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# Detectable Anti-Respiratory Viruses IgM and IgG Antibodies among Children with Acute Respiratory Tract Infections in Owo, Ondo State, Nigeria

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***Abstract***
*Globally, in children, less than 5 years of age, acute respiratory tract infections (ARTIs) are a major cause of morbidity and mortality. Long-lasting immunity is not induced by respiratory infections as reinfection can occur throughout life. This study aimed to determine the seroprevalence of six respiratory viruses specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies in children with ARTIs in Owo, Ondo State. The sera samples of two hundred (200) subjects who consented to participate in the study were collected and tested using serum-specific Enzyme-Linked Immunosorbent Assay (ELISA) kits, IgM and IgG antibodiestothe influenza A virus (FLU-A), respiratory syncytial virus (RSV), parainfluenza virus (PIV), coronavirus (CoV), rhinovirus (RV) and adenovirus (AdV) respectively (IgM and IgG ELISA Kits; Melsin Medical Co., China). The mean age of the subjects tested was 3.49 ± 1.41 years. The total anti-respiratory viruses IgM seropositivity was detected in 83% of the children with the highest being AdV 91 (45.5%), followed by PIV 89 (44.5%), FLU-A and RV with 88 (44%) respectively, CoV 85 (42.5%), and RSV 80 (40%). The total anti-respiratory viruses IgG seropositivity was detected in 87.5% of the children with the highest being PIV 152 (76%), followed by RSV 135 (67.5%), RV 93 (46.5%), AdV 81 (40.5%), CoV and FLU-A with 76 (38%) respectively. The study revealed the presence of current and previous infections of respiratory viruses among children in Owo which calls for the need for preventive and control measures against respiratory tract viruses are suggested.*
***Keywords:*** *Human respiratory viruses, immunoglobulin M (IgM), immunoglobulin G (IgG), Enzyme-Linked Immunosorbent Assay (ELISA), Sera*

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## INTRODUCTION

Annually, the World Health Organisation (WHO) estimates that acute respiratory infections (ARIs) are a leading cause of mortality among children under 5 years with over 4 million death worldwide (WHO, 2018). In humans, the most common illness of the upper and lower respiratory tracts is caused by viruses. The major burden of infection is borne by children and infants, usually recurring with 5 to 6 episodes yearly (Chonmaitree *et al.,* 2008). ARIs are caused mainly by viruses primarily associated with the upper respiratory tract which commonly include influenza viruses, respiratory syncytial viruses (RSV), parainfluenza viruses (PIV), coronaviruses (CoV), rhinoviruses (RV), adenoviruses (AdV), and enteroviruses (Brodzinski and Ruddy, 2009; Liu *et al.*, 2014). Other respiratory viruses have been reported, including human bocavirus (HBoV), human metapneumovirus (hMPV) (Kling *et al.*, 2005), human polyomaviruses, human coronaviruses such as Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), human coronavirus 229E (HCoV-229E), human coronavirus OC43 (HCoV-OC43), human coronavirus NL63 (HCoV-NL63), human coronavirus HKU1 (HCoV-HKU1) and Middle East Respiratory Syndrome coronavirus (MERS-CoV) (Akinloye et al., 2011; Kolawole *et al.*, 2017).

Children under 5 years of age are majorly at risk for severe influenza and complications. In humans, a major public health problem is caused by Influenza viruses leading to mild to severe respiratory infections. According to the WHO, worldwide, approximately 3–5 million severe cases and 290,000–650,000 deaths annually are caused by Influenza viruses. (WHO, 2018; Krammer, 2019; Suntronwong *et al.*, 2021). Also, across the world, a major cause of childhood morbidity and mortality in low to middle-income countries is Respiratory syncytial virus (RSV) (Shi *et al.*, 2017). Upper respiratory tract infection is usually caused by RSV. Children (25-40%) in their first year of life experiencing infections may develop severe respiratory diseases requiring hospitalization (Pecchini *et al.*, 2008; Nair *et al.*, 2010). Human parainfluenza virus (HPIV) types are major causative agents of laryngotracheobronchitis (croup), and to a lesser extent are frequently associated with bronchiolitis and pneumonia in infants under six months of age who are unable to mount a robust antibody response (Thomazelli *et al.*, 2018).

Rhinovirus (RV) commonly infects all age groups. A wide spectrum of clinical syndromes is associated with RV which is one of the most common causative agents of upper respiratory tract infections in infants, young

children and the elderly. Commonly, approximately 90% of children have antibodies against RV by 2 years of age (Blomqvist *et al.*, 2002). The colloquial term for mild, self-limiting upper respiratory infections is the "common cold" and the primary causative agent implicated, not only in children but also in adults is the RV (Makela *et al.*, 1998). Also, RV is responsible for otitis media, croup, rhinosinusitis and more important clinical manifestations, including associations with wheezing, asthma, and community-acquired pneumonia (CAP) (Ruotsalainen *et al.*, 2013; Jain *et al.,* 2015). In children, there is a well-established link between human adenovirus (HAdV) and respiratory tract infections (RTIs). A broad range of respiratory diseases of varying severity, particularly in immunocompromised children is caused by HAdV (Echevarría, 2008). Adenoviruses may cause epidemic keratoconjunctivitis and gastroenteritis. More rarely, HAdV infections may lead to haemorrhagic cystitis (Chen *et al.*, 2013). Severe disease in children, immunodeficient patients and the elderly has also been documented (Abbas *et al.*, 2013). Infections with adenovirus may occur sporadically or in epidemics and can be detected throughout the year. In childhood, human coronaviruses (HCoVs) are usually identified and mostly isolated from the nasopharynx of children causing mild upper respiratory tract infections (URTIs). However, severe lower respiratory tract infections (LRTIs) can occur in neonates with low birth weight, premature infants, and children with underlying chronic diseases (Gerna et al., 2006; Kuypers *et al.*, 2007). Co-infections with other respiratory viruses, commonly RSV, influenza viruses, and human metapneumovirus have also been implicated in some cases (Smut *et al.*, 2008). This study aimed to determine the seroprevalence of IgM and IgG antibodies to six of the most common respiratory viruses, namely influenza A virus, respiratory syncytial virus, parainfluenza virus, coronavirus, rhinovirus and adenovirus among children ≤ 5 years with ARTIs in Owo, Nigeria.

