RESEARCH PAPER

Serum IgG and IgA Levels in Polio and Non-polio Acute Flaccid Paralysis Cases in Western Uttar Pradesh, India

MADHU C MOHANTY, UMA P NALAVADE AND JAGADISH M DESHPANDE

From Enterovirus Research Center, Indian Council of Medical Research, Haffkine Institute Campus, Acharya Donde Marg, Parel, Mumbai, India.

Correspondence to:
Dr Jagadish Mohanrao Deshpande,
Director, Enterovirus Reseach Center,
Indian Council of Medical Research,
Haffkine Institute Campus,
Acharya Donde Marg, Parel,
Mumbai 400 012, India.
deshpandejm@gmail.com
Received: May 30, 2014;
Initial review: August 04, 2014;
Accepted: December 20, 2014.

Objective: IgG and IgA immunocompetence of children with wild poliovirus poliomyelitis and non-polio acute flaccid paralysis.

Methods: 932 cases of acute flaccid paralysis, reported in 2008-2009, were tested for presence of polio and non-polio enteroviruses according to the WHO standards. Serum IgA and IgG levels were determined by sandwich ELISA.

Results: Mean (SD) IgA levels [0.87 (0.62)g/L; *n*=28] of virologically confirmed poliomyelitis cases were lower than those of virus negative [1.21 (0.83)g/L; *n*=612] and non-polio Enterovirus positive [1.22 (0.79)g/L; *n*=240] cases of acute flaccid paralysis. No significant difference was observed in the concentration of IgG among these groups.

Conclusion: IgA plays an important role in protection against poliomyelitis.

Keywords: *Acute flaccid paralysis, Poliovirus, Poliomyelitis, Serum immunoglobulins*

Since 2007, polio antibody sero-prevalence studies were undertaken in Bihar and Uttar Pradesh, to understand why polio eradication faced challenges in these two states. A sero-survey of acute flaccid paralysis (AFP) cases for polio antibody prevalence in 25 districts in Western Uttar Pradesh was conducted in 2008-09. We reported that there was no abnormal prevalence of immunodeficiency in children in Western Uttar Pradesh that could have delayed achieving zero-polio [1].

Success of polio eradication initiative depends on breaking all chains of wild poliovirus transmission. Neutralization of virus infectivity by the serum antibody, mostly IgG, is the main modality of protection against invasion of poliovirus into the central nervous system, whereas IgA antibody is the most important defense at the mucosal surfaces of the nasopharynx and gastrointestinal tract [2]. Recent studies provide evidence that poliovirus specific IgA intestinal antibody is a determinant of virus excretion and that IgA functions through neutralization of the virus infectivity [3]. Circulating phagocytes may also play a role in the defense against poliovirus, mediated through serum IgA [4]. We compared serum IgG and IgA levels of children with paralytic poliomyelitis and non-polio AFP with the objective to explore any correlation of these immunoglobulins with the susceptibility to paralytic poliomyelitis.

METHODS

Stool samples of AFP cases were collected as per the AFP surveillance guidelines [5]. Venous blood samples (1 to 2 mL) were collected from AFP cases up to 5 years of age at the time of clinical examination by the surveillance medical officers of the National Polio Surveillance Unit (NPSU). Polio and non-polio Enterovirus (NPEV) isolation and identification were carried out as per the standard WHO protocol for virological investigations of AFP cases [6]. IgG and IgA concentrations of the serum samples were estimated by sandwich ELISA, as described earlier [1].

Student's t test was used for comparing the mean immunoglobulin values between different groups of AFP children. Sigma Plot was used for statistical analysis.

RESULTS

Stool and serum samples of 932 AFP cases reported in 25 districts in Western Uttar Pradesh in 2008-2009 were investigated. Wild poliovirus (WPV) was isolated from stools of 28 (3.0%) cases of which 11 were WPV1 and 17 were WPV3. Sabin OPV strains were isolated from 46 (5%) cases and NPEV from 240 (25.7%) cases. No enterovirus was detected in stools of 618 (66.2%) cases. AFP cases were thus divided into four groups (WPV, NPEV, Sabin PV, EV negative) on the basis of virological test results. Median (range) age of the AFP

cases were 12 (1 to 46), 18 (0 to 60), 23 (0 to 58) and 20 (0 to 59) months in WPV, NPEV, Sabin PV and EV negative groups, respectively.

