VER
Vascular & Endovascular Review

Predisposing Infection with Orthopneumovirus (Hopv) and Orthorubulavirus (Horuv) Causes Increase Susceptibility To Infections with Human Metapneumovirus (Hmpv) Leading To High Severity of (Artis) in Infants

Sattar Gaber Ajeel, Rusul Sahib Hussien Mohmmed Shubber

[1]PhD, department for Microbiology, Assistant Professor , medicine college , University of Ibn Sina for Medical and Pharmacological science . Iraq – Baghdad
[2]College for medical department, Ibn Sina University of Medical and Pharmaceutical Science Baghdad -Iraq.
Email– sattar.gaber.ajeel@ ibnsina.Edu .
Drstaargaber@gmail.com
rusul_shubber88@ibnsina.edu.iq

ABSTRACT

Viruses are the important causes of acute respiratory tract infections (ARTIs) in infants . (hOPV, and (hORUV) that included respiratory syncytial viruses whom predisposing viruses for infected with hMPV . Human metapneumovirus (hMPV) , human type 2 orthopneumoviruses hOPV and human orthopnjeumovirus hORUV are among viruses that causes severe (ARTIs) in infants .In this study we aimed to determine the role of (hOPV, hORUV) in decrease of immunity and causes infected with hMPV.That lead to severe (ARTIs).

In the current study we aimed to study the human type 2 orthopneumovirus (Hopv) and human orthorubulavirus (Horuv) in increase susceptibility to infectants with human metapneumovirus (HMPV) that lead to high severity of (ARTIs) in children between (two months to thirteen months)of age .

Methodes :- we collected swabs from nasopharyngeal from (180) infants with age less than sex months , started December 2024 to April 2025 taken the samples and diagnosis by real time polymerase chain reactions (RT-PCR) were used to determined for present of human metapneumovirus (hMPV) , human type 2 orthopneumovirus ((hOPV) include respiratory syncytial virus RSV) and human orthorubulavirus (hORUV), also taken the date for entry the hospital and after that taken the history for each patients and diagnosed if present of present three viruses during first three days and after five days of entry the central teaching hospital of peadiatric , in Baghdad , also determine clinical feature by the chest x-ray .

Results :- A total samples that collection from children (180) nasopharyngeal swabs were screened for present of predisposing infection (hMPV) in infants infected with (hOPV) and ((hORUV) include (respiratory syncytial virus)(RSV) , and the impact with the (hOPV) and (hORUV), for increase severity of (ARTIs) , we observed that higher infection with (hOPV)(from male 54(51.42%) and female 29(38.66%)),(hORUV) from male 24 (22.85%) and female17 (22.66%)) , rather than (hMPV) in male 3(2.85%) and female 2 (2.77%) , during the first three days of enter the hospital . While after five days of enter the hospital observed increase severity of ARTIs and increase infected of patients with hMPV,who infected with (hOPV) and (hORUV), during the first week . In this study observed infectious infants, 86(47.8%) in groups coinfected (hMPV , hOPV), also seen 28(15.6%) in group patients coinfection with (hORUV ,hMPV) and 60 (33.4%)in group of infants infected with the three viruses (hMPV , hOPV and hORUV) , while 23(12.8%) in group infected with hMPV only, non negative results detection in all infants

KEYWORDS: Human metapneumovirus (hMPV) , human type 2 orthopneumovirus (hOPV)and human type 2 orthopneumoviruse (hOPV), and human orthorubulavirus (hORUV), acute respiratory tract infections (ARTIs) , infants . chest x-ray.

How to Cite: Sattar Gaber Ajeel, Rusul Sahib Hussien Mohmmed Shubber, (2025) Predisposing infection with orthopneumovirus (hOPV) and orthorubulavirus (hORUV) causes increase susceptibility to infections with human metapneumovirus (hMPV) leading to high severity of (ARTIs) in infants, Vascular and Endovascular Review, Vol.8, No.8s, 336-342.

