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## Children were less frequently infected with SARS-CoV-2 than adults during 2020 COVID-19 pandemic in Warsaw, Poland

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3 **Children were less frequently infected with SARS-CoV-2 than adults**  
4 **during 2020 COVID-19 pandemic in Warsaw, Poland**

5

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34

## 35 **Abstract**

36 *Purpose:* Clinical data suggest that during the current COVID-19 pandemic children are less  
37 prone than adults to SARS-CoV-2 infection. Our purpose was to determine the frequency of  
38 SARS-CoV-2 in children vs. adults during the 2020 pandemic in Warsaw, Poland and to  
39 investigate whether RSV and/or influenza A/B infections were associated with SARS-CoV-2  
40 infections.

41 *Methods:* We present results of RT-PCR tests for SARS-CoV-2 performed in Warsaw,  
42 Poland. Some of the pediatric subjects were also PCR-tested for RSV, and A and B influenza.  
43 We compared the test results from the four groups of symptomatic and asymptomatic  
44 subjects: 459 symptomatic pediatric patients (children 0-18 years old), 1774 symptomatic  
45 adults, 445 asymptomatic children, and 239 asymptomatic adults.

46 *Results:* 3.26% (15/459) of symptomatic pediatric patients were positive for SARS-CoV-2 in  
47 contrast to 5.58% (99/1774) of symptomatic adults ( $p=0.0448$ ). There were no SARS-CoV-2  
48 positive cases in the group of asymptomatic children (0/445) and two positive cases in the  
49 group of asymptomatic adults (2/239), i.e. 0.83%. In the group of symptomatic pediatric  
50 patients 17.14% (6/35) ( $p=0.0002$ ) were positive for RSV, 8.16% (4/49) were positive for  
51 influenza A, and 2.04% (1/49), thus 10.20% (5/49) ( $p=0.0176$ ) for influenza A/B.

52 *Conclusion:* Children were less prone to SARS-CoV-2 infection than the adults during the  
53 COVID-19 pandemic in Warsaw. Higher percentage of symptomatic children was infected  
54 with RSV or influenza A/B than with SARS-CoV-2. This suggests a necessity for the testing  
55 for all these viruses for an early identification and isolation of SARS-CoV-2-positive patients  
56 for an ensuing 2020 autumn return of COVID-19.

57  
58 **Key words:** COVID-19, SARS-CoV-2, 2020 pandemic, pediatric patients

## 60 **Introduction**

61 Severe Acute Respiratory Syndrome coronavirus-2 or SARS-CoV-2 emerged in Wuhan in  
62 Hubei province in China in December 2019 and rapidly had propagated all over the world  
63 causing the COVID-19 pandemic, declared by WHO on March 11 (WHO Director-General's  
64 opening remarks at the media briefing on COVID-19 - 11 March 2020;  
65 [https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-  
66 media-briefing-on-covid-19---11-march-2020](https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020)). The pandemic and number of cases are still  
67 unfolding in many countries while we report this data. In Poland, the first case was reported  
68 on March 4<sup>th</sup>, 2020. During the first two weeks of the epidemic, the whole Masovia area,  
69 including the Polish capital, Warsaw, became one of the major infected areas in Poland, with  
70 3581 cases by 1<sup>st</sup> June 2020.

71 There is a growing body of evidence from different countries with COVID-19 pandemic that  
72 children are less frequently infected with SARS-CoV-2. Children are mostly asymptomatic or  
73 experience much milder symptoms than the adults (Balasubramanian et al., 2020; Cristiani et  
74 al., 2020; Dong et al., 2020; Jiatong et al., 2020; Lee et al., 2020; Marraro and Spada, 2020  
75 Morand et al., 2020; Zimmermann and Curtis, 2020), although a low percentage of the

76 infected children developed the pediatric multi-system inflammatory syndrome (Viner and  
77 Whittaker, 2020). Severe (2-3%) or critical illness (0.61%) have been reported in pediatric  
78 patients analyzed in two systematic reviews and meta-analysis of data from several countries  
79 (Liguoro et al., 2020; Dhir et al., 2020). The purpose of our study was to establish if a lower  
80 frequency of infection, and lesser severity in children were also true for the 2020 COVID-19  
81 pandemic in Warsaw, Poland.

82

## 83 **Material and Methods**

### 84 *Patients*

85 Analyses were performed on two main groups of patients: children – from 1 month to 18  
86 years old, and adults – over 18 years old. Patients from two Warsaw hospitals were enrolled:  
87 the Pediatric Teaching Clinical Hospital of Medical University of Warsaw and the Hospital  
88 for Infectious Diseases (Warsaw, Poland). Each of these two groups was divided into two  
89 subgroups: symptomatic (separately children and adults) and asymptomatic (separately  
90 children and adults). Patients presenting with fever, respiratory tract infection syndromes,  
91 gastrointestinal symptoms, dyspnea, cough, chest pain, and seizures were included in the  
92 symptomatic groups. Two asymptomatic groups were: 1. asymptomatic children who  
93 underwent screening for SARS-CoV-2 at the admission for planned hospitalisation unrelated  
94 to COVID-19, 2. asymptomatic legal guardians of the asymptomatic children and medical  
95 staff involved in contact tracing.

