

Original Research Article

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Seroincidence Studies on Enterovirus 71 (EV71) and Coxsackievirus A16 (CVA16) Infections in Pregnant Women Attending Antenatal Clinics at Yusuf Dan Tsoho and Kawo General Hospitals in Kaduna, Kaduna State, Nigeria

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ABSTRACT

Enteroviruses infect people of all age groups, however, younger children are more affected and occasionally with permanent paralysis and neurological complications such as Brainstem Encephalitis (BE), Aseptic Meningitis (AM) and Acute Flaccid Paralysis (AFP). The viruses depend on the host's physiological features, including age, sex, immune response and nutritional status. This study was carried out to know whether the healthy pregnant women silently shed Non-Polio Enteroviruses (NPEVs), because pregnant women are usually immunocompromised in nature. Therefore, rapid strip tests (cassettes) IgM antibody was used to screen human EV71 and CVA16 from serum samples. Out of sixty (60) blood samples collected from Kawo and Yusuf Dan Tsoho General Hospitals in Kaduna, Kaduna state, Nigeria, none of the samples was found positive for Enteroviruses (i.e. Enterovirus 71 (EV71) and Coxachie virus A16 (CVA16). These cassettes (tests) demonstrated sensitivity of 88.5% (23/26) and specificity of 95.2% (177/186). Therefore, standard hygienic practice is required to prevent unforeseen Enterovirus diseases in Kaduna State, Nigeria.

Keywords

Enterovirus,
Coxsackievirus,
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Introduction

Enteroviruses (EVs) infections have emerged as a major public health problem, with outbreaks occurring frequently in summer and early fall throughout the world (Kim *et al.*, 2014; Bian *et al.*, 2015 and Guan *et al.*, 2015). Human Enteroviruses are divided into seven groups and many species including: Polioviruses (3 types), Coxsackieviruses A (23 types), Coxsackieviruses B (6 types), ECHO viruses (31 types), Rhinovirus A (28

types), Rhinovirus B (8 types) and Enteroviruses (4 types, EV-68 to EV-71).

Enteroviruses are small (20-30nm), non-enveloped, single-stranded RNA viruses with icosahedral capsid composed of 60 subunits consisting of four structural proteins (VP1 to VP4) Enterovirus RNA is approximately 7.5 kb long and encodes a polyprotein that is processed to yield the mature structural and nonstructural proteins (Brown and Pallansch 1995). The coding region is

bounded by non-translated regions at the 5' and 3' ends and the viruses depend on the host's physiological features, including age, sex, immune response and nutritional status (Bible and Field, 2007). Enteroviruses infect people of all age groups, however younger children are more affected and occasionally with permanent paralysis and neurological complications (Ooi *et al.*, 2012). Growing evidence indicates that Enteroviruses have caused symptomatic infections in North America, Malaysia, Singapore, Australia and Taiwan (Singh *et al.*, 2002; Ryu *et al.*, 2010; Pons *et al.*, 2015). Although because of the poor standard of hygiene, Enteroviruses infections are very common in developing countries (Rifqiyah *et al.*, 2009). Their transmission is through fecal-oral route and through respiratory droplets during acute infections. Enteroviruses is shedding in the faeces of persons and continue for three weeks after being infected, the infections occur all year round with higher rates during rainy seasons (Attoh *et al.*, 2014).

Enterovirus 71 (EV71)

Enterovirus 71 (EV71) is one of the main causative pathogens of hand, foot and mouth disease (HFMD) which occasionally involves the central nervous system (CNS) and can cause serious and potentially fatal neurological complications among pediatric infectious diseases (McMinn, 2006 and Ooi *et al.*, 2012). EV71 can also cause fatal diseases as pulmonary edema, encephalomyelitis or even neurologic and psychiatric symptoms (Wang *et al.*, 2004 and Chang *et al.*, 2007). EV71 causes a serious complication such as brainstem encephalitis, aseptic meningitis and acute flaccid paralysis (Wang *et al.*, 1999; McMinn *et al.*, 2001 and Lee *et al.*, 2015).