INTRODUCTION

Acute respiratory infections (ARI) are the most important causes of morbidity and mortality in children (neonates and infants) (1).The World Health Organization (WHO) started a program to control and reduced acute respiratory tracts infections (ARTIs) that causes high incidence for public health problem. ARTIs causes (30%-50%) of pediatric medical admissions (2) . although many pathogens can leading to infections of respiratory tracts (3) .The main causes are viruses that lead to acute lower respiratory tracts infections (ARTIs) . Which is the second causes of death and the primary causes enter of children to hospital. (4). Viral causative agents are represent about (30%-40%) for respiratory infections (5). The major causes of lower respiratory trank infections is viral (6).

Respiratory diseases are the main causes of mortality in children under five years of age old , with more than 150 million

individual per year . human metapneumovirus (hMPV) , human type 2 orthopneumovirus (hOPV) and human orthorubulavirus (hORUV) (7) . are causes pneumonitis and bronchiolitis in infants (8) .

The main etiological agents are viruses such as , human metapneumovirus (hMPV) , human type 2 orthopneumovirus (hOPV) and human orthorubulavirus (hORUV) . and co infections with other RSV (9).

Human metapneumovirus (hMPV) is a respiratory pathogen that emerge newly causes upper and lower respiratory infections in all ages of individuals especially in older adults with weakened immune systems and young children (10) . The first discovered of the virus in 2001 ,hMPV from family of the pneumoviridae along with respiratory syncytial virus (RSV) (11). Human metapneumovirus (HMPV) causes a highly contagious disease that spread through respiratory secretion such as coughing and sneezing (12). hMPV primary associated with pneumonia and bronchiolitis ,and the sever infection with this virus can lead to causes severe climical symptoms that complications such as asthma and exacerbations of chronic pulmonary disease (13) .

The Word Health Organizations seeks to reduce mortality in younger children that currently amounts (37%) per year which is occurs with the first month of life , (43%) associated with other respiratory disease (14).

More than (25%) of children enter the hospital are causes acute respiratory diseases . human metapneumovirus (hMPV) and human type 2 orthopneumovirus (hOPV) are responsible for (80%) of infections , that estimated by The Word Health Organizations (15).

Increase incidence of infections with these agents in younger children during December , January and February throughout the year, infants and premature newborns with bronchopulmonary dyspasia , congenital heart disease and asthma m are more susceptible for infections with these agents (16).

The lower respiratory tract infections due to childhood morbidity , causes infectious diseases which reported among the top of ten causes death children under 5 years (17). the clinical practices observing in respiratory disease is rales , shortness of breath ,cough , wheezing children seen failure of respiration , lead to death (18) . However the incidence of viral coinfection , despite impact of viral infection in the world(19) .The coinfection are associated with increase morbidity and mortality for the individuals (20).

Human type 2 orthopneumovirus (Hopv) and human orthorubulavirus (Horuv) are two genera within pneumoviridae family of viruses , orthopneumovirus includes human respiratory syncytial virus (RSV) , who a major disease causes of young children and infants that lead to causes pneumonia , ,fever wheezing and coughing and bronchiolitis (21) . human orthorubulavirus (Horuv) is a virus that causes mumps (22) . infects the salivary glands , that causes swelling of salivary glands ,headache ,fever wheezing and coughing (23).

Orthorubulavirus especially parainfluenza virus that causes infections in upper and lower respiratory tracts leading to common cold , pneumonia and croup . while Orthopneumovirus and orthorubulavirus infectiions in upper and lower respiratory tracts (24). Orthopneumovirus , which includes human respiratory syncytial virus (RSV) is the main cause of lower respiratory tracts infections (LRTIs) , also lead to pneumonia and bronchitis , especially in infants (25).

METHODES

Methodology for this study was conducted between December 2024 - April 2025 . Molecular diagnosis by (RT-PCR) reverse transcriptase – polymerase chain reaction for infants with (respiratory infections) . after enter the central teaching hospital of paediatrics , in Baghdad get approval for taken nasopharyngeal swabs , and recorded date of entry , history , and diagnosed for present of the three viruses that determine for each infants We taken swabs and date for all infants during entry the hospital and observed the history for each patients and diagnosed if present or non present three viruses during first three days and after five days of entry the hospital , also determine clinical feature by the chest x-ray .