Mean (SD) serum immunoglobulin concentrations of the 932 AFP cases were IgG 9.62 (3.47) g/L and IgA 1.2 (0.82) g/L. There were 5 AFP cases with IgG level less than 2 g/L and four AFP cases with IgA level below 0.07 g/L, all in the virus negative group.

Comparison of serum IgG and IgA levels in the four groups of AFP cases is presented in the ***Table* 1**. Serum IgG concentrations were not significantly different between any of the four groups. However serum IgA levels of wild poliovirus cases were significantly lower than the IgA levels in AFP cases with either NPEV (n=240, $P<0.025$) or no enterovirus in the stools (n=618, $P<0.03$). (***Fig.* 1**).

We also compared the IgA levels by stratifying the data using 6-month intervals. IgA levels of WPV cases up to the age of 12 month were significantly lower than NPEV and virus negative AFP cases (***Table* II**). The values could not be confidently evaluated for the higher age groups because of the small number of WPV cases.

TABLE I MEAN (SD) IGG AND IGA CONCENTRATION ACCORDING TO RESULTS OF VIRUS ISOLATION FROM STOOL SAMPLE OF AFP CASES

Virus Isolation	*No.*	*IgG (g/L)*	*IgA (g/L)*
WPV	28	8.71 (3.66)	0.87 (0.62)
Sabin PV	46	9.51 (4.14)	1.19 (0.88)
NPEV	240	9.70 (3.45)	*1.22 (0.79)
EV Negative	618	9.65 (3.42)	*1.21 (0.83)

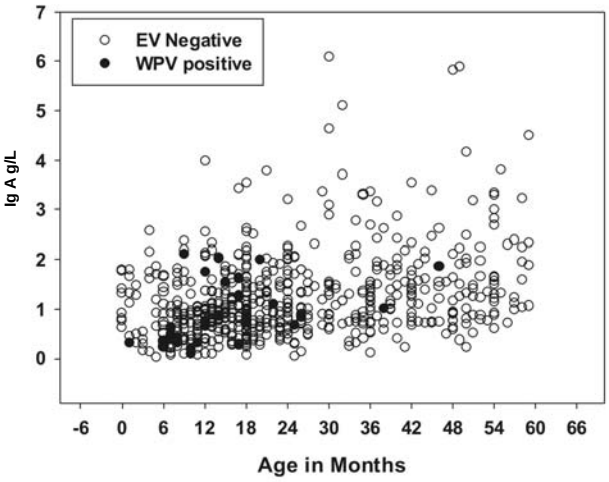
P <0.05 for comparison with WPV.

TABLE II AGE-STRATIFIED SERUM IGA LEVELS OF EV NEGATIVE, NPEV AND WPV AFP CASES

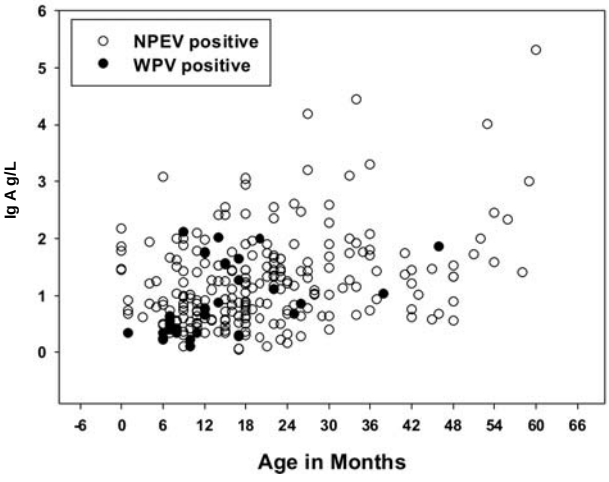
Age (mo)	*Serum IgA Levels, Mean* ± SD (*n*), g/L		
	EV Negative	*NPEV*	*WPV*
0-6	1.04± 0.61 (46)	1.14± 0.7(21)	0.30± 0.050 (3)
7-12	0.86 ±0.62 (96)	0.92± 0.53 (52)	0.65±0.61 (13)
13-18	1.02 ±0.60 (49)	1.05 ± 0.67 (61)	1.20± 0.61 (6)
19-24	1.14 ± 0.64 (87)	1.18± 0.59 (39)	1.54± 0.63 (2)
25-30	1.39 ± 1.08 (52)	1.51 ±0.92 (26)	0.77± 0.12 (2)
31-36	1.41 ± 1.00 (50)	1.91± 1.01 (15)	Nil
37-42	1.53 ± 0.71(45)	1.18 ±0.38 (8)	1.02 (1)
43-48	1.48 ± 1.04 (32)	1.03± 0.38 (9)	1.86(1)
49-54	1.70 ± 1.09 (44)	2.34 ±0.98 (5)	
55-60	1.98± 1.056 (17)	3.01 ±1.66 (4)	

