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Influenza & Respiratory Virus Epidemiological Characteristics among Children in Georgia

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Abstract

Introduction. Influenza and Respiratory Syncytial Virus (RSV) are important causes of severe acute respiratory illnesses among pediatric patients worldwide. The aim of this study was comparison of the epidemiological characteristics of infections associated with RSV and Influenza viruses in hospitalized children in Georgia. The existence of epidemiological data regarding differences between these two major respiratory viral infections could have implications for appropriate management of cases. **Methodology** included retrospective case series study. For this purpose, special questionnaire was elaborated for withdrawal necessary of epidemiological data such as age, sex, residence, hospitalization duration etc. Obtained data were reviewed and analyzed using EPI Info 7.2.5.0. **Results.** Influenza and RSV both viruses can lead to serious respiratory problems especially in young children with chronic diseases. Therefore, timely antiviral treatment and annual Influenza vaccination are recommended to children with underlying conditions to avoid complications and shorten hospitalization time.

Key words: Influenza, Respiratory Syncytial Virus, children care, Georgia.

Quote: Nutsa Piradashvili, Barbare Tabidze. Influenza & Respiratory Virus Epidemiological Characteristics among Children in Georgia. Health Policy, Economics and Sociology, 2023; 7 (1)

გრიპის და რესპირატორული ვირუსის ეპიდემიოლოგიური მახასიათებლები ბავშვებში

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აბსტრაქტი

შესავალი. გრიპი და რესპირატორული სინციტიალური ვირუსი (RSV) არის მძიმე მწვავე რესპირატორული დაავადებების მნიშვნელოვანი მიზეზები პედიატრიულ პაციენტებში მთელ მსოფლიოში. კვლევის მიზანი იყო საქართველოში ჰოსპიტალიზირებულ ბავშვებში რესპირატორული სინციტიალური ვირუსის და გრიპის ვირუსებთან დაკავშირებული ინფექციების ეპიდემიოლოგიური მახასიათებლების შედარება. ამ ორ ძირითად რესპირატორულ ვირუსულ ინფექციას შორის განსხვავებების შესახებ კლინიკური მონაცემების არსებობა შეიძლება გავლენა იქონიოს შემთხვევების სათანადო მართვაზე. **მეთოდოლოგია** მოიცავდა რეტროსპექტულ შემთხვევის სერიას. ამ მიზნით შემუშავდა სპეციალური კითხვარი.

შესწავლილ იქნა ლაბორატორიულად დადასტურებული გრიპის და RSV შემთხვევების 2021-2022 და 2022-2023 წლებში გრიპის სეზონზე ბავშვთა საავადმყოფოში არსებული მონაცემები. მიღებული მონაცემები გაანალიზდა EPI Info 7.2.5.0-ის გამოყენებით. **შედეგები.** გრიპმა და რესპირატორული სინციტიალური ვირუსმა შეიძლება გამოიწვიოს სერიოზული რესპირატორული პრობლემები, განსაკუთრებით ქრონიკული დაავადებების მქონე მცირეწლოვან ბავშვებში. ამიტომ, დროული ანტივირუსული მკურნალობა და ყოველწლიური გრიპის ვაქცინაცია რეკომენდირებულია ძირითადი დაავადების მქონე ბავშვებისთვის გართულებების თავიდან ასაცილებლად და ჰოსპიტალიზაციის დროის შემცირების მიზნით.

საკვანძო სიტყვები: გრიპი, რესპირატორული სინციტიალური ვირუსი, საქართველო.

ციტატა: ნუცა პირადაშვილი, ბარბარე ტაბიძე. გრიპის და რესპირატორული ვირუსის ეპიდემიოლოგიური მახასიათებლები ბავშვებში. ჯანდაცვის პოლიტიკა, ეკონომიკა და სოციოლოგია, 2023; 7 (1)

Introduction

Influenza and Respiratory Syncytial Viruses (RSV) are among the leading Influenza and respiratory syncytial viruses (RSV) are among the leading causes of Lower respiratory tract infections. Influenza virus associated pandemics are described since the end of 19th century while RSV was discovered in late fifties of 20 century (CDC, WHO).

Social distancing and COVID-19 preventive measures implemented by government reflected in circulation of these two major viruses causing hospitalization of children worldwide. According to MDPI (Multidisciplinary Digital Publishing Institute), a research carried out in USA, flu activity had significantly diminished throughout the pandemic while a sudden upsurge in RSV in June 2021 was a public health concern indicative of possible resurgence of other viruses.

As of 2022-2023 season, influenza epidemic is off to an early start in the European region as concerns over RSV rise and Covid-19 is still being a threat (Mondal P. et al, 2022)

In general, a thorough knowledge of influenza and RSV characteristics, epidemiology across age groups and health care settings, and in particular of the spatial and temporal dynamics of their seasonal epidemics, is a pre-requisite for countries to enhance the effectiveness of public health interventions aimed at reducing their disease burden (eg, influenza vaccine, palivizumab (PVZ) prophylaxis, and hospital preparedness and response).