96

### 97 *SARS-CoV-2 analysis*

98 Throat or nasopharynx swabs were obtained from the symptomatic and asymptomatic  
99 subjects. Immediately after collection, the swabs were placed in viral preservation medium,  
100 transported to laboratory in temperature 2-8°C and stored in such conditions until processing.  
101 Total RNA was extracted from 140 µl specimen with manual centrifuge column isolation kit  
102 (Viral RNA Isolation Kit, ZJ Bio-Tech C, China) according to manufacturer's instruction.  
103 Extraction volume of 60 µl was obtained for each sample. A 5 µl aliquot of RNA was used  
104 for real-time RT-PCR, which targeted simultaneously 3 genes specific for SARS-CoV-2: gene  
105 E, N, and ORF1ab (Liferiver Novel Coronavirus (2019-nCoV) Real Time Multiplex RT-PCR  
106 Kit, Shanghai ZJ Bio-Tech C, Shanghai, China). Real time PCR was performed upon  
107 CFX96™ Real-Time PCR Detection System (Bio-Rad, USA). The specificity of the test is  
108 98.1 %, analytical sensitivity  $1 \times 10^3$  copies/ml. The protocol was performed according  
109 manufacturer's instruction. Real-time RT-PCR was performed under the following  
110 conditions: 45°C for 10 min and 95°C for 15 min, followed by 45 cycles of amplification at  
111 95°C for 15 sec and 60°C for 1 min. Criteria for judging results: CT value < 43 positive; 43 ≤  
112 CT value ≤ 45 suspicious positive and ≥ 45 negative. The positive should meet for all 3 genes  
113 tested. Internal control was added into extraction mixture on isolation stage to monitor the  
114 whole process. Positive and negative control was included in each run of amplification.

115

### 116 *RSV and Influenza A/B analysis*

117 Selected samples of pediatric symptomatic patients were also tested for the presence of RSV  
118 and Influenza A/B virus with qualitative real-time PCR test Xpert® Xpress Flu/RSV  
119 (Cepheid, USA). 35 patients were tested for RSV and 49 patients for influenza A and B.

120 Nasopharyngeal specimen were collected from selected paediatric symptomatic patients.  
121 After collection the swab were placed in universal transport medium (UTM, Copan  
122 Diagnostics). The samples were tested immediately after collection with qualitative real-time  
123 PCR test Xpert® Xpress Flu/RSV (Cepheid, USA) according manufacturer's instruction on  
124 GeneXpert I apparatus. The volume of 300 µl was transferred to the cartridge. Isolation and  
125 amplification stage was done automatically by the instrument. Each test was equipped in  
126 internal control which monitored whole process. External positive and negative controls were  
127 tested with each new applied lot of Xpert Xpress Flu/RSV. The RT-PCR test targets few  
128 genes of examined viruses: genes encoding matrix protein, PB2 and PA for Flu A, genes  
129 encoding matrix protein and non-structural protein for fly B, genes encoding nucleocapsid of  
130 RSV A and RSV B. Sensitivity of the test is estimated on 99%, specificity on 98%.  
131 Results were presented as the percentage of all patients in the given group.

### 132 *Statistical analysis*

133 The data from the adults and children, as well as RSV positive, and influenza A and B  
134 positive cases within the selected samples in the symptomatic children group, were analyzed  
135 by Chi-square test. The P-value <0.05 was considered as statistically significant. We also  
136 analyzed data using the Fisher test.

137

## 138 **Results**

139 SARS-CoV-2 RT-PCR tests were performed in two centers in Warsaw, Poland, during 3  
140 months between March and May 2020, which corresponded to the first three months of  
141 COVID-19 epidemics in Poland. Patients were divided into four groups.

- 142 1. symptomatic pediatric patients (n = 459),
- 143 2. symptomatic adult patients (n = 1774),
- 144 3. asymptomatic children (n = 445),
- 145 4. asymptomatic adults (n = 239).

146 The age strata in each group are showed in Suppl. Materials 1 section.

147 The tests showed 3.26% (15/459) positive cases among the symptomatic pediatric patients,  
148 5.58% (99/1774) among the symptomatic adults, none in the the asymptomatic children  
149 (0/445), and 0.83% (2/239) in the asymptomatic adults.

150 The statistical analysis performed with the chi-square test has shown significantly (p=0.0448)  
151 lower incidence of SARS-CoV-2 infection in the symptomatic pediatric population than in the  
152 symptomatic adults. This trend was also observed in the asymptomatic groups, however the  
153 result was not stiatistically significant (p=0.0533) (Fig. 1). The Fisher test analysis gave  
154 similar results (Fig. 1 Suppl. Materials).