In this study divided the patients in four groups before detection the three viruses via taken nasopharyngeal swabs (a) infants infected with hmpv and hopv (b) infants infected with hmpv only (c) infants infected with hmpv and horuv (d) infants infected with three viruses , The age of children under six months hospitalized , during four months collection with a diagnosis of (1) severe (ARTIs) ,(2) severe pneumonia or bronchiolitis ,(3) tachypea(respiratory rate of 50 breaths per minute , 40 breathe per minute in infants > months age , (4) . Chest indrawing and (5) other danger symptoms (headache ,vomiting , unconsciousness or both and other respiratory symptoms).

The study excluded the infants with nosocomial ARTIs and infants with non respiratory distress . the cases subjected for the history (age ,sex ,presenting symptoms , estimated risk factors , course of disease and onset of it .

The data of this study on general and examination locally ,admission radiology and laboratory investigation , that need for oxygen therapy also secondary complication, detection of bacterial coinfections , duration in hospital .

RESULTS

In this study detected 180 infants with severe ARTIs, 105 (58.3%) males and 75(41.7%) were females . higher infections observed with hMOPV, in male **54(51.42%) and29(38.66%)In female ,and with hORUV ,from male** 24 (22.85%) for female ,**29(38.66%) , and lower infected infants with hMPV ,** male 3(2.85%) and female 2 (2.77%) during three days of entry hospital seen in table 1.

Table 1:- Detection of three viruses during the first three days hospitalizations

Sex	**Male**	**female**	df	OR	p-value
total	105 (58.3%)	75(41.7%)			
Infection					
hOPV	**54(51.42%)**	**29(38.66%)**			
hORUV	24 (22.85%)	17 (22.66%)			
hMPV	3(2.85%)	2 (2.77%)			
hOPV@hORUV	24(22.85%)	17 (22.66%)	3	0.609	0.253
hOPV @hMPV	3(2.85%)	2 (2.77%)			
With three viruses	3(3.85%)	2(2.77%)			
%	(100.00%)	(100.00%)			

p > 0.05, so not significant independence of two categorical variables.
Assumptions are satisfied (expected counts > 5 in each cell).

The results of this study after five days of hospitalization infants , determine the higher prevalence of male infection than females in all groups , also the groups infected with two hOPV co with hMPV , 55(52.38%) , 31 (41.33%) and hORUV co with hmpv 15(14.28%), 13(17.33%) and three viruses 22(20.95%) 21(29.16%), which higher severty of infection than group infected with hMPV, only 13(12.38%) , 10 (13.33%)from male and female respectively , in table 2.

Table 2 :- Detection of three viruses after five days of hospitalization

Sex	**Male**	**female**	df	OR	p-value
total	105 (58.3%)	75(41.7%)			
Infection					
hOPV @ hMPV	55(52.38%)	31 (41.33%)			
hORUV @ hMPV	15(14.28%)	13(17.33%)			
Only hMPV	13(12.38%)	10 (13.33%)	3	0.682	0.292
With three viruses	22(20.95%)	21(29.16%)			
%	(100.00%)	(100.00%)			

p > 0.05, so not significant independence of two categorical variables.
Assumptions are satisfied (expected counts > 5 in each cell).

The results for viral research , by used PCR method , detection higher infections and severity of ARTIs in group coinfection of hMPV with hOPV, 86(47.8%) also in group of infants infected with the three viruses (hMPV , hOPV , hORUV) 43 (23.88%), and present 28(15.6%) of hORUV group , while low infection and severity of ARTIs with hMPV infectious group 23(12.8%) . in positive patients,while non negative results detection in all groups shown in table 3 .

Table 3:-The role of Predisposing infection with hOPV and /or hMPV to infection with hMPV after five days of hospitalizations .

	Total	hOPVCoinfected with hMPV	Only infected with hMPV	hORUVCoinfected with hMPV	Infected with 3 viruses
Positive	180	86	23	28	43
%	(100.00. %)	(47.8%)	(12.8%)	(15.6%)	(23.88%)
Negative	0	0	0	0	0
	(100.00. %)	(100.00. %)	(100.00. %)	(100.00. %)	(100.00. %)

The results for determine depended on the chest x- ray that found of each group were categorized and diagnosed that infection with respiratory viruses48(26.66%) in patients infected with bronchiolitis , 95(52.77) in pneumonic patients , 34(18.88%) bronchiolitis and pneumonia and 3(1.66%) in asthma also estimation high infections in group of hopv Coinfected with hmpv and group infected with three viruses rather than group of infants infected with hmpv only observed in table 4.