## MATERIALS AND METHODS

### Study Design and Ethics Issues

The cross-sectional study was carried out at the Federal Medical Centre (FMC), Owo, Ondo State, Nigeria. Children (≤ 5 years) who presented within 7 days of the start of respiratory infections, attending the Children Out Patients' Department (COPD) of the hospital were recruited consecutively into the study. The study was approved by the Federal Medical Centre, Health Research Ethics Committee (HREC). Before enrolment into the study, written informed consent was obtained from the parent/guardian of the children. A structured questionnaire was administered to obtain patients' sociodemographic information, history of past and present medical status, and risk factors.

### Sample Collection (Blood)/Processing

A total of two hundred (200) samples were collected between April 2019 and January 2020. Each child was bled via venipuncture, five (5 ml) of whole blood was collected in labelled sterile tubes without anticoagulant and allowed to clot. The blood samples were spun on a bench centrifuge at 3,500 rpm for 5 minutes to obtain the serum. The sera were separated immediately and stored at -20°C until further processed.

### Assay Procedure for Detection of IgM and IgG Antibodies

The qualitative evaluation of all sera samples was tested for the presence of IgM and IgG antibodies to influenza A virus (FLU-A), respiratory syncytial virus (RSV), parainfluenza virus (PIV), coronavirus (CoV), rhinovirus (RV) and adenovirus (AdV) respectively in human sera using the Enzyme-Linked Immunosorbent Assay (ELISA) kits according to the assay procedure provided by Melsin Medical Co., Limited, China. Each kit contained microwells which were pre-coated with the virus antigen. The solid phase was treated with the diluted sample to capture the IgM and IgG antibodies to the virus if present by antigens on the wells. The optical density of the sample was read at a reference wavelength of 450 nm using a microtiter plate reader (BIOBASE EL-10B) within 15 minutes after stopping the reaction (Melsin Medical Co., Limited, China). The mean optical densities (ODs) of the positive and negative controls were used to calculate the cut-off value of the samples. Samples with higher ODs are positive, and samples with lower ODs are negative. The interpretation of the results was done accordingly.

### Data analysis

Data generated were analyzed using the IBM Statistical Package for Social Sciences Version 23 (IBM SPSS Inc.). Pearson Chi-square test was used to establish the association between the seroprevalence of each virus antibody tested and demography, predisposing factors and symptoms evaluated in the study with the p-value $< 0.05$ accepted as statistically significant.

## RESULTS

The study subjects consisted of 200 children, aged 0-5 years with a mean age of 3.49 ± 1.41 years, suffering from ARTIs. There were 129 (64.5%) males and 71 (35.5%) females. Among the study subjects, both 0 - 1

year and 1 - 2 years age groups were 26 (13%) each, 20 (10%) were 2 - 3 years, 74 (37%) were 3 - 4 years, and 54 (27%) were 4 - 5 years as shown in Figure 1.

The total IgM seropositivity was detected in 83% of the children with the highest being AdV 91 (45.5%), followed by PIV 89 (44.5%), FLU-A and RV with 88 (44%) respectively, CoV 85 (42.5%), and RSV 80 (40%) as shown in Figure 2. While the total IgG seropositivity was detected in 87.5% of the children with the highest being PIV 152 (76%), followed by RSV 135 (67.5%), RV 93 (46.5%), AdV 81 (40.5%), CoV and FLU A with 76 (38%) respectively as shown in Figure 3.

The children in preschool were 46 (23%), nursery 40 (20%), primary school 95 (47.5%) and others 19 (9.5%), with the majority of the children residing in the urban area 174 (87%). The association of the demography of subjects with the detection of respiratory virus IgM antibody are shown in Table 1. A significant association was observed between gender, with FLU A IgM (p=0.014) and AdV IgM (p=0.022). In terms of age, there was a significant association between the age of the subjects and FLU A IgM (p=0.005), RSV IgM (p=0.034), RV IgM (p=0.015) and AdV IgM (p=0.003). In contrast, no significant association was observed between gender, age group, residential area and respiratory viruses IgG antibodies (Table 2). However, there was a significant association between the educational level of the children enrolled in the study and AdV IgG (p=0.030).

