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A Serological Survey of Human Parainfluenza Viruses (HPIVs) among Children in Kaduna Metropolis, Nigeria

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Abstract: *This study was done to carry out a survey of Human Parainfluenza Virus in children aged 1-12years in Kaduna Metropolis, Nigeria using the Enzyme Linked Immunosorbent Assay Diagnostic kits. Of the 376 samples tested for IgG antibody of HPIV 1, 2 and 3, 288 were seropositive (76.6%). Risk and demographic factors such as age of the children parental occupation, parental educational status, vitamin A deficiency, frequency of eating, household size, duration of breastfeeding, environmental smoke, respiratory symptoms, fever, sickle cell and underlying diseases were analysed. Age (χ^2=17.408, p=0.001), parental occupation (χ^2=10.116, p=0.039), duration of breastfeeding (χ^2=8.439, p=0.015), presence of respiratory symptoms (χ^2=5.116, p=0.024) were significantly associated with the infection. Observation from the study showed the importance of Human Parainfluenza Virus as an agent of respiratory tract infection in children. As antiviral drugs are not readily available, preventive measures should be adhered to in the control of the infection.*

Keywords*: Human Parainfluenza Virus, Children, Nigeria*

I. Introduction

Respiratory infections have a significant impact on health worldwide and the majority of these infections are of viral origin. Moreover, 10%–50% of patients will develop a secondary bacterial infection as children are the most afflicted with acute otitis media, sinusitis, or pneumonia. In very young or older individuals or individuals with chronic medical conditions, viral respiratory infections may induce a severe illness (Hayden *et al*., 2006). Furthermore, most acute respiratory infections are caused by Rhinovirus, Respiratory Syncytial Viruses, Enteroviruses, Influenza A and B viruses, Parainfluenza viruses, or Adenovirus (Allander *et al*., 2007). Ray (2004), have also suggested that the viruses that are the major causes of acute respiratory disease (ARD) include influenza viruses, parainfluenza viruses, rhinoviruses, adenoviruses, respiratory syncytial virus (RSV), and respiratory coronaviruses.

Human parainfluenza viruses (HPIVs) have been associated with every type of upper and lower respiratory tract illness, including common cold with fever, laryngotracheobronchitis (croup), bronchiolitis, and pneumonia. HPIVs are also a cause of community-acquired respiratory tract infections of variable severity even in adults. Weinberg *et al* found that HPIV accounted for 6.8% of all hospitalizations for fever, acute respiratory illnesses, or both in children younger than 5 years (Weinberg *et al*., 2009). Furthermore, Human parainfluenza viruses (HPIVs) are common community-acquired respiratory pathogens without ethnic, socio-economic, gender, age or geographical boundaries. Many factors have been found that predispose individuals to these infections, including malnutrition, overcrowding, vitamin A deficiency, concomitant diseases (e.g. diarrhoea, heart disease, asthma), day care attendance, lack of breast feeding and environmental smoke or toxins (Laurichesse *et al*., 1999; Rudan *et al*., 2008). Besides, in most developing countries, a significant proportion of these disease burdens have been found to be respiratory infections. A hallmark of infection by respiratory viruses is productive infection of and the subsequent destruction of the airway epithelium (Gorski *et al*., 2012). Human parainfluenza viruses (HPIVs) are a common cause of acute respiratory illness throughout life. Infants, children, and the immunocompromised are the most likely to develop severe disease (Schomacker *et al*., 2012). In the past few decades, infectious diseases have moved steadily back up the health agenda, prompting new emphasis on developing strategies for prevention and control.

