3)</td>
<td>2,893(66.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>414(32.6)</td>
<td>381(38.5)</td>
<td>454(33.7)</td>
<td>1,433(33.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>296(23.3)</td>
<td>49(5.0)</td>
<td>161(12.2)</td>
<td>71(1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-11</td>
<td>255(20.1)</td>
<td>107(10.8)</td>
<td>143(10.6)</td>
<td>226(5.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-47</td>
<td>634(50.0)</td>
<td>547(55.3)</td>
<td>838(62.3)</td>
<td>2,996(69.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥48</td>
<td>81(6.4)</td>
<td>285(28.8)</td>
<td>204(15.2)</td>
<td>1,031(23.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever history</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-fever</td>
<td>1032(81.3)</td>
<td>557(56.3)</td>
<td>753(55.9)</td>
<td>2,255(52.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>225(17.7)</td>
<td>420(42.5)</td>
<td>587(43.6)</td>
<td>2,048(47.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blank</td>
<td>11(0.9)</td>
<td>12(1.2)</td>
<td>6(0.4)</td>
<td>23(0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GBS</td>
<td>274(21.6)</td>
<td>337(34.1)</td>
<td>247(18.4)</td>
<td>834(19.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPEV</td>
<td>47(3.7)</td>
<td>120(12.1)</td>
<td>71(5.3)</td>
<td>595(13.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>51(4.0)</td>
<td>43(4.3)</td>
<td>32(2.4)</td>
<td>114(2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic neuritis</td>
<td>197(15.5)</td>
<td>115(11.6)</td>
<td>244(18.1)</td>
<td>653(15.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>499(39.3)</td>
<td>287(29.0)</td>
<td>543(40.3)</td>
<td>1,468(33.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blank</td>
<td>201(15.8)</td>
<td>87(8.8)</td>
<td>209(15.5)</td>
<td>663(15.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 dose</td>
<td>318(25.1)</td>
<td>30(5.1)</td>
<td>127(9.4)</td>
<td>100(2.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dose</td>
<td>369(29.1)</td>
<td>51(5.2)</td>
<td>187(13.9)</td>
<td>95(2.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 doses</td>
<td>150(11.8)</td>
<td>77(7.8)</td>
<td>140(10.4)</td>
<td>179(4.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3 doses</td>
<td>350(27.6)</td>
<td>728(73.6)</td>
<td>817(60.7)</td>
<td>3,723(86.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>75(5.9)</td>
<td>74(7.5)</td>
<td>63(4.7)</td>
<td>202(4.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 “None” only calculate the result from stools regarded as “adequate”.
2 The information of gender in 1 AFP belonged to “Non-residual paralysis” and no enterovirus isolates cases was “unknown”.
3 Wrongly filled: the filled date of illness onset was prior to birth date.
4 Interval: Time interval between vaccination and paralysis onset in days.
5 No/Unknown: with no OPV vaccination history or unknown OPV vaccination status.

Abbreviations: PV, Sabin-poliovirus; NPEV, Non-Polio Enterovirus; GBS, Guillain Barre Syndrome.

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**Figure 6**