The predisposing factors considered in the study included daycare attendance, a family member with recent ARTIs symptoms, type of apartment, number of people sleeping in a room, change of environment and duration of exclusive breastfeeding. The association of predisposing factors with the detection of respiratory virus IgM antibodies in children is shown in Table 3. There was a significant association between daycare attendance and RSV IgM antibody (p=0.024). Also, a significant association was observed between a family member with recent ARTI symptoms and CoV IgM antibody (p=0.010). FLU A IgM, PIV IgM, and AdV IgM antibodies were all significantly associated (p<0.05) with the type of apartment. A significant association was observed between the number of people sleeping in a room and PIV IgM (p=0.008). Duration of exclusive breastfeeding was found to be significantly associated with CoV IgM and AdV IgM (p<0.05). However, no significant association was recorded between the change of environment and any of the respiratory viruses IgM (p>0.05)

Tables 4 showed the association of predisposing factors with the detection of respiratory viruses IgG antibody in children enrolled in the study. A significant association between daycare attendance and PIV IgG antibody (p=0.006) was observed. Also, a significant association was observed between a family member with recent ARTI symptoms and RV IgG antibody (p=0.010) and, the type of apartment was significantly associated with RV IgG antibody (p=0.006). A significant association was observed between the number of people sleeping in a room and FLU A IgG (p=0.023). Change of environment was significantly associated with AdV IgG (p=0.029) and also, and lack of exclusive breastfeeding was significantly associated with RV IgG (p=0.002).

Out of the tested children, 34 (17%) had symptoms of difficulty in breathing, 133 (16.5%) had a cough, 97 (48.5%) had cold, 113 (56.5%) were sneezing and 153 (76.5%) had a fever. The association of symptoms with the detection of respiratory viruses IgM antibody in enrolled children is shown in Table 5. Difficulty in breathing is significantly associated with PIV IgM and RV IgM (p<0.05). Sneezing is significantly associated with FLU A IgM (p=0.036). However, there was no statistical association (p>0.05) between cough, cold and fever with any of the respiratory viruses IgM antibodies in the study. The association of symptoms with the detection of respiratory viruses IgG antibody in enrolled children is shown in Table 6. Difficulty in breathing is significantly associated with CoV IgG (p=0.022). Fever was significantly associated with RSV IgG (p=0.025) and PIV IgG (p=0.039). However, there was no statistical association (p>0.05) between cough, cold and sneezing with any of the respiratory viruses IgG antibodies in the study.

**Discussion**

Respiratory infections have been widely investigated by specific IgM and IgG antibodies against viruses. This study depicts the detection of IgM and IgG antibodies to six (6) human respiratory viruses using ELISA. To the best of our knowledge, this is one of the first reports that attempts to describe the seroprevalence of respiratory viruses including RSV, PIV, AdV, RV, FLUA and CoV, and to evaluate the potential risk factors associated with respiratory tract infections among children in Owo, Ondo State, Nigeria. The total IgM seropositivity was 83% while IgG seropositivity was 87.5% detected in the children enrolled in the study.

The seroprevalence of FLU A IgM was 44% in this study. A previous study retrospectively analyzed serum IgM antibodies to influenza viruses and reported that FLU A IgM antibody seropositivity in children was

0.80% which is far lower than the findings of this study, this is due to the large population size considered in the earlier study (Yao *et al.*, 2019). The seroprevalence of FLU A IgG was 38% and is not in agreement with a similar study which reported a higher seroprevalence of antibodies against FLU A IgG with 67% among children aged 0-6 years (Sauerbrel *et al.*, 2014).

RSV is among the frequent causative agent of severe RTIs in infants and children with 76% of children being re-infected by the second year of life (Faneye *et al.*, 2014). The seroprevalence of RSV IgM was 40% among the tested subjects and is similar to an earlier study by Sulaiman *et al*. (2017) who reported that the seroprevalence of RSV IgM was 47.3% among children aged 0-5 years. However, previous studies by Idris and Kolawole (2022) and Lin *et al.* (2015) recorded a lower seroprevalence of RSV IgM with 7.5% and 10.27% respectively among children aged 0-5 years and its at variance with this study. The difference in seroprevalence reported in this study and others reported in previous studies might be due to the differences in population sizes, geographical location, or seasonal variations considered in the studies. Furthermore, this study recorded the seroprevalence of RSV IgG as 67.5% among the tested subjects. Similarly, another study reported seroprevalence of RSV IgG with 75% among children in Ilorin, Nigeria (Odebisi-Omokanye *et al.*, 2017). Also, a study by Faneye *et al*. (2014) recorded seroprevalence of RSV IgG was 85.7%. Likewise, a recent study also recorded the seroprevalence of RSV IgG as 73% in consistence with this study (Idris and Kolawole, 2022).

In this study, the seroprevalence of PIV IgM was 44.5% among the tested subjects. However, a very low seroprevalence of PIV IgM with 1.57% was reported by Lin *et al*. (2015). The difference in seroprevalence reported in this study and the findings by Lin et al. is due to the differences in population sizes, geographical location and possibly seasonal variations. Also, the seroprevalence of PIV IgG was 76% among the tested subjects studied. In agreement with our study, a previous study reported the seroprevalence of PIV IgG as 70% among the tested children (Odebisi-Omokanye *et al.*, 2018). Also, another study reported human parainfluenza virus type 2 (HPIV-2) IgG antibodies among children aged 1-5 years with a seroprevalence of 46.4% (Sale *et al.*, 2010), although the studied population size was much higher than the population in our study.

The human coronaviruses (hCoVs) 229E, HKU1, NL63 and OC43 circulate globally, and commonly infect children (Heimdal *et al.*, 2019). The seroepidemiologic studies in children and adults have shown clearly that the prevalence of immunoglobulin G (IgG) against SARS-CoV was low (Leung *et al.*, 2004); this implies a limited spread and also SARS-CoV had a restricted period of circulation. Although, this study detected the antibody to coronavirus before the outbreak of the recent pandemic. A previous study in Nigeria conducted before the recent pandemic Coronavirus infectious disease-2019 (COVID-19), detected Coronavirus OC43 as the most common virus in Ilorin community (13.3%) and Coronavirus OC 229 E/NL63 was also detected among subjects from the clinic (12.5%) (Kolawole *et al.*, 2017). In this study, the seroprevalence of CoV IgM was 42.5% and CoV IgG was 38% among the tested children. The CoV antibodies detected in this study might be for CoV-OC43, as this study was carried out before the outbreak of the recent pandemic COVID-19.