Acute Respiratory Infection symptoms (cough and difficult/fast breathing) frequently overlap with those of malaria which sometimes make diagnosis difficult. In Nigeria, children with these pneumonia symptoms which can be caused by HPIVs are frequently overlooked by the home management strategy that seeks to treat all childhood fevers as malaria (Ukwaja *et al*., 2010). The majority of deaths occur in Africa and South-East Asia (Rudan *et al*., 2008). The incidence of clinical pneumonia, a respiratory tract infection among children ranges from 0.34 to 1.3 episodes per child-year (Akanbi *et al*., 2009). Over 6 million new cases are estimated annually with expected mortality of 204,000 children (Rudan *et al*, 2008). However, many children with pneumonia do not receive timely, appropriate treatment at health facilities, (UNICEF, 2007) especially children from poorer families – for economic and social reasons (Schellenberg *et al*., 2003). Also, most clinical cases of respiratory infections are regarded as bacterial and there is a tendency of not focusing enough attention

to viral causes of respiratory tract infections. Sometimes the viruses cause only a runny nose and other symptoms that may be diagnosed as a simple cold rather than Human Parainfluenza Infection.

Although respiratory viral infections are much studied in developed countries and their impact on health care is well understood, there is a gap in information on the burden of respiratory viral infections in developing countries. From the public health point of view, it would be valuable to know which viruses are the most common causative agents, what their disease manifestations are, how often virus alone causes severe respiratory infection, and how severe lower respiratory infections could be prevented (Rudan and Conseus, 2005). This study therefore attempts to survey the prevalence of HPIVs among children, ages 1 to 12 years and determine the risks and demographic factors associated with the infection in the study area.

II. Materials And Methods

Study area

This study was conducted in Kaduna Metropolis, Kaduna State which is located in the Northern Guinea Savanna ecological zone. It occupies almost the entire central portion of the Northern part of Nigeria and share common borders with Zamfara, Katsina, Niger, Kano, Bauchi, Nassarawa and Plateau States. To the Southwest, the state shares border with the Federal Capital Territory, Abuja. The global location of the state is between longitude $06^{o}00$ and $09^{o}00$ East of the Greenwich Meridian and also between latitude $09^{o}00$ and $11^{o}30$, north of the equator. The state occupies an area of about 48,473.2 square kilometres. It has a population of 6,066,562 people (NBS, 2007); and a projected population of 6,527,620 in 2009. Kaduna State is the successor to the old Northern Region of Nigeria, which had its capital at Kaduna. In 1967 this was split up into six states, one of which was the North-Central State, whose name was changed to Kaduna state in 1976. This was further divided in 1987, losing the area now part of Katsina State.

The study was conducted in four major hospitals in Kaduna Metropolis which included; Barau Dikko Specialist Hospital, Yusuf Dantsoho Memorial Hospital, Kawo General Hospital, Gwamna-Awan General Hospital Kaduna situated in North and South regions of Kaduna Metropolis.

Sample collection and processing

The various clinics were visited after obtaining ethical approval from Kaduna State Ministry of Health. Children aged 1 – 12 years were recruited in the study. Blood samples were collected only from children whose parents/guardians signed an informed consent. Sterile syringe (2ml) was used for blood collection. Samples were collected aseptically by venous puncture from each. The samples were collected into plain specimen bottles and centrifuged at 1500 revolution per minute (1500 rpm/min) for five minutes and the sera were collected into clean and dry plain specimen bottles using clean and dry Pasteur pipettes. The sera were stored at -20^{0}C until the assay time (Cheesbrough, 2003). The serum assay for HPIV was carried out in the Department of Microbiology, Ahmadu Bello University Zaria. Using Enzyme Linked Immunosorbent Assay (HPIV 1/2/3 IgG antibody test kit IMMUNOLAB GmbH ELISA, Germany), samples were assayed for specific IgG antibody against the HPIV-1, 2 and 3 virus. Manufacturer's instructions were duly followed. The optical density (OD) values were read at 405nm, using Sigma Diagnostic EIA multi well reader II. The kit has 99% specificity and 100% sensitivity.

III. Results

The ELISA result showed that 288 (76.6%) samples tested positive to Human Parainfluenza Virus IgG antibody while 88(23.4%) samples tested negative to HPIV IgG antibody giving a total seroprevalence of 76.6%.

It was discovered that there was significant association ($p = 0.039$) between parents' occupation and the HPIV infection. Children whose parents were teachers had the highest infection rate of 84.1% followed by those whose mothers were fulltime housewives (81.1%), 76.9% of civil servants' children were infected while children of self-employed parents had the least infection (70.9%) (Table 1).