Coxsackievirus A16

Coxsackievirus A16 (CVA16) tends to infect the skin and mucous membranes causing

herpangina (sores in the throat), acute hemorrhagic conjunctivitis (AHC), and hand-foot-and mouth (HFMD) disease (Lim *et al.*, 2013). Both Coxsackie virus A16 (CA16) and Enterovirus 71 (EV71) are the major pathogens responsible for HFMD. While CA16 infections generally causes mild symptoms such as blisters/ulcers on the hands and feet and in the mouth as well as pharyngitis in infants and children under five years old (Wang *et al.*, 2004; Legay *et al.*, 2007).

Materials and Methods

Sixty (60) blood sample was carried from pregnant women attending antenatal clinics from Kawo and Yusuf Dan Tsoho General Hospitals in Kaduna state, Nigeria. Ethical approval for the collection of the blood samples was approved by the ministry of Health and Human Services Kaduna state, Nigeria. Exactly 2ml of blood was collected by venipuncture from each pregnant woman, deposited into appropriately labeled sterile EDTA (Ethylene Diamine Tetraacetic acid) bottles, and transported to the laboratory and stored at stored in the refrigerator at -70°C till further analysis.

EV71 IgM and CVA16 IgM rapid test kit were used to determine the presence of enterovirus 71 and coxsackie virus 16 respectively following the method of Zhang *et al.*, (2016). A positive test would have showed red bar on the cassette while negative or false positive showed no bar after 30 minutes.

Results and Discussion

The result below shows that of the 60 blood sample collected from pregnant woman attending, none was found positive for Enterovirus 71 and Coxsackievirus A16. Rapid strips tests IgM antibodies cassettes were used for detecting Human Enterovirus

71 (EV71) and Coxsackievirus A16 (CVA16) from serum samples in pregnant women attending antenatal clinics from the above Hospitals (Table 1). This methodology was employed for EV71 and CVA16 detection because of its convenience and fast especially

when dealing with large amount of sample. Enteroviruses such as polioviruses, coxsackieviruses and echoviruses are among the most common and significant causes of infectious diseases in infants and children (Ooi *et al.*, 2012).

Table.1 Rapid strip test results for EV71 and CVA16

Enterovirus 71 (EV71)	Outcome	Coxsackie virus A16 (CVA16)	Outcome
1	-	1	-
2	-	2	-
3	-	3	-
4	-	4	-
5	-	5	-
6	-	6	-
7	-	7	-
8	-	8	-
9	-	9	-
10	-	10	-
11	-	11	-
12	-	12	-
13	-	13	-
14	-	14	-
15	-	15	-
16	-	16	-
17	-	17	-
18	-	18	-
19	-	19	-
20	-	20	-
21	-	21	-
22	-	22	-
23	-	23	-
24	-	24	-
25	-	25	-
26	-	26	-
27	-	27	-
28	-	28	-
29	-	29	-
30	-	30	-

NB*** - (Negative)

Most Enteroviruses infections are self-limiting and do not require hospitalization care with the exception of poliovirus and Enterovirus 71 which frequently cause neurologic complication such as central nervous system (CNS) (Wang *et al.*, 2009 and Ooi *et al.*, 2012). Screening of the viruses was carried out in Nigeria because a study indicated that non-polio Enteroviruses (NPEVs) were in circulation in Borno and Adamawa states, Nigeria from children aged 5 to 16 years, according to Baba *et al.*, (2012). This study test was conducted for pregnant women because, a study reported that the viruses depend on the host's physiological features, including age, sex, immune response and nutritional status (Bible and Field, 2007). The virus transmitting through fecal-oral route and through respiratory droplets during acute infections and is shedding in faeces of the infectious persons continues for three (3) weeks after being infected and the infections occur all year round with higher rates during rainy seasons (Attoh *et al.*, 2014). According to Diedrich *et al.*, (2009), pregnant women in Jiangsu province (China) were found to have 78.4% and 83.8% and 48 found positives for EV71 and CVA16 respectively which is in contrast in pregnant women in Nigeria. Because of poor standard of hygiene and sanitation, the infections are very common in a developing country, which is not in agreement with the findings in Kaduna, Nigeria (Rifqiyah *et al.*, 2009).