Table 4:- Clinical features for infants in different group

Features	Total	hOPVCoinfected with hMPV	Only infected with hMPV	hORUV Coinfected with hMPV	Infected with 3 viruses		X2	P-value
Bronchiolitis	48(26.66%)	20(41.66%)	7(14.58%)	7(3.88%)	14 (7.77%)			
Pneumonia	95(52.77)	45(47.36%)	11(11.57%)	17(9.44%)	22(12.22%)			
Asthma	3(1.66%)	1(33.33%)	2(66.66%)	0(0.00%)	0(0.00%)	9	11.44	0.247
Bronchiolitis and Pneumonia	34(18.88%)	20(58.82%)	3(8.82%)	4(2.22%)	7(3.88%)			
%	(100.00%)	(100.00%)	(100.00%)	(100.00%)	(100.00%)			

Interpretation: Since $p > 0.05 \rightarrow$ no significant association between infection category and clinical diagnosis.
In current study observed the higher infection in December 55(30.55%) and January 76(42.22%) rather than February 28(15.55%) and march 21 (11.66%) in table 5.

Table 5:- Duration of infection according to months.

Months	No	hOPV Coinfected with hMPV	Only infected with hMPV	hORUV Coinfected with hMPV	Infected with 3 viruses	df	X2	p-value
December	55(30.55%)	27(49.09%)	9(16.36%)	5(9.09%)	14 (25.45%)			
January	76(42.22%)	40(52.63%)	13(17.10%)	7(9.21%)	16(21.05%)			
February	28(15.55%)	11(39.28%)	7(25.00%)	4(14.28%)	6(21.42%)			
March	21 (11.66%)	8(38.09%)	4(19.04%)	3(14.28%)	6(28.57%)			
%	(100.00%)	(100.00%)	(100.00%)	(100.00%)	(100.00%)	9	3.55	0.939

interpretation: Very high p-value → strong evidence of no difference. Infection categories appear evenly distributed across months.

High severity of infections in male 70(66.66%) and female 45(60.00%)in group Hopv co infection with hmpv, in coinfection of hmpv with horuv observed male 11(11.42%) and female 8(10.66%) , from infants male infected with hmpv only 4(3.80%) and female 6(8.00%) , while infected male with three viruses observed in male 19(18.09%) and 16(21.33%) female table 6 .

Table 6 :- Co- morbidity on admission in infants infected with hMPV , hORUV and hOPV .

	No	hOPV Coinfected with hMPV	Only infected with hMPV	hOURV Coinfected with hMPV	Infected with 3 viruses	df	X2	p-value
Respiratory	70(38.88%)	30(42.86%)	14(20.00%)	7(10.00%)	18(25.71%)			
Previous admission	44(24.44%)	18(40.90)	8(18.18%)	8(18.18%)	10(22.72%)			
Co infection with bacteria	32(17,77%)	15(46.87%)	7(21.87%)	6(18.75%)	4(12.50%)			
Coronary heart disease	28(15.55%)	11(39.28%)	3(10.71)	5(17.85%)	9(32.14%)	12	10.15	0.603
Down-syndrome	6(3.33%)	2(33.33%)	3(50.00%)	0(0.00%)	1(16.66%)			
%	(100.00%)	(100.00%)	(100.00%)	(100.00%)	(100.00%)			

interpretation: $p > 0.05 \rightarrow$ no significant association between risk factors and infection category.

Statistic analysis :- In current study the categories were analysis used a chi -square test , the associated between explanatory variables and outcomes was analysed by used the univariate and then using multivariate logistic regression . The outcomes variables were treated as binary variable according to median value of these variables. The confounding variables the breastfeeding and age were used as variables . Also the variables were analysed as categories . The statistical significance level was set up $p>0.05$ for statical analyses .