RSV is a globally prevalent virus transmitted via respiratory droplets. Symptoms include runny nose, low appetite, coughing, sneezing, fever, wheezing. In very young infants with RSV, the only symptoms may be irritability, decreased activity, and breathing difficulties. RSV can also cause more severe infections such as bronchiolitis, pneumonia, and other complications that sometimes can be fatal. Diagnosis is done by assessment of patient's history, medical exam, other blood and virus screening tests like can be ordered. Sometimes patients require hospitalization, additional oxygen therapy, IV fluids, and intubation with mechanical ventilation, if they have trouble breathing or are dehydrated. According to CDC, each year in the United States, an estimated 58,000-80,000 children younger than 5 years old are hospitalized due to RSV infection.

There is no vaccine yet to prevent RSV infection, but scientists are working hard to develop one. Infected patients can control temperature at home with medications like Paracetamol, and other antipyretic drugs, before the condition gets severe. Medication called Palivizumab that can help protect some babies at high risk for severe RSV disease, which must be prescribed by a doctor to very premature infants and young children with certain heart and lung conditions as a series of monthly shots during RSV season.

Seasonal influenza is an acute respiratory infection caused by influenza viruses which circulate in all parts of the world. There are 4 types of influenza viruses, types A, B, C and D. Subtype A is known to cause pandemics. Transmitted via respiratory droplets. The incubation period is characteristic and it ranges from one to four days.

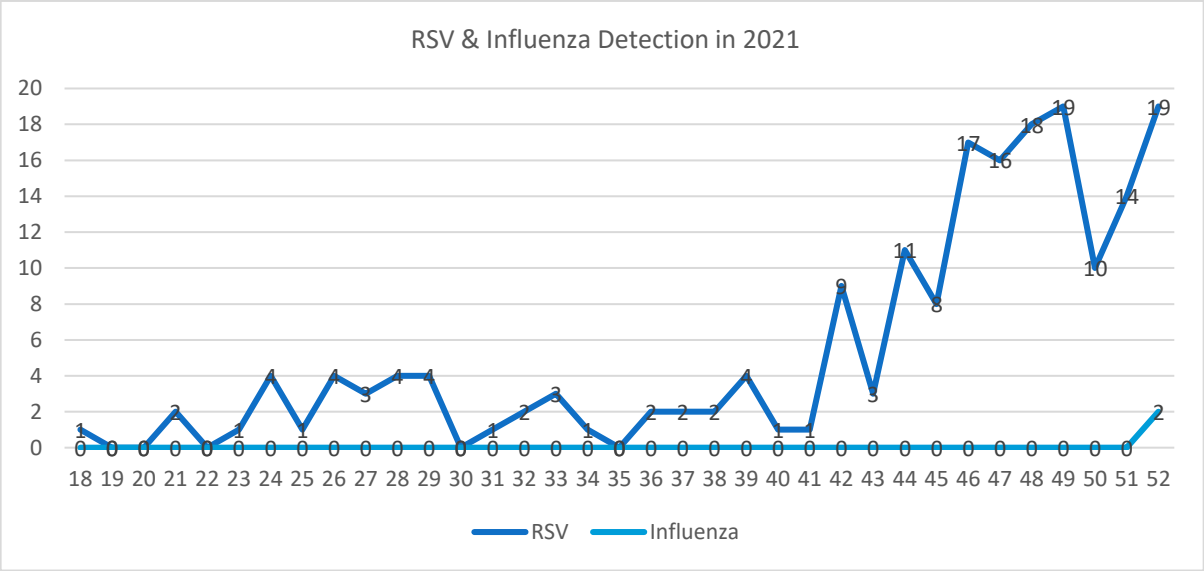
Influenza can cause mild to severe illness. Flu symptoms may include: fever or feeling feverish/chills, cough, sore throat, runny/stuffy nose, muscle/body aches, fatigue, even vomiting and diarrhea may be present, more common in children. Most people who get flu will recover in a few days to less than two weeks, but some people will develop complications, some of which can be life-threatening and result in death. Sinus and ear infections are examples of moderate complications from flu, while pneumonia is a serious one.

Hospitalization and death occur mainly among high risk groups. Diagnosis is made by laboratory confirmation of influenza virus from throat, nasal and nasopharyngeal secretion with PCR, rapid antigen tests. Treatment focuses on relieving symptoms of influenza such as fever with over the counter medications.

Based on above the aim of this study was comparison of the epidemiological characteristics of infections associated to RSV and Influenza viruses in hospitalized children in Georgia.

Methodology

For this study retrospective case series study methodology was used. The data in this study are based on information obtained from Severe Acute Respiratory Infection (SARI) cases collected at Iashvili Children's hospital that serves SARI sentinel site for Georgia since 2009. Specimens were tested at Lugar Center, NCDC. In this study we only analyzed data regarding hospitalized children diagnosed with Influenza



and RSV during 2021 and 2022 at Iashvili Children's hospital. For this purpose, special questionnaire was elaborated for withdrawal of necessary clinical and epidemiological data such as age, sex, underlying clinical conditions, complications, hospitalization duration, need of ICU, antibiotic treatment, vaccination status, outcome etc. Obtained data were reviewed and analyzed using Epi Info 7.2.5.0. Differences between RSV and influenza cases were assessed.