Generally, children by the age of 2 years have antibodies against RV (Blomqvist *et al.*, 2002). This study observed that age is significantly associated with RV IgM ($p<0.05$). Also, the seroprevalence of RV IgM and RV IgG was 44% and 46.5% respectively. Similarly, a previous study reported 38% seropositivity of rhinovirus infection in children (Kolawole *et al.*, 2015).

The seroprevalence of AdV IgM with 45.5% was recorded in this study. A recent study by Idris and Kolawole (2022) reported a lower AdV IgM of 8.5% among children. Also, a lower AdV IgM with 6.63% had been reported by Lin *et al.* (2015) among children with ARTIs and this is at variance with this study. This study reported a 40.5% seroprevalence of AdV IgG among the tested children. However, another investigation on AdV IgG with HIV coinfection reported a seroprevalence of 33% among the tested subjects (Kolawole *et al.*, 2014). Also, previous studies had reported a lower seroprevalence of AdV IgG (12.5%) among children aged 11-27 months (Trojnar *et al.*, 2014) and this is at variance with our study. An earlier study reported a higher seroprevalence of AdV IgG (98.5%) in Ado-Ekiti (Idris and Kolawole, 2022).

The differences in the seroprevalence reported in this study and others reported in previous studies might be linked to several factors including geographical or seasonal variations during which samples were collected, sample sizes, and differences in the methodology employed in the virus assay in the studies (Lin *et al.*, 2015).

In our study, there were more males 129 (64.5%) than females 71 (35.5%) with ARTIs. Generally, previous studies had reported higher seropositivity in

males than in females. This study also observed that seropositivity to all the virus antibodies was higher in males than in females and the difference was statistically significant only in FLUA IgM (p=0.014) and AdV IgM (p=0.022). This study observed no statistical association between gender, age group, residential area and respiratory viruses IgG antibodies. In contrast, a significant statistical relationship had been reported between gender and IgG (RSV and HPIV) seroprevalence in Iran and other studies of these types (Karimi *et al.*, 2010). Also, similar studies in Germany reported an age-dependent increase of antibodies to FLU A IgG among children until the age of nine to ten years (Sauerbrel *et al.*, 2014). However, a statistical significance was recorded between the age of the subjects and FLU A IgM (p=0.005), RSV IgM (p=0.034), RV IgM (p=0.015) and AdV IgM (p=0.003). The highest RSV IgM seropositivity of 57.6% per group was found within the 0-1 year age group. Similar studies had also reported the highest seroprevalence within age grade 0-1 year with 15.4% (Sulaiman *et al.*, 2017).

The predisposing factors considered in the study included daycare attendance, a family member with recent ARI symptoms, type of apartment, number of people sleeping in a room, change of environment and exclusive breastfeeding. There was a significant association between daycare attendance and RSV IgM antibody (p=0.024) and PIV IgG antibody (p=0.006) observed in this study. Odebisi *et al.* (2018) reported a significant association between daycare attendance and HPIV IgG (p=0.017) and is in agreement with this study.

Also, a significant association was observed between a family member with recent ARTI symptoms with CoV IgM antibody (p=0.010) and RV IgG antibody (p=0.010). This implied that possible transmission could occur between an infected family member and children within the home. A statistical significance between HPIV IgG and a family member recently diagnosed with respiratory infection with a high prevalence had been reported in a previous study (Odebisi *et al.*, 2018). In contrast, this study did not observe a significant association between HPIV IgG and a family member recently diagnosed with a respiratory infection.

Type of apartment was significantly associated with FLU A IgM, PIV IgM, AdV IgM and RV IgG antibodies (p<0.05). Forty per cent (≥ 40%) of the children sleep in rooms with 3-4 people. PIV IgM (p=0.008) and FLU A IgG (p=0.023) are significantly associated with the number of people sleeping in a room. Similar studies reported that the probability of developing ARTI was higher with the under-five age (49.1%) of the children sleeping with 3 or more adults in a room (Oluremi et al., 2018). Also, overcrowding is associated with a high ARIs prevalence (Goel *et al.*, 2012).

A previous study reported a significant protective factor against RSV infection in children who were breastfed for > 2 months (Figueras-Aloy *et al.*, 2004) and this is not in agreement with this study as there was no significant association (p>0.05) observed between duration of breastfeeding and RSV. However, the duration of breastfeeding was significantly associated with CoV IgM, AdV IgM and RV IgG (p<0.05) respectively in this study. Consistent with this study, Odebisi *et al.* (2018) reported that there was no significant association (p>0.05) between exclusive breastfeeding and human parainfluenza virus infection in children. There was no statistical significance recorded between the change of environment and any of the respiratory viruses IgM (p>0.05). However, a statistical significance was recorded between the change of environment and AdV IgG (p=0.029).