Similarly, test of association of parents' level of formal education with the infection was carried out. Though there was no significant association ($\chi^2 = 4.768$, $p = 0.092$), children of parents with primary education had the highest rate of infection; those with tertiary level of education, their children had 78.9% infection rate and the least (70.9%) was observed amongst children of parents with secondary level of education (Table 1).

Table 2 presents the result of the assessment of the association of number of meals eaten daily; this shows no significant association ($\chi^2 = 2.132$, $p = 0.344$) with human parainfluenza virus infection but the daily eating pattern revealed that children that ate once a day had the least rate of infection while those that ate twice daily had 80.0%. Household size was not significantly associated ($\chi^2 = 0.194$, $p = 0.907$) but households with 7-12 persons had higher (77.0%) infection rate compared to those with 1-6 persons where the infection rate was 75.9% (Table 2).

Other risk factors assessed include but not limited to vitamin A deficiency, duration of breastfeeding, whether or not parents smoke. There was no significant association between vitamin A and human parainfluenza virus infection in children (Table 2). Table 2 further shows significant association (p = 0.015) between duration of breastfeeding and the infection. Children who were breastfed for 1-6 months had 41.7% infection rate followed by those breastfed for 7-12 months (77.6%) and 77.8% for those that were breastfed for more than 1 year.

Children of parents that smoke had higher (80.0%) infection with human parainfluenza virus than those of non-smoking parents (76.4%) though smoking was not significantly associated with the infection.

Table 1: Association of demographic data with human parainfluenza virus infection in children

Parameter	No. of sample tested	No. Positive (%)	χ^2	P
Age group (years)				
1-3	151	99(65.6)	17.408	0.001**
4-6	76	65(85.5)		
7-9	84	69(82.1)		
10-12	65	55(84.6)		
TOTAL	**376**	**288(76.6)**		
Parents' Occupation				
Civil servant	52	40(76.9)	10.116	0.039*
Teacher	69	58(84.1)		
Housewife	90	73(81.1)		
Self-employed	165	117(70.9)		
TOTAL	**376**	**288(76.6)**		
Education				
Primary	81	67(82.7)	4.768	0.092
Secondary	148	105(70.9)		
Tertiary	147	116(78.9)		
TOTAL	**376**	**288(76.6%)**		

χ^2 = chi square
p = level of significance
* = significant association exists at p < 0.05
** = significant association exists at p < 0.01

Table 2: Effect of household number and nutrition on human parainfluenza virus infection

Parameter	No. of samples tested	No. Positive (%)	χ^2	P
Daily eating				
Once	16	10(62.5)	2.132	0.344
Twice	55	44(80.0)		
Thrice	305	234(76.7)		
TOTAL	**376**	**288(76.6)**		
Household number				
1-6	137	104(75.9)	0.194	0.907
1-12	239	184(77.0)		
TOTAL	**376**	**288(76.6)**		
Vitamin A				
Yes	294	226(76.9)	0.057	0.812
No	82	62(75.6)		
TOTAL	**376**	**288(76.6)**		
Breastfeeding				
1-6 months	12	5(41.7)	8.439	0.015*
7-12 months	98	76(77.6)		
>12 months	266	207(77.8)		
TOTAL	**376**	**288(76.6)**		

χ^2 = chi square
p = level of significance
* = significant association exists at p < 0.05
** = significant association exists at p < 0.01

In like manner, environmental smoke was not significantly associated with the infection (Table 3).

Of the 319 children with respiratory symptoms, 251 (78.7%) had human parainfluenza virus infection while 37(64.9%) of those without respiratory symptoms did not have the infection. Significant association (p = 0.024) was observed (Table 4). Fever, sickle cell and underlying diseases showed no significant association with the infection in children (Table 4).

Table 3: Effect of smoking on human parainfluenza infection

Parameter	No. of samples tested	No. Positive (%)	χ^2	P
Parental smoking				
Yes	25	20(80.0)	0.173	0.677
No	351	268(76.4)		
TOTAL	**376**	**288(76.6)**		
Environmental smoke				
Yes	195	143(73.3)	0.405	0.121
No	181	145(80.1)		
TOTAL	**376**	**288(76.6)**		

χ^2 = chi square
p = level of significance

Table 4: Relationship between symptoms, risk factors and human parainfluenza virus.