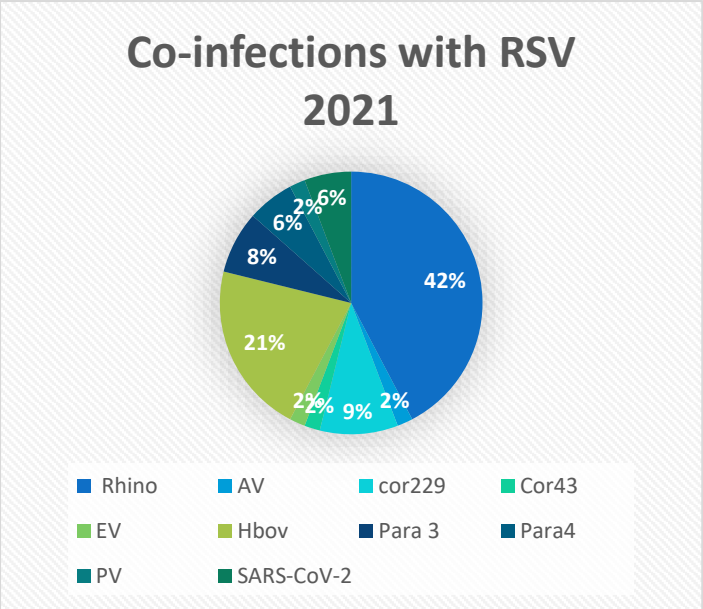
Results

Overall 393 patients tested positive on Influenza and RSV during our study period. For epidemiological review we used total data. For clinical characterization we were able to obtain information regarding 364 cases.

Epidemiological review of 2021

In 2021, of 1102 specimens screened on influenza virus A/H3N2 was detected in three cases only, all children were under age of 5 years. All detections were observed in December, 2021. Out of 1102 samples, a total of 187 (17%) were positive on RSV, among which 45 had co-infections with other respiratory viruses including 3 cases with SARS-CoV-2. RSV mainly predominantly circulated in November and December of 2021 that was slightly early compared to previous pre-pandemic seasons in Georgia.

We found out that in 2021 season, most RSV positive patients had co-infections with other viruses, out of which 41% was RSV with Rhinovirus; 23% with COVID-19 and 18% with Adenovirus. Those three viruses were most common during that period.

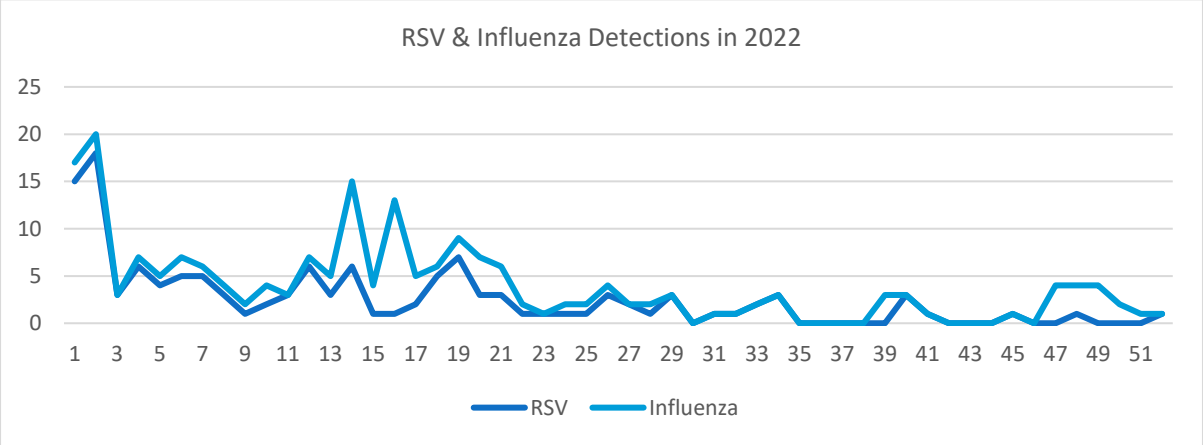


Epidemiological review of 2022

From the year of 2022, out of 832 tested samples 75 were positive on Influenza viruses (1A/H1N1 and 73 A/H3N2). Sporadic detections were observed during cold months in early 2022, majority of positive detections were in late spring and rest of the cases started to be seen from late fall when normally influenza season begins in northern hemisphere countries.