The symptoms considered in this study were difficulty in breathing, cough, cold, sneezing, and fever. A significant association (p<0.05) was observed between difficulty in breathing and PIV IgM, RV IgM (p<0.05) and CoV IgG. Similarly, sneezing is significantly associated with FLU A IgM (p=0.036) in the children studied. In contrast, Karimi *et al.* (2010) reported that there was no significant relationship between clinical syndromes and HPIV IgM seroprevalence in children. Also, this study observed no significant association (p>0.05) between cough, cold and sneezing with any of the respiratory viruses IgG antibodies in children. However, Niang *et al.* (2017) reported a significant association (p=0.0028) between cough and patients infected by adenovirus. Fever was significantly associated with RSV IgG (p=0.025) and PIV IgG (p=0.039). A similar study also reported a significant association (p<0.05) between fever and RSV IgG (Idris and Kolawole, 2022).

**Conclusion**

In conclusion, IgM and IgG antibodies to six respiratory viruses including influenza A, respiratory syncytial virus, parainfluenza virus, coronavirus, rhinovirus and adenovirus showed a high total IgM (83%) seropositivity with the highest being AdV IgM (45.5%) and IgG (87.5%) seropositivity with the highest being PIV IgG (76%) was found among children with acute respiratory tract infections attending FMC, Owo, Nigeria. There is a need for mass surveillance in other parts of Nigeria to provide a better picture of the circulating virus antibodies. Elaborate investigations

on antigen detection of these respiratory viruses are necessary to determine the pattern of respiratory virus circulation among children.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