Parameter	No. of sample tested	No. Positive (%)	χ^2	P
Respiratory symptoms				
Yes	319	251(78.7)	5.116	0.024*
No	57	37(64.9)		
TOTAL	**376**	**288(76.6)**		
Fever				
Yes	275	209(76.0)	0.203	0.653
No	101	79(78.2)		
TOTAL	**376**	**288(76.6)**		
Sickle cell				
Yes	29	26(89.7)	2.990	0.084
No	347	262(75.5)		
TOTAL	**376**	**288(76.6)**		
Underlying diseases				
Diarrhoea	21	17(81.0)	4.450	0.217
Asthma	6	6(100.0)		
Blood diseases	7	258(75.4)		
None	342			
TOTAL	**376**	**288(76.6)**		

χ^2 = chi square
p = level of significance
* = significant association exists at $p < 0.05$

IV. Discussions

The IgG antibody was measured to determine the proportion of sero-positivity and the level of the antibody with deference to such factors as age of children, parental occupation, highest educational level of the parent, environmental pollution (smoke), duration of breastfeeding, presence of respiratory symptoms, sickle cell disease, and any other underlying diseases.

The study revealed a rate of 76.6% of Human Parainfluenza Virus in the population of children in Kaduna Metropolis. This marked an increase in prevalence rate as compared with previous results from Sale *et al*., (2010) which showed a prevalence of 46.4% among children aged 1-5years in Zaria, Kaduna and Calvo *et al*., (2011) in Spain with prevalence 11.8% can be due to the fact that the ELISA kit used in this study tested for IgG antibodies for Parainfluenza 1, 2 and 3. This means that the children may have had the IgG antibody however may not have come down with the infection. Also the study was carried out during the Harmattan (equivalent to the winter season) which usually is the peak period of the infection in children especially (Ray, 2004). The result is however similar to the report of Glezen and Denny (1997) which showed that 75% of children aged 5 years had antibodies to HPIV-1 and 2 as well as that of Akinloye *et al* (2011) in Ibadan who discovered that 80% of children have antibodies to the virus by ten years of age. The study also revealed that there was increase in seropositivity with age. This could be as a result of reinfection of older children that occurs in the presence of antibodies elicited by an earlier infection. Since there is no permanent immunity to the infection those antibodies modify the disease, as such reinfection usually present simply as nonfebrile upper respiratory infection. This agrees with the findings of Brooks *et al* (2007) as well as that of Sale *et al* (2010). Infection with the human paramyxoviruses such as the HPIVs can occur throughout life Hall (2001); however unlike primary infection in the very young, subsequent infections are often milder or subclinical Hall (2001). The mechanism behind the ability of these viruses to reinfect has been attributed to the incomplete and waning immunity that develops after primary infection with specific emphasis being placed on the serum neutralizing antibody and mucosal IgA levels (Okamoto *et al*., 2010; Kawasaki *et al*., 2004).

In terms of the occupation of parents of the children in relation to human parainfluenza virus infection, it was discovered that there was significant association ($p = 0.039$) between parents' occupation and the infection. Children whose parents were teachers had the highest infection rate of 84.1% followed by those whose mothers were fulltime housewives (81.1%), 76.9% of civil servants' children were infected while children of self-employed parents had the least infection (70.9%). This may possibly be explained by the fact that some of these teachers may have come in contact with other children in their schools who could have been infected and so passed it on to their children at home since HPIV infection is transmitted via contact and air particles (Burke *et al*., 2013).

The test of association of parents' level of formal education with the infection showed there was no significant association. Children of parents with primary education had the highest rate of infection; those with tertiary level of education, their children had 78.9% infection rate and the least (70.9%) was observed amongst children of parents with secondary level of education. The parents with the primary education as the highest educational status are more likely not to be informed and mindful of methods of controlling the transmission of the virus such as the use of disinfectant, proper hygienic practices and environmental control of short-range transmission. This agrees with the findings of Rudan *et al* (2008) who stated that Mother's education is a possible risk factor of the pneumonia an infection caused by Parainflenza virus 3 specifically.