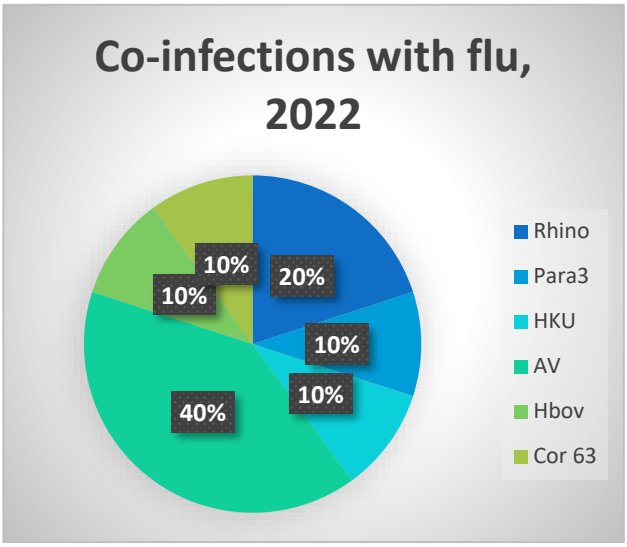
Out of 832 specimens a total of 129 tested positive on RSV, among which 23 had co-infections with other respiratory viruses, including one case of SARS-CoV-2; 3 patients had more than 2 viruses. RSV continued circulation in cold months, then detections were reduced among hospitalized children.

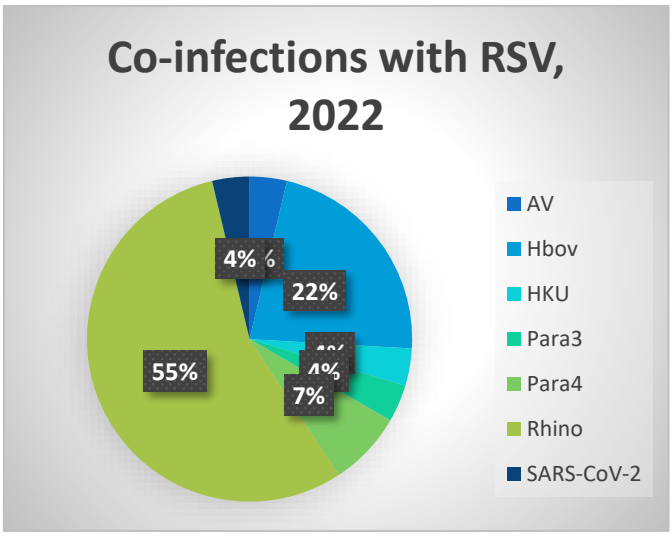
Co-infections of Influenza with other respiratory viruses were registered only in 6 children, 3/6 had more than 3 viruses simultaneously. In both years, 2021 and 2022, Rhinovirus was mostly detected virus among RSV co-infections.