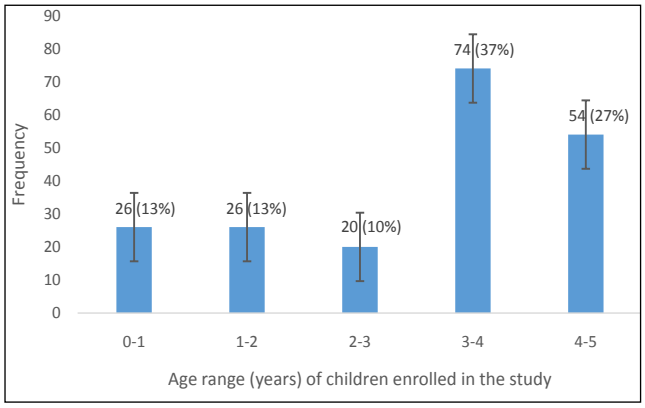


**Figure 1:** Age distribution of children enrolled in the study.

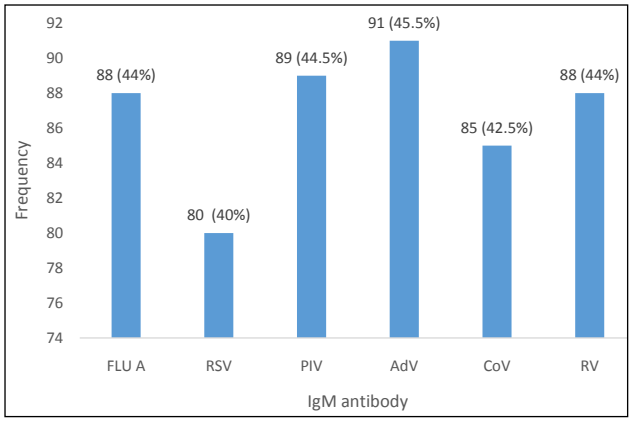


**Figure 2:** Seroprevalence of IgM antibody to respiratory viruses in children enrolled in the study.

**Key:** IgM, Immunoglobulin M; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus

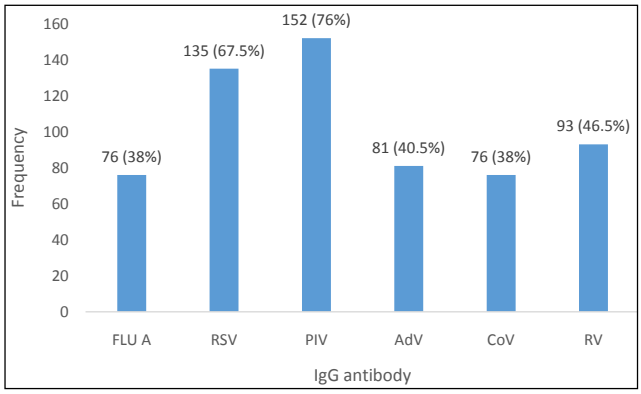


**Figure 3:** Seroprevalence of IgG antibody to respiratory viruses in children enrolled in the study

IgG, Immunoglobulin G; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus

**Table 1:** Association of demography of subjects with detection of respiratory viruses IgM antibody

| Demography | | No. of subjects tested (N=200) | FLU A IgM seropositivity per group No. (%) | p-value | RSV IgM seropositivity per group No. (%) | p-value | PIV IgM seropositivity per group No. (%) | p-value | COR IgM seropositivity per group No. (%) | p-value | RV IgM seropositivity per group No. (%) | p-value | AdV IgM seropositivity per group No. (%) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gender | Male | 129 | 65 (50.3) | **0.014*** | 47 (36.4) | 0.165 | 59 (45.7) | 0.635 | 60 (46.5) | 0.122 | 63 (48.8) | 0.063 | 51 (39.5) | **0.022*** |
| | Female | 71 | 23 (32.3) | | 33 (46.4) | | 30 (42.2) | | 25 (35.2) | | 25 (35.2) | | 40 (56.3) | |
| Age group (years) | 0-1 | 26 | 4 (15.3) | **0.005*** | 15 (57.6) | **0.034*** | 16 (61.5) | 0.412 | 9 (34.6) | 0.356 | 8 (30.7) | **0.015*** | 20 (76.9) | **0.003*** |
| | 1-2 | 26 | 9 (34.6) | | 14 (53.8) | | 11 (42.3) | | 9 (34.6) | | 13 (50) | | 15 (57.6) | |
| | 2-3 | 20 | 7 (35) | | 10 (50) | | 9 (45) | | 6 (30) | | 7 (35) | | 9 (45) | |
| | 3-4 | 74 | 41 (55.4) | | 26 (35.1) | | 29 (39.1) | | 37 (50) | | 43 (58.1) | | 27 (36.4) | |
| | 4-5 | 54 | 27 (50) | | 15 (27.7) | | 24 (44.4) | | 24 (44.4) | | 17 (31.4) | | 20 (37) | |
| Educational level of children | Pre-school | 46 | 18 (39.1) | 0.005* | 25 (54.3) | 0.051 | 15 (32.6) | 0.053 | 18 (39.1) | 0.014* | 19 (41.3) | 0.630 | 14 (30.4) | 0.000* |
| | Nursery | 40 | 17 (42.5) | | 14 (35) | | 16 (40) | | 26 (65) | | 21 (52.5) | | 16 (40) | |
| | Primary | 95 | 51 (53.6) | | 31 (32.6) | | 45 (47.3) | | 35 (36.8) | | 41 (43.1) | | 42 (44.2) | |
| | Others | 19 | 2 (10.5) | | 10 (52.6) | | 13 (68.4) | | 6 (31.5) | | 7 (36.8) | | 19 (100) | |
| Residential area | Rural | 26 | 8 (30.7) | 0.145 | 8 (30.7) | 0.303 | 11 (42.3) | 0.809 | 11 (42.3) | 0.983 | 13 (50) | 0.509 | 16 (61.5) | 0.078 |
| | Urban | 174 | 80 (45.9) | | 72 (41.3) | | 78 (44.8) | | 74 (42.5) | | 75 (43.1) | | 75 (43.1) | |

**Key:** IgM, Immunoglobulin M; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus; *Significant association $p < 0.05$.

**Table 2:** Association of demography of subjects with detection respiratory viruses IgG antibody

| **Demography** | | **No. of subjects tested (N=200)** | **FLU A IgG seropositivity per group No. (%)** | **p-value** | **RSV IgG seropositivity per group No. (%)** | **p-value** | **PIV IgG seropositivity per group No. (%)** | **p-value** | **CoV IgG seropositivity per group No. (%)** | **p-value** | **RV IgG seropositivity per group No. (%)** | **p-value** | **AdV IgG seropositivity per group No. (%)** | **p-value** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gender | Male | 129 | 51 (39.5) | 0.547 | 82 (63.5) | 0.109 | 95 (73.6) | 0.293 | 47 (36.4) | 0.539 | 66 (51.1) | 0.075 | 53 (41) | 0.820 |
| | Female | 71 | 25 (35.2) | | 53 (74.6) | | 57 (80.2) | | 29 (40.8) | | 27 (38) | | 28 (39.4) | |
| Age group (years) | 0-1 | 26 | 10 (38.4) | 0.274 | 17 (65.3) | 0.569 | 18 (69.2) | 0.881 | 8 (30.7) | 0.223 | 11 (42.3) | 0.175 | 16 (61.5) | 0.071 |
| | 1-2 | 26 | 11 (42.3) | | 16 (61.5) | | 19 (73) | | 12 (46.1) | | 10 (38.4) | | 11 (42.3) | |
| | 2-3 | 20 | 6 (30) | | 11 (55) | | 16 (80) | | 5 (25) | | 5 (25) | | 9 (45) | |
| | 3-4 | 74 | 34 (45.9) | | 54 (72.9) | | 58 (78.3) | | 34 (45.9) | | 39 (52.7) | | 22 (29.7) | |
| | 4-5 | 54 | 15 (27.7) | | 37 (68.5) | | 41 (75.9) | | 17 (31.4) | | 28 (51.8) | | 23 (42.5) | |
| Educational level of children | Pre-school | 46 | 15 (32.6) | 0.357 | 33 (71.7) | 0.066 | 30 (65.2) | 0.272 | 11 (23.9) | 0.105 | 20 (43.4) | 0.745 | 15 (32.6) | **0.030*** |
| | Nursery | 40 | 19 (47.5) | | 32 (80) | | 31 (77.5) | | 19 (47.5) | | 19 (47.5) | | 11 (27.5) | |
| | Primary | 95 | 33 (34.7) | | 61 (64.2) | | 76 (80) | | 37 (38.9) | | 47 (49.4) | | 43 (45.2) | |
| | Others | 19 | 9 (47.3) | | 9 (47.3) | | 15 (78.9) | | 9 (47.3) | | 7 (36.8) | | 12 (63.1) | |
| Residential area | Rural | 26 | 11 (42.3) | 0.628 | 20 (76.9) | 0.271 | 20 (76.9) | 0.906 | 13 (50) | 0.177 | 15 (57.6) | 0.220 | 9 (34.6) | 0.512 |
| | Urban | 174 | 65 (37.3) | | 115 (66) | | 132 (75.8) | | 63 (36.2) | | 78 (44.8) | | 72 (41.3) | |

**Key:** IgG, Immunoglobulin G; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus; *Significant association $p < 0.05$.