DISCUSSION

Acute respiratory infection causes high mortality among infants world wide and the main causes of respiratory difficulties that lead to respiratory failure among the infants under the age of three years (26).in this study detected 180 infants with severe ARTI S, 105 (58.3%) males and females 75(41.7%) .

In current study observed high severity of (ARTIs) in infants for groups (a,c,d) rather than group (b) who infected infants with hmpv , also the number of patients infected in three groups were more than number of patients in group (b) the etiology of ARTIs in infants in three groups rather than group (b) also observed the number of patients infected with hmpv after five days in all groups more than infected during the first three days of hospitalizations , because because the causative agents of the other predisposed viruses this result agreement with Shafik et al. (27).

In acurrent study conducted with Egypt by Shafik et al. that detected the ARTIs in children under 5 years of age infected with respiratory viruses (27) this results conducted with our result that found infected infants under six months of age .

Also our results agreement with the study that observed The proportion of infected infants for ARTIS was similar to the study Cuevas et al that found 48%of children were infection with RSV , the other study seen 17% were infected with (HMPV) (28) .

Also respiratory infection seen in one study which detected from November and in med February , Anther study by McGuiness et, al .(29) Revealed that respiratory viruses season in united states by season on set occurred in October , November of each year rather than march , April of the following year , the same of our results estimated the higher infection in Desamber 2024 55(30.55%)and January 2025 76(42.22%) rathar than other months(February28(15.55%) and march 21(11.66%)) because the cold months in Iraq .Leung etal (30) observed infection in November or December and peak infection in February and end by the end of March .in our study , we non found statisticaly significant differences between months

Papadopoules et al (31) determined that respiratory infections results from infection with more than one virus ,in hospitalized infants , also Hornsleth et al (32) estimated that infected infants with ARTIs depened on tha hospital stay . this a agreement with our result that etological causes of infected infants with hmpv present them in hospital and infected with other viruses horuv an hopv that lead to decrease the immunity and the transmitted for non infected child with this viruses to anther this agreement with Papadopoules et al (31) and Hornsleth et al (32)

(that seen in our results , in infants infected only with hmpv 23 (12.8%) , 86 47.8%) in infants infected with hopv and hmpv , 28(15.6%) in patients infected with horuv and hmpv and 43(23.88%) in infants infected with three viruse) this detected the role of predisposing infection with the other respiratory viruses to infected with hmpv which lead to high severity of ARTIS from infantes ,than other group and seen low the infants infected with hmpv .our results agreement with Legg et al (33) found multiple viruses infected the same infants causes respiratory infection of (7.6%) children . (33)

Also Brouard et al (34) observed that up to (27%)of patients had coinfections , Semple etal found coinfection of RSV with hMPV (35).This studies conducted with our results from frequency of hMPV, infection in infants who dual infected with hORUV ,hOPV ,was due to nosocomial infection.

The clinical feature of all viruses in in this study were largely similar .However bronchitis and pneumonia were frequently observed in infants.

The current study demonstrated the role of infected infants with (hORUV ,hOPV)as importance pathogens for respiratory caused hospitalization of infants that lead to increase suitable to infected with hMPV, causes ARTIs , the causes of severity ARTIs , Can be attributed to decrease of cellular immunity after infection with the respiratory viruses before infect with hMPV, also in reals that lower cellular immunity in infants , the acquired immunity for maternally decrease with half life one month that associated with lower of humeral immunity to h MPV ,in infants exposure to three viral infection . also one causes of severity of ARTIs and infected the same infant with hMPV , recurrent infections are allergies , secondary infection and don't taken vaccine or low effectiveness of vaccinations , recurrent infections refer to repeated of infections caused by same pathogens which may indicate underlying immune deficiencies.

CONCLUSIONS

In our study found hMPV , synergistic with predisposing respiratory viruses infected of same infants in the same time causes a strong sever ARTIs . The prevalence of hMPV , infection in cases with dual viruses (hORUV, hOPV). Several clinical studies are currently investigations the immunopathogenesis of viruses that causes RTIs lead to decrease of immune cells that lead to infection with hMPV , severity of infection with viruses in an infant can be understood to be a function of host response to a virus , to improve our understand of immune response of the host .In this study we must search for multiple viral pathogens and examine the time of infection with the viruses and study sequences for each virus .

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