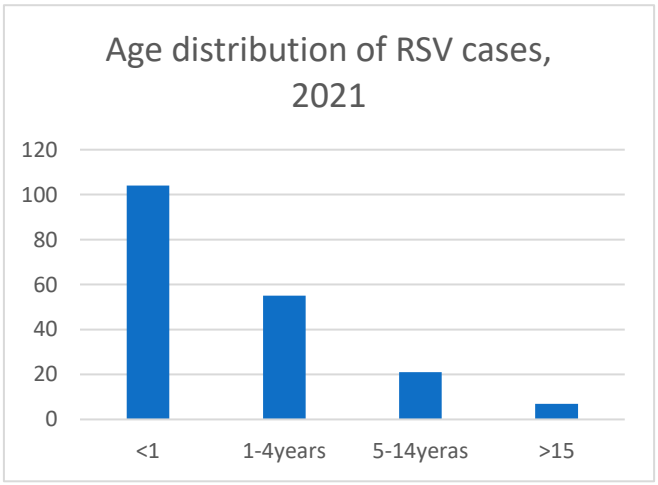


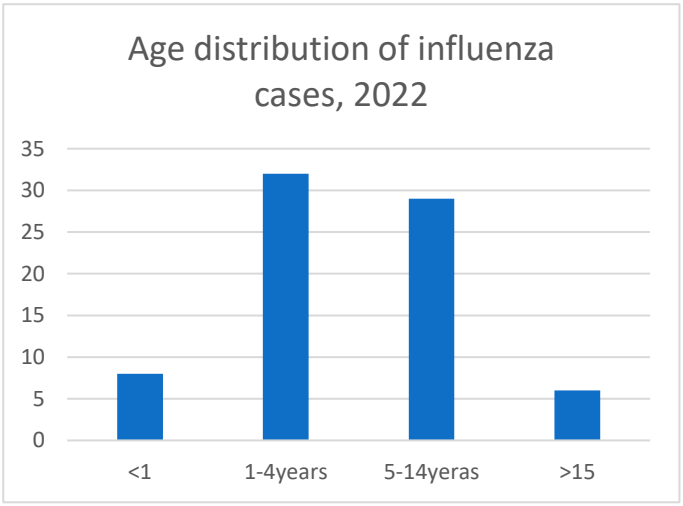
Age group comparison

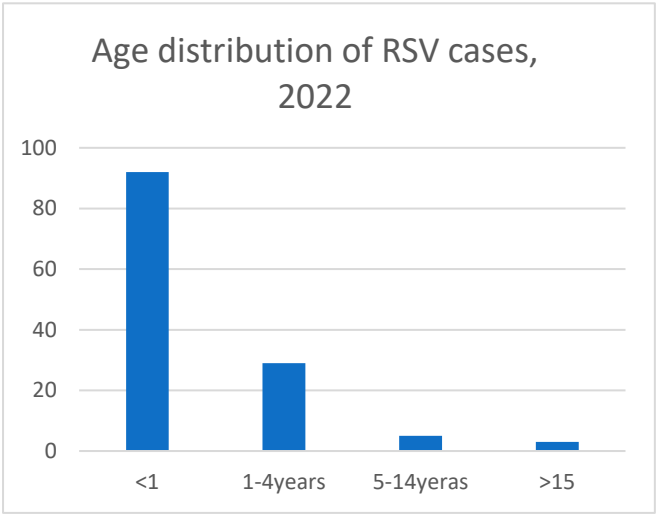
Based on our data, most of RSV detections were related to age group <1 (OR=6, p<0.005) so young children are at higher risk to acquire severe infection associated with this virus compared to influenza.









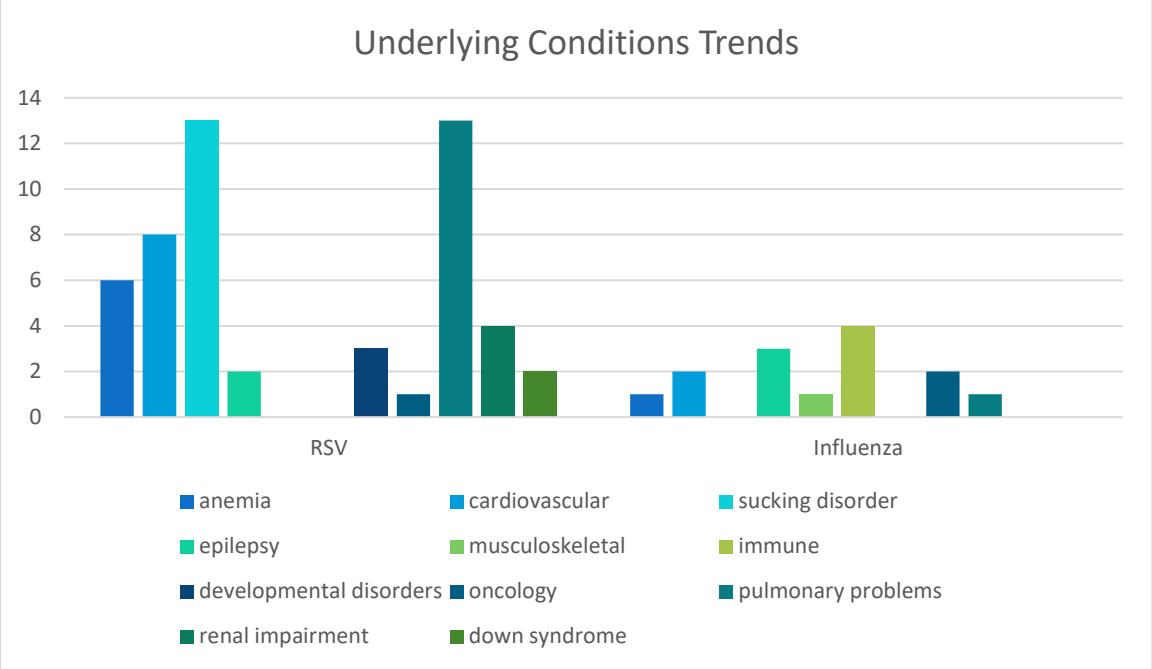


Majority of hospitalizations due to influenza were among young children of age 1-4 years followed by age group 5-14 years.