**Table 3:** Association of some predisposing factors with detection of respiratory viruses IgM antibody in enrolled children

| Predisposing factor | | No. of subjects tested (N=200) | FLU A IgM seropositivity per group No. (%) | p-value | RSV IgM seropositivity per group No. (%) | p-value | PIV IgM seropositivity per group No. (%) | p-value | CoV IgM seropositivity per group No. (%) | p-value | RV IgM seropositivity per group No. (%) | p-value | AdV IgM seropositivity per group No. (%) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Attendance of daycare | No | 154 | 73 (47.4) | 0.076 | 55 (35.7) | 0.024* | 72 (46.7) | 0.241 | 65 (42.2) | 0.878 | 68 (44.1) | 0.935 | 70 (45.4) | 0.981 |
| | Yes | 46 | 15 (32.6) | | 25 (54.3) | | 17 (36.9) | | 20 (43.4) | | 20 (43.4) | | 21 (45.6) | |
| Family member with recent ARI symptoms | No | 174 | 79 (45.4) | 0.301 | 66 (37.9) | 0.122 | 78 (44.8) | 0.809 | 80 (45.9) | 0.010* | 79 (45.4) | 0.301 | 80 (45.9) | 0.726 |
| | Yes | 26 | 9 (34.6) | | 14 (53.8) | | 11 (42.3) | | 5 (19.2) | | 9 (34.6) | | 11 (42.3) | |
| Type of appartment | | | | | | | | | | | | | | |
| | F to F | 61 | 22 (36) | 0.001* | 22 (36) | 0.092 | 22 (36) | 0.046* | 30 (49.1) | 0.436 | 23 (37.7) | 0.448 | 40 (65.5) | 0.000* |
| | Self contain | 19 | 2 (10.5) | | 12 (63.1) | | 13 (68.4) | | 8 (42.1) | | 8 (42.1) | | 15 (78.9) | |
| | 2/more rooms flat | 120 | 64 (53.3) | | 46 (38.3) | | 54 (45) | | 47 (39.1) | | 57 (47.5) | | 36 (30) | |
| Number of people sleeping in a room | | | | | | | | | | | | | | |
| | 1-2 | 46 | 21 (45.6) | 0.948 | 18 (39.1) | 0.414 | 15 (32.6) | 0.008* | 21 (45.6) | 0.833 | 14 (30.4) | 0.106 | 18 (39.1) | 0.611 |
| | 3-4 | 141 | 61 (43.2) | | 59 (41.8) | | 72 (51) | | 58 (41.1) | | 68 (48.2) | | 67 (47.5) | |
| | 5-6 | 13 | 6 (46.1) | | 3 (23) | | 2 (15.3) | | 6 (46.1) | | 6 (46.1) | | 6 (46.1) | |
| Change of environment | | | | | | | | | | | | | | |
| | No | 167 | 69 (41.3) | 0.086 | 67 (40.1) | 0.938 | 76 (45.5) | 0.518 | 71 (42.5) | 0.992 | 77 (46.1) | 0.177 | 81 (48.5) | 0.055 |
| | Yes | 33 | 19 (57.5) | | 13 (39.3) | | 13 (39.3) | | 14 (42.4) | | 11 (33.3) | | 10 (30.3) | |
| Exclusive breastfeeding | | | | | | | | | | | | | | |
| | < 6 months | 80 | 32 (40) | 0.352 | 33 (41.2) | 0.768 | 34 (42.5) | 0.642 | 43 (53.7) | 0.009* | 33 (41.2) | 0.522 | 46 (57.5) | 0.005* |
| | > 6 months | 120 | 56 (46.6) | | 47 (39.1) | | 55 (45.8) | | 42 (35) | | 55 (45.8) | | 45 (37.5) | |

**Key:** IgM, Immunoglobulin M; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus; F to F: face to face; *Significant association $p < 0.05$.

**Table 4:** Association of some predisposing factors with detection of respiratory viruses IgG antibody in enrolled children

| Predisposing factor | | No. of subjects tested (N=200) | FLU A IgG seropositivity per group No. (%) | p-value | RSV IgG seropositivity per group No. (%) | p-value | PIV IgG seropositivity per group No. (%) | p-value | CoV IgG seropositivity per group No. (%) | p-value | RV IgG seropositivity per group No. (%) | p-value | AdV IgG seropositivity per group No. (%) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Attendance of daycare | No | 154 | 60 (38.9) | 0.608 | 105 (68.1) | 0.706 | 124 (80.5) | 0.006* | 64 (41.5) | 0.058 | 68 (44.1) | 0.224 | 62 (40.2) | 0.899 |
| | Yes | 46 | 16 (34.7) | | 30 (65.2) | | 28 (60.8) | | 12 (26) | | 25 (54.3) | | 19 (41.3) | |
| Family member with recent ARI symptoms | No | 174 | 67 (38.5) | 0.703 | 117 (67.2) | 0.840 | 133 (76.4) | 0.708 | 67 (38.5) | 0.703 | 87 (50) | 0.010* | 70 (40.2) | 0.840 |
| | Yes | 26 | 9 (34.6) | | 18 (69.2) | | 19 (73) | | 9 (34.6) | | 6 (23) | | 11 (42.3) | |
| Type of appartment | | | | | | | | | | | | | | |
| | F to F | 61 | 23 (37.7) | 0.374 | 45 (73.7) | 0.305 | 49 (80.3) | 0.525 | 25 (40.9) | 0.750 | 38 (62.2) | 0.006* | 19 (31.1) | 0.091 |
| | Self contain | 19 | 10 (52.6) | | 14 (73.6) | | 13 (68.4) | | 6 (31.5) | | 10 (52.6) | | 11 (57.8) | |
| | 2/more rooms flat | 120 | 43 (35.8) | | 76 (63.3) | | 90 (75) | | 45 (37.5) | | 45 (37.5) | | 51 (42.5) | |
| Number of people sleeping in a room | | | | | | | | | | | | | | |
| | 1-2 | 46 | 10 (21.7) | 0.023* | 27 (58.6) | 0.176 | 33 (71.7) | 0.308 | 12 (26) | 0.050 | 19 (41.3) | 0.716 | 19 (41.3) | 0.160 |
| | 3-4 | 141 | 62 (43.9) | | 97 (68.7) | | 107 (75.8) | | 56 (40) | | 68 (48.2) | | 60 (42.5) | |
| | 5-6 | 13 | 4 (30.7) | | 11 (84.6) | | 12 (92.3) | | 8 (61.5) | | 6 (46.1) | | 2 (15.3) | |
| Change of environment | | | | | | | | | | | | | | |
| | No | 167 | 67 (40.1) | 0.165 | 112 (67) | 0.768 | 130 (77.8) | 0.169 | 67 (40.1) | 0.165 | 73 (43.7) | 0.075 | 62 (37.1) | 0.029* |
| | Yes | 33 | 9 (27.2) | | 23 (69.6) | | 22 (66.6) | | 9 (27.2) | | 20 (60.6) | | 19 (57.5) | |
| Exclusive breastfeeding | | | | | | | | | | | | | | |
| | No | 80 | 33 (41.2) | 0.439 | 56 (70) | 0.538 | 60 (75) | 0.787 | 31 (38.7) | 0.858 | 48 (60) | 0.002* | 32 (40) | 0.906 |
| | Yes | 120 | 43 (35.8) | | 79 (65.8) | | 92 (76.6) | | 45 (37.5) | | 45 (37.5) | | 49 (40.8) | |