There was no significant association between the number of meals eaten daily with Human Parainfluenza Virus infection. The daily eating pattern revealed that children that ate once a day had the least rate of infection while those that ate twice daily had 80.0%. The sample size was limited for children that ate once a day than for the others. Also, the other risk factors such as contact with infected persons and fomites, may have been more common among the older children that made them more susceptible to the infection.

There was no significant association between sources of vitamin A and human parainfluenza virus infection in children. Although, household size was not significantly associated, households with 7-12 persons had higher (77.0%) infection rate compared to those with 1-6 persons where the infection rate was 75.9%. This suggests that overcrowding which results in indoor air pollution and eventually person to person contact is a risk factor for contacting the HPIV infection. This result agrees with that of Rudan *et al* (2008).

Duration of breastfeeding and the infection was statistically significant. Children who were breastfed for 1-6 months had 41.7% infection rate followed by those breastfed for 7-12 months (77.6%) and 77.8% for those that were breastfed for more than 1 year. This could be due to the fact that a larger number of the children involved in the study were breast fed for 1-2 years than for 6-12 months and 1-6 months. Also some of the children were already above 1-2 years so they may have been more exposed to other means of transmission of the virus. The action of maternal antibodies in stronger in children for the first six months of life than when they get older (Schomacker *et al*., 2012).

Children of parents that smoke had higher infection with human parainfluenza virus than those of non-smoking parents though smoking was not significantly associated with the infection. In like manner, environmental smoke was not significantly associated with the infection and this is consonance with the finding of Johnson *et al* (2008). It is however in contrast with the findings of Laurichesses *et al* (1999) who identified environmental smoke as a predisposing factor to the infection in England and Wales. This contrast may also be due to the fact that there is a larger number of smoking parents in such a place than in Nigeria where smoking is not so socially acceptable.

The results showed that of the 29 subjects tested to have sickle cell disease, seropositivity was observed in 26 (89.7%) but was not statistically significant. This could be due to the fact that there was a limited number of sickle cell individuals involved in the study and this result agrees with that of Sale *et al* (2010).

Fever and underlying diseases showed no significant association with the infection in children. This is in contrast with the findings of Laurichesses *et al* (1999) and Rudan *et al* (2008) who identified concomitant diseases (underlying diseases) as a predisposing factor to the infection in England and Wales. This could be due to the fact that there were a limited number of children with concomitant diseases involved in the study. Also fever and concommitant diseases such as Diarrhoea, Heart disease etc could have been caused by other microbial agents than Human parainfluenza virus.

Out of the 319 children with respiratory symptoms, 251 (78.7%) had human parainfluenza virus infection while 37 (64.9%) of those without respiratory symptoms did not have the infection. Significant association was observed. Parainfluenza infection is a respiratory tract infection and as such patients should show respiratory symptoms such as cold, cough and catarrh. Early infections however may not show such symptoms. Also a large proportion of the children studied had respiratory symptoms due to the season when the sampling was done i.e the Harmattan season which resulted to the high seropositivity. This result however, is in contrast to the findings of Sale *et al* (2010) whose findings showed that respiratory symptom is not statistically significant to HPIV infection. The result however agrees with that of Brooks *et al* (2007).

V. Conclusion and Recommendations

Observation from the study showed the importance of Human Parainfluenza Virus (Types 1, 2 and 3) as an agent of respiratory tract infections in children. Age, Parental occupation, duration of breastfeeding and presence of respiratory symptoms are important demographic and risk factors of Human Parainfluenza Infection in children This study suggests the need for rapid, easy and less expensive methods of diagnosis for clinical management and availability of vaccines. A better understanding of HPIV pathogenesis will aid the design and evaluation of live attenuated HPIV vaccines and therapeutic drugs. As antiviral drugs are not readily available, preventive measures such as proper hygienic practices and parental supervision should be adhered to in the control of the infection.

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