Therefore, the results were negatives, which is also not in agreement with earlier report of Attoh *et al.*, (2014) that the virus were isolated from patients with variety of illnesses and occasionally from apparently normal people. Although, Zhu *et al.*, (2013), reported that the detection efficiencies of Enterovirus 71 (EV71) and Coxsackievirus A16 (CA16) were lower in severe hand, foot and mouth diseases, and cases by Real Time (RT-PCR) thus spontaneously detection of IgM

antibodies needs to be considering in routine laboratories.

In conclusion, the study shows the negative results of the viruses among pregnant women attending antenatal in the clinics. Although 70 to 80% of the infections are asymptomatic. Therefore, standard hygienic practice is required to prevent unforeseen Enterovirus diseases.

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References

- Attoh, J., Obodai, E., Adiku, T., and Odoom, J.K. (2014). Prevalence of human Enteroviruses among apparently healthy nursery school children in Accra. *Pan Africa Medical Journal*. 18: 66-66.
- Baba, M.M., Oderinde, B.S., Patrick, P.Z., and Jarmai, M.M. (2012). Sabin and wild polioviruses from apparently healthy primary school children in northeastern Nigeria. *Journal of Medicine Virology*. 84: 358-364. PMID: 22170559.
- Bian, L., Wang, Y., Yao, X., Mao, Q., Xu, M., and Liang, Z. (2015). Coxsackievirus A6: A new emerging pathogen causing hand, foot and mouth disease outbreaks worldwide. *Expert Review of Anti-Infection Therapy*. 13, 1061-1071.
- Bible, J. M., Pantelidis, P., Chan, P. K., and Tong, C.Y. (2007). Genetic evolution of Enterovirus 71 Epidemiological and pathological implications. *Review in Medical Virology*. 17, 371-379.
- Brown, B. A., and Pallansch, M. A. (1995). Complete nucleotide sequence of