**Key:** IgG, Immunoglobulin G; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus; F to F: face to face; *Significant association $p < 0.05$.

**Table 5:** Association of symptoms with the detection of respiratory viruses IgM antibody in enrolled children

| Symptom | No. of subjects tested (N=200) FLU A IgM seropositivity per group No. (%) | p-value | RSV IgM seropositivity per group No. (%) | p-value | PIV IgM seropositivity per group No. (%) | p-value | CoV IgM seropositivity per group No. (%) | p-value | RV IgM seropositivity per group No. (%) | p-value | AdV IgM seropositivity per group No. (%) | p-value | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Difficulty in breathing | 34 | 13 (38.2) | 0.457 | 11 (32.3) | 0.318 | 21 (61.7) | **0.026*** | 10 (29.4) | 0.090 | 9 (26.4) | **0.024*** | 14 (41.1) | 0.578 |
| Cough | 133 | 64 (48.1) | 0.098 | 53 (39.8) | 0.951 | 60 (45.1) | 0.086 | 58 (43.6) | 0.655 | 65 (48.8) | 0.050 | 57 (42.8) | 0.290 |
| Cold | 97 | 42 (43.2) | 0.846 | 40 (41.2) | 0.729 | 45 (46.3) | 0.601 | 41 (42.2) | 0.949 | 41 (42.2) | 0.632 | 44 (45.3) | 0.969 |
| Sneezing | 113 | 57 (50.4) | **0.036*** | 50 (44.2) | 0.162 | 51 (45.1) | 0.837 | 45 (39.8) | 0.383 | 50 (44.2) | 0.936 | 45 (39.8) | 0.066 |
| Fever | 153 | 72 (47) | 0.116 | 62 (40.5) | 0.785 | 69 (45) | 0.759 | 62 (40.5) | 0.307 | 71 (46.4) | 0.216 | 65 (42.4) | 0.122 |

**Key:** IgM, Immunoglobulin M; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus; *Significant association $p < 0.05$.

**Table 6:** Association of symptoms with the detection of respiratory viruses IgG antibody in enrolled children

| Symptom | No. of subjects tested (N=200) | FLU A IgG seropositivity per group No. (%) | p-value | RSV IgG seropositivity per group No. (%) | p-value | PIV IgG seropositivity per group No. (%) | p-value | CoV IgG seropositivity per group No. (%) | p-value | RV IgG sero-positivity per group No. (%) | p-value | AdV IgG seropositivity per group No. (%) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Difficulty in breathing | 34 | 9 (26.4) | 0.128 | 21 (61.7) | 0.433 | 27 (79.4) | 0.609 | 7 (20.5) | **0.022*** | 16 (47) | 0.943 | 13 (38.2) | 0.768 |
| Cough | 133 | 53 (39.8) | 0.448 | 84 (63.1) | 0.065 | 102 (76.6) | 0.747 | 51 (38.3) | 0.887 | 60 (45.1) | 0.579 | 54 (40.6) | 0.967 |
| Cold | 97 | 37 (38.1) | 0.967 | 60 (61.8) | 0.098 | 69 (71.1) | 0.118 | 31 (31.9) | 0.088 | 51 (52.5) | 0.094 | 40 (41.2) | 0.837 |
| Sneezing | 113 | 44 (38.9) | 0.755 | 74 (65.4) | 0.488 | 88 (77.8) | 0.479 | 42 (37.1) | 0.782 | 47 (41.5) | 0.113 | 50 (44.2) | 0.219 |
| Fever | 153 | 61 (39.8) | 0.326 | 97 (63.3) | **0.025*** | 111 (72.5) | **0.039*** | 57 (37.2) | 0.695 | 75 (49) | 0.197 | 65 (42.4) | 0.303 |

**Key: IgG,** Immunoglobulin G; FLU A, Influenza virus; RSV, Respiratory syncytial virus; PIV, Parainfluenza virus; AdV, Adenovirus; CoV, Coronavirus; RV, Rhinovirus; *Significant association $p < 0.05$.

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