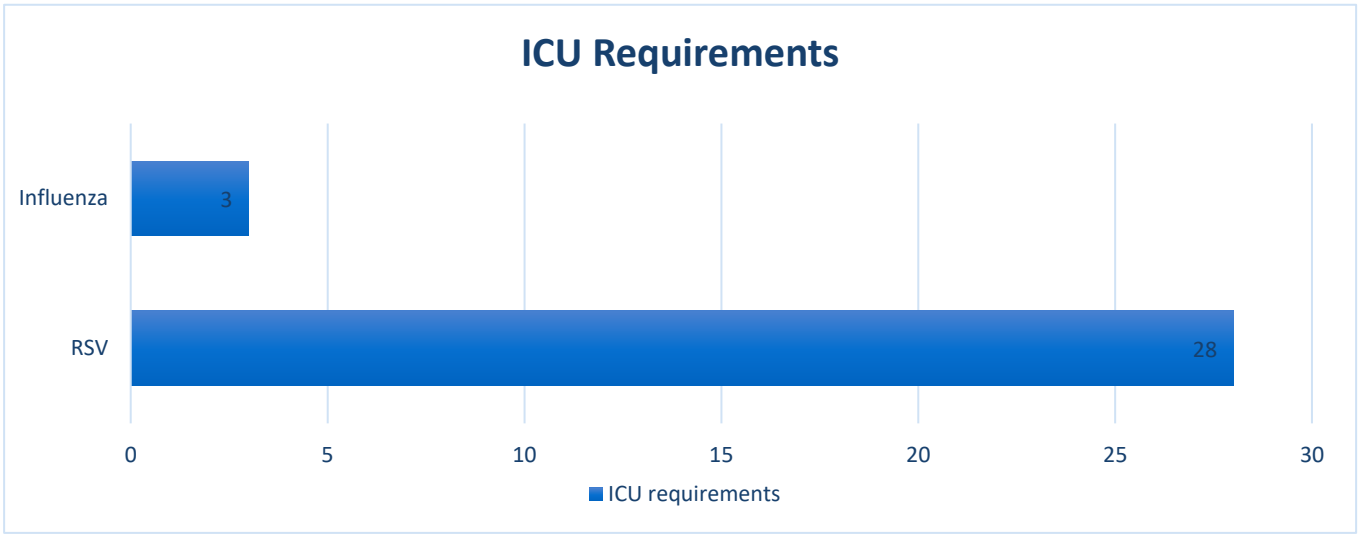
As observed in 2021 most of RSV detections, in 2022, also were among young children under 1 year of age followed by age group 1-4 years.

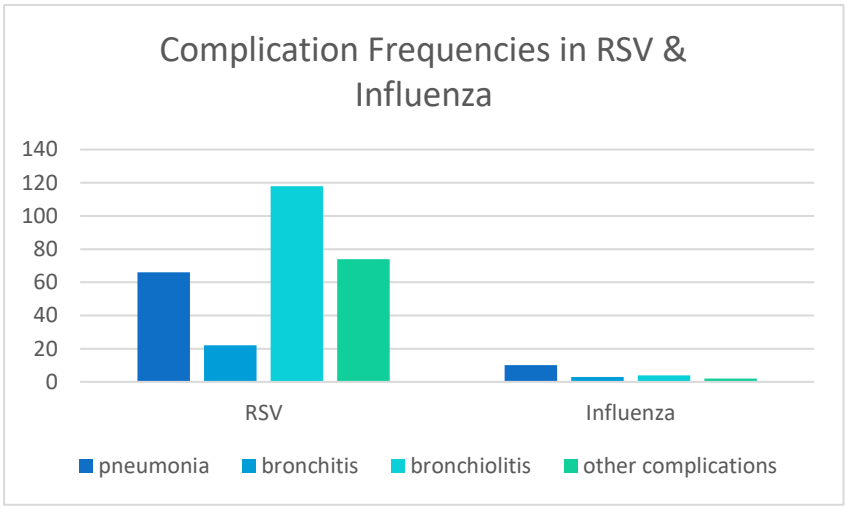
The most common underlying condition in positive RSV infections is seen to be sucking disorder in newborns and pulmonary problems, such as asthma, interstitial lung disease, followed by cardiovascular defects such as

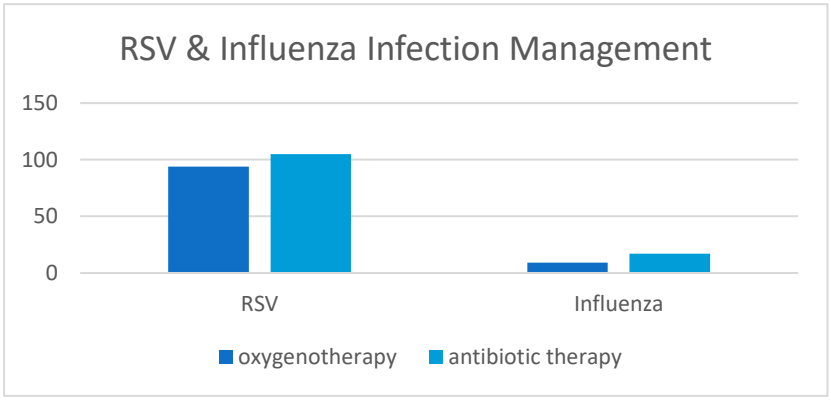
AVSD and ASD. In Influenza cases, immune disorders were the most prevalent, such as Hemolytic-Uremic syndrome