- Enterovirus 71 is distinct from poliovirus. *Virus Research*. 39:195-205; PMID: 8837884.
- Chang, L.Y., Huang, L. M., Gau, S. S., Wu, Y.Y., Hsia, S. H., Fan, T.Y., Lin, K. L., Huang, Y. C., Lu, C.Y., and Lin, T.Y., (2007). Neurodevelopment and cognition in children after Enterovirus 71 infection. *The New England Journal of Medicine*. 356, 1226– 1234.
- Diedrich, S., Weinbrecht, A., and Schreier, E. (2009). Seroprevalence and molecular epidemiology of Enterovirus 71 in Germany. *Archives Virology*. 154:1139-42; PMD: 19506798.
- Guan, H., Wang, J., Wang, C., Yang, M., Liu, L., Yang, G., and Ma, X. (2015). Etiology of multiple Non- EV71 and non-CVA16 Enteroviruses associated with hand, foot and mouth disease in Jinan, China, 2009—June 2013. *PLoS ONE*. 10, e0142733.
- Kim, H., Kang, B., Hwang, S., Lee, S.W., Cheon, D.S., Kim, K., Jeong, Y.S., and Hyeon, J.Y., (2014). Clinical and Enterovirus findings associated with acute flaccid paralysis in the Republic of Korea during the recent decade. *Journal of Medical Virology*. 86, 1584–1589.
- Lee, K. Y., and Yeh, H. R., (2015). Continuous myocloni and tonic spasms in a 2-month-old infant with Enterovirus 71 brain stem encephalitis. *PediatricsNeurology*. 46:52–55.
- Legay, F., Lévêque, N., Gacouin, A.,Tattevin, P., Bouet, J., Thomas, R., and Chomelt, J. J. (2007). Fatal coxsackievirus A-16 pneumonitis in adult. *Emerging Infectious Diseases*. 13:1084-6; PMID: 18214187.
- Lim, B. K., Ju, E. S., Lao, D. H., Yun, S. H., Lee, and Y. J. (2013). Development of a Enterovirus diagnostic assay system for diagnosis of viral myocarditis in humans. *Microbiology Immunology*. 57(4): 281-287.
- McMinn, P. C. (2006). The emergence of Enterovirus 71 as a major cause of acute neurological disease in young children of the Asia-Pacific region. *Journal of Pediatrics Infectious Disease*. 17–23.
- McMinn, P., Stratov, I., Nagarajan, L., and Davis, S. (2001). Neurological manifestations of Enterovirus 71 infection in children during an outbreak of hand foot and mouth disease in Western Australia. *Clinical Infection Disease*. 32:236–242.
- Ooi, M. H., Wong, S. C., Lewthwaite, P, Cardosa, M. J., and Solomon, T. (2012). Clinical features, diagnosis, and management of Enterovirus 71. *Lancet Neurology*. 9:1097– 1105.
- Ryu, W.S., Kang, B., Hong, J., Hwang, S., Kim, A., Kim, J., and Cheon, D.S. (2010). Enterovirus 71 infection with central nervous system involvement, South Korea. *Emerging Infectious Disease*. 16, 1764–1766.
- Rifqiyah, N.U., R. Dhenni, A., Jajuli, Y., Nishimura, and H., Shimizu, (2009). Detection and identification of human Enteroviruses among healthy children in Antajaya, Bogor. *Journal of Biotechnology Resin Tropical Region*. 1: 2-9.
- Singh, S., Chow, V. T., Phoon, M. C., Chan, K. P., and Poh, C. L., (2002). Direct detection of Enterovirus 71 (EV71) in clinical specimens from a hand, foot, and mouth disease outbreak in Singapore by reverse transcription- PCR with universal Enterovirus and EV71-specific primers. *Journal of Clinical Microbiology*. 40: 2823-7; PMID: 12149336.
- Wang, C. Y., Li, Lu, F., Wu, M. H, Lee, C. Y., Huang, L. M., (2004). Fatal coxsackievirus A16 infection. *Pediatrics Infectious Disease Journal*. 23: 275-6; PMID: 15014311.

- Wang, S. M., Liu, C. C., Tseng, H. W., Wang, J. R., Huang, C. C., Chen, Y. J., Yang, Y. J., Lin, S. J., and Yeh, T.F. (1999). Clinical spectrum of Enterovirus 71 infection in children in southern Taiwan, with an emphasis on neurological complications. *Clinical Infectious Diseases*. 29, 184–190.
- Wang, S. M., and Liu, C. C. (2009). Enterovirus 71: epidemiology, pathogenesis and management. *Expert Review Anti-infective Therapy*. 7:735–742.
- Xu, J., Qian, Y., Wang, S., Serrano, J. M., Li, W., Huang, Z., and Lu, S., (2010). EV71: An emerging infectious disease vaccine target in the Far East? *Vaccine*. 28, 3516–3521.
- Zhang, J., Weng, Z., Du, H., Xu, F., He, S., He, D., Cheg, T., Zhang, J., Ge, S. and Xia, N. (2016). Development and evaluation of rapid point-of-care tests for the detection of Enterovirus 71 and Coxsackievirus A16 specific immunoglobulin M antibodies. *Journal of virological methods*, 23, 44-47.
- Zhu, D., Zhao, X. Y., Yao, Y., Dai, F. F., He, H., Li, R. Q., Jin, R. H., Liang, L. C., Li, N., (2013). A new factor influencing pathogen detection by molecular assay in children with both mild and severe hand, foot, and mouth disease. *Diagnosis Microbiology for Infectious Disease*. 76: 162- 7; PMID: 23535205.

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