155 The age of 15 positive paediatric symptomatic patients, uniformly covering the whole period  
156 between 0.6 and 14.1 years of age, was as follows: 0.6; 0.6; 0.8; 1.0; 1.8; 4.2; 5.0; 7.3; 9.8;  
157 10.0; 11.0; 11.3; 13.0; 14.0 and 14.1 years.

158 The analysis of the symptomatic non-SARS-CoV-2 patients showed that 17.14% (6/35)  
159 (p=0.0002) of children were positive for RSV, 8.16% (4/49) for influenza A, and 2.04%

160 (1/49) for influenza B; thus 10.20% (5/49) ( $p=0.0176$ ) were positive for A and B influenza  
161 together (the same 49 patients were tested for influenza A and B). These data were also  
162 analyzed using two statistical tests: chi-square (Fig. 2) and the Fisher test (Fig. 2 Suppl.  
163 Materials). In other words, 17.14% of pediatric patients negative for SARS-CoV-2 were  
164 positive for RSV, and 10.20% for influenza A/B. Thus, statistically significantly higher  
165 number of pediatric symptomatic patients were positive for either RSV or influenza A/B than  
166 for SARS-CoV-2. There was also a single pediatric case of pertussis (whooping cough)  
167 diagnosed based on the clinical symptoms. These data show that during the first three months  
168 (March-May 2020) of the COVID-19 pandemic in Warsaw, Poland, significantly less  
169 pediatric patients were infected with SARS-CoV-2 than RSV and influenza together. Thus,  
170 children were more likely to be infected with RSV or influenza A/B than with SARS-CoV-2.

171

## 172 **Disussion**

173 Our study showed that children presenting symptoms suggestive of COVID-19 and requiring  
174 hospitalisation or an emergency assessment, had significantly lower SARS-CoV-2 infection  
175 than hospitalised adults. This data are consistent with the previous studies from different  
176 countries during the 2020 COVID-19 pandemic. Asymptomatic, mild, and moderate  
177 symptoms were observed in more than 90% of all COVID-19 positive children, severe and  
178 critical cases were observed in 5.9% of children in comparison to 18.5% in adults (Dong et  
179 al., 2020). Cristiani et al. (2020) report that among the total number of 44,672 positive cases,  
180 the Chinese Centre of Disease Control and Prevention report showed only 416 pediatric cases  
181 in 0–9 years age group (0.9%) with no fatalities and 549 cases in 10–19 years age group  
182 (1.2%) with 1 fatality (0.2%). Brodin (2020) reports Korean data showing that 6.3% of all  
183 positive cases were children under 19 years of age. (reviewed also by Balasubramanian et al.,  
184 2020; Jiatong et al., 2020; Lee et al., 2020; Marraro and Spada, 2020; Morand et al., 2020;  
185 Zimmermann and Curtis, 2020).

186 Interestingly, SARS-CoV-1 infection rate during 2002-2003 epidemic had shown similar  
187 characteristics regarding children vs. adults in China, and other countries (Cao et al., 2020;  
188 Dong et al., 2020; Sørensen et al., 2006; Stockman et al., 2007; Zhao et al., 2006). Therefore,  
189 it seems that children are more resistant to both SARS-CoV-1 and SARS-CoV-2 infection.

190 There are several factors that might explain this phenomenon. First of all, children, because  
191 the milder symptoms of SARS-CoV-2 infection are tested less frequently than the adults.  
192 There may be also an input from the environmental/social factors. Children may be better  
193 protected and sheltered against the virus during the pandemic than the adults, and the rate of  
194 children infection may be influenced by the quality of the parental care (Zimmermann and  
195 Curtis, 2020).

196 Alternatively, some endogenous factors may play a role. They may include a different age-  
197 dependent expression and/or distribution of ACE2 receptor for SARS-CoV-1 and SARS-  
198 CoV-2 (suggested by Li et al., 2003; Lovren et al., 2008; Tai et al., 2020; Tipnis et al., 2000;  
199 Walls et al., 2020; Wysocki et al., 2010; Brodin, 2020; Miri et al., 2020; Xu et al., 2020).  
200 Indeed, a lower level of ACE2 expression in the nasal epithelial cells of children, especially  
201 the youngest children, was confirmed by a recent study of Bunyavanich (2020) suggesting

202 that this can be a reason for a lower infectability of children with SARS viruses. Nevertheless,  
203 the data about the impact of ACE2 expression pattern are still fragmentary.

204 One of the reasons for the severity of the COVID-19 is the over-reactivity of the immune  
205 response in the lungs, where the alveolar macrophages induce the cytokine storm (Merad and  
206 Martin 2020). In children, the immune system is immature (Kloc et al., 2020), thus aggressive  
207 cytokine response is rarely seen (Simon et al., 2015) resulting in milder COVID-19  
208 symptoms. The severity of COVID-19 in children was recently reviewed by two meta-analyses  
209 (Liguoro et al., 2020; Dhir et al., 2020). Even though the reviews had large cohorts (7480,  
210 4857 patients), the severity of illness was described only in 20-34% of all patients (1475 and  
211 1666 respectively). In the review by Liguoro et al. (2020), 12% of neonates were severely ill.  
212 In