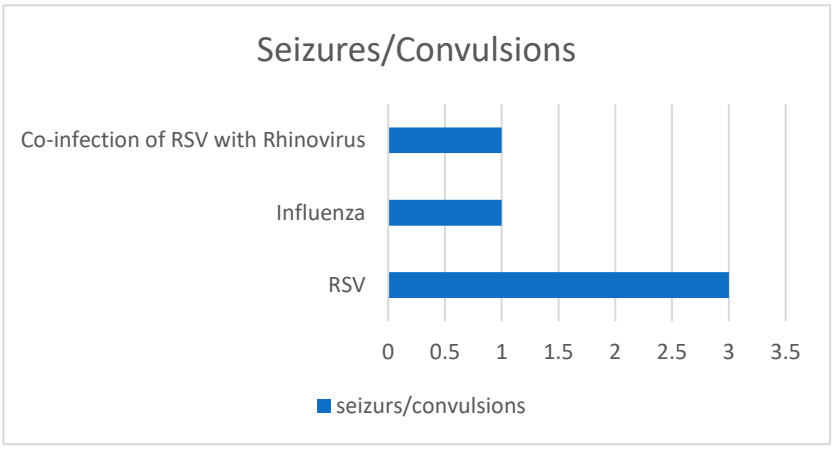


Out of total 77 detected Influenza cases, only 3 of them needed ICU admission, only 1/3 presenting with oncologic underlying condition.
Out of total 313 detected RSV cases, 28 of them needed ICU admission. 1/28 presenting with prematurity, oncologic, hepatic and cardiovascular conditions was reported as deceased.









Multiple complications have been seen in RSV and Influenza Infections. As it is seen, RSV causes higher frequency in complications than influenza. LRTI such as bronchiolitis is the most common in RSV infections, while pneumonia has the highest frequency in Influenza infections.

In RSV infections, antibiotic therapy was much more used than oxygen therapy. The same relativity is shown in regard to the Influenza infections.

Out of 77 positive Influenza patients, seizures/convulsions were present in only one patient, present with epilepsy and cerebral palsy. And out of 313 positive RSV patients, seizures/convulsions were present in 3 cases. 1/3 of the cases had neurologic underlying conditions, including epilepsy, developmental disorder, and renal impairment.

Discussion

In this research, we observed that RSV detection rate was more common than Influenza. During the pandemics those viruses were less noticeable, but after some time when social distancing and other preventive measures were mitigated, RSV cases started to spread.

Non-pharmaceutical interventions targeted at SARS-CoV-2 has presumably affected the activity of other respiratory pathogens. Strong measures implemented by government reflected in circulation of RSV as a noticeable decrease in RSV infections, however new generations without natural immunity to RSV, raised the potential for increased RSV incidence, out-of-season activity. Moreover, we can suppose, that cancellation of different policies to restrict SARS-CoV-2 transmission has let the RSV spread with much less difficulty.

Increased immunogenicity and speed of evolution in minor-group lineages may have contributed to the very large number of Rhinovirus serotypes and co-infections with influenza and RSV.

In the first weeks of the year of 2022, number of detections of both viruses were high, but it didn't last long. Majority of positive detections were in late spring and rest of the cases were seen from late fall.

As for coinfections, Rhinovirus was still a leading co-infection with RSV. However, in Influenza detections, the most frequent co-infection was with Adenovirus. Half of the co-infections detected involved more than 2 viruses.

Based on our data, we differentiated age groups which were more affected by RSV and Influenza viruses. Based on our data, most of RSV detections were related to age group <1 in 2021 as well as in 2022, followed by age group 1-4 years.

As for the Influenza distribution, majority of patients were of age 1-4 years, followed by age group 5-14 years and this result could be explained by the fact that children of those age group are more active due to their lifestyle, such as going to kindergarten, having close contact with many children of their age.

Overall children aged < 1 were at higher risk so to acquire severe infection associated with RSV compared to influenza.

As for clinical review of the total data, hospitalization ranges were nearly equal. But these durations are exceptions since they have appeared to be caused not directly by the viral infections, but other conditions, such as prematurity.

It's natural to presume that hospitalization duration was not only based on patient's virus type but also on underlying conditions and complications. Patients who were infected with only one virus had relatively lower hospitalization duration.

The most common underlying condition is reported to be sucking disorder in newborns and pulmonary problems such as asthma, interstitial lung disease, followed by cardiovascular defects such as AVSD and ASD. In influenza infections, immune system impairment was the most frequent underlying complication, e.g. HUS.

The viral infection has a nonsignificant role in the death of the said patient, since the report showed multiple much more serious problems, which actually determined the circumstances.

As the reports have shown, RSV causes higher frequency in complications overall than Influenza. LRTI such as bronchiolitis is the most common in RSV infections, while pneumonia has the highest frequency in Influenza cases.

In RSV reports, antibiotic therapy and oxygen therapy was used more than in Influenza infections, presumably due to the ability of the virus to cause much more severe illness.

According to MDPI (Multidisciplinary Digital Publishing Institute), RSV was studied as an uncommon cause of Febrile Seizures. Although RSV is often associated with high risk of neurological complications, less cases of FS were reported than in SIV infections (Ricco M. et al, 2022).

During the research, only 4 medical forms were discovered holding the information about the vaccination status against Influenza. None of the vaccinated cases required ICU admission, ¾ cases were <5 years old, presented with bronchiolitis, with no further complications.

Our study had several limitations which could influence the results of analyses performed: False negative laboratory results may have been obtained due to the late referral of patients to clinics; since we only analyzed one hospital data it might not reflect other pediatric patients; medical record are filled by different physicians so there might be incomplete data or recall bias from patient's or parent's side regarding clinical symptoms or underlying condition.

Literature Review

Multiple creditable researches have been carried out regarding the same or similar issues.

According to Frontier original research article, the outbreak of coronavirus disease 2019 (COVID-19) was reported to bring changes to the transmission pattern of respiratory pathogens including RSV. Virus usually peaked in winter and declined by early spring in China (Jia R. et al, 2022). In their study, they observed an unusual increase of the RSV detection rate in the summer of 2021 in Shanghai. Interestingly, the abnormal reemergence of RSV during COVID-19 was also observed during the summer months in both northern hemisphere countries including Japan, America, Canada, Israel, Italy, and southern hemisphere countries

including Australia and New Zealand. Continuous surveillance of RSV infection at both local and global scales is needed to provide more clues to explain the phenomenon.

Non-pharmaceutical interventions targeted at SARS-CoV-2 have affected the activity of other respiratory pathogens. In another study of medical journal Lancet, researchers describe changes in the epidemiology of RSV among children younger than 5 years in England since 2020 (Bradsley M. et al, 2022). The extraordinary absence of RSV during winter 2020–21 probably resulted in a cohort of young children without natural immunity to RSV, thereby raising the potential for increased RSV incidence, out-of-season activity, and health-service pressures when measures to restrict SARS-CoV-2 transmission were relaxed.

As for epidemiological characteristics of influenza, according to CDC, the effects of seasonal influenza epidemics in developing countries are not fully known, but research estimates that 99% of deaths in children under 5 years of age with influenza related lower respiratory tract infections are found in developing countries.

During periods of low influenza activity, the infection of other respiratory viruses e.g. rhinovirus, respiratory syncytial virus, and others can also present as Influenza-like Illness (ILI) which makes the clinical differentiation of influenza from other pathogens difficult. Worldwide, annual epidemics of influenza are estimated to result in about 3 to 5 million cases of severe illness, and about 290 000 to 650 000 respiratory deaths. (WHO)

According to journal of Global Health, a comparative analysis of the epidemiology of influenza and respiratory syncytial virus was carried out in Russia, from time periods of 2013/14 to 2018/19 years. As a result, the overall positivity rate was 13.5% for influenza and 4.4% for RSV. The median age was older among influenza (15 years) than among RSV patients (3 years); Influenza and RSV epidemiology differed in many regards in Russia, especially in the timing of epidemics and the age distribution of infected subjects (Caini S. et al, 2022).

To compare the frequency and the severity of influenza and RSV infections among children < 24 months hospitalized with respiratory symptoms, researchers analyzed data from prospective study during the peak of five influenza seasons in province of Quebec, Canada. They detected higher frequency of RSV compared to influenza viruses (55.3% vs. 16.3%). Radiologically confirmed pneumonia was significantly more frequent in children with RSV (39%) than those with influenza (18%) and the clinical course was more severe in RSV than influenza-infected children, especially among infants < 3 months. Even during peak weeks of influenza season, a higher burden and severity of RSV was found compared with influenza virus disease in hospitalized children < 24 months (Amini R. et al, 2019).

Apart from pediatric patients and individual virus infections, we tried to search for relatable issues. According to Elsevier Journal, a retrospective study analyzed adult patients with acute respiratory infection from January 2017 to June 2019 in China-Japan Friendship Hospital in Beijing, China. Coinfection of Flu/RSV in adults is associated with a high adverse outcome. Compared to flu-only infected and RSV-only infected patients, both rates of intensive care unit admission and use of invasive mechanical ventilation in flu/RSV coinfected patients were higher. Thus, such coinfections should be increasingly appreciated (Zhang Y. et al, 2020).

Another retrospective cohort study of comparative analysis between RSV and Influenza in admitted children under 2-years-old, carried out in 2023 April, in USA, RSV admissions were associated with a higher risk for a complex hospital course and required higher rates of respiratory support than influenza admissions (Tang M K. et al, 2023).

Conclusion

Seasonal Influenza vaccines are available in Georgia. Routine immunization is recommended for all persons aged 6 months and older. WHO and CDC recommends annual vaccination to pregnant women, children aged between 6 months to 5 years, elderly, individuals with chronic medical conditions, health-care workers. Even when flu vaccination does not prevent illness entirely, it has been shown in several studies to reduce severity of illness.

CDC estimates that from the 2010-2011 season to the 2019-2020 season, among reported flu-related deaths in children, about 80% occurred in children who were not fully vaccinated. Also, even though each flu death in a child is supposed to be reported to CDC, it is likely that not all flu-related deaths in children are captured and that the actual number of deaths is higher. Multiple RSV vaccines are in development to try to counter this challenge using a variety of traditional and new technologies. The approaches used need to be tailored to each population owing to differences in risk factors for severe disease and immunological factors that vary among populations. Although the road has been long, we are now entering an era where an RSV vaccine is likely to become available that could revolutionize pediatric and older adult medicine.

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