DISCUSSION

Humoral antibodies of IgG type play important role in protection against paralytic disease whereas the IgA antibodies (especially secretory IgA) may be critical to stop poliovirus infection and replication at the primary sites [7]. We compared the immunoglobulin levels in AFP children grouped on the basis of virological results, and found that patients with WPV paralysis had significantly lower IgA levels than NPEV positive and enterovirus negative cases.



(a)



(b)

FIG. 1 *Scatter Plots of serum IgA levels in (a) WPV vs. EV negative cases; (b) WPV vs. NPEV cases, plotted against the age at onset of paralysis.*

WHAT THIS STUDY ADDS?

- Paralytic poliomyelitis cases have lower levels of serum IgA than non-polio AFP cases.

There were a few limitations in our study. We quantified total serum IgA because poliovirus-specific IgA antibody assays were not readily available. As the study was done in the late stage of polio eradication initiative, the number of WPV cases were fewer than before.

Our observation that lower levels of serum IgA in AFP classified as WPV poliomyelitis than non-polio AFP suggests that poliovirus replication/excretion is dependent mainly on IgA response.

Contributors: JMD: conceived the study, helped in designing the study, revised and approved the manuscript for important intellectual content; MCM: designed the study, conducted the laboratory tests, collected and analyzed the data and drafted the paper; UPN: conducted virus isolation work, collected and analyzed the data. The final manuscript was approved by all authors.

Funding: Indian Council of Medical Research (ICMR); *Competing interest*: None stated.

REFERENCES

1. Mohanty MC, Deshpande JM. Investigation of the prevalence of antibody immunodeficiency in a polio endemic area in India. Trans R Soc Trop Med Hyg. 2014;108:258-63.
2. Medical Microbiology, Chapter 1, Immunology overview by Armond S Glodman and Bellur S Prabhakar, 4th edition, Edited by Samuel Baron. University of Texas Medical Branch at Galveston; 1996. Available from: *www.ncbi.nlm.nih.gov/books/NBK7795/#A201*. Accessed September 9, 2014.
3. Wright PF, Wieland-Alter W, Ilyushina NA, Hoen AG, Arita M, Boesch AW, *et al*. Intestinal immunity is a determinant of clearance of poliovirus after oral vaccination. J Infect Dis. 2014;209:1628-34.
4. Buisman AM, Abbink F, Schepp RM, Sonsma JA, Herremans T, Kimman TG. Preexisting poliovirus-specific IgA in the circulation correlates with protection against virus excretion in the elderly. J Infect Dis. 2008;197:698-706.
5. Field Guide: Surveillance of Acute Flaccid Paralysis, Third Edition, September 2005, Available from: *www.searo.who.int/india/.../poliomyelitis/Field_guide_for_Surveillance_of_Acute_Flaccid_ Paralysis_ 3rd_ edition.pdf*. Accessed September 9, 2014.
6. WHO Polio Laboratory Manual, 4th edition, November 2004. Available from: *www.who.int/vaccines/en/poliolab/WHO-Polio-Manual-9.pdf*. Accessed September 9, 2014.
7. Grassly NC, Jafari H, Bahl S, Sethi R, Deshpande JM, Wolff C, *et al*. Waning intestinal immunity after vaccination with oral poliovirus vaccines in India. J Infect Dis. 2012;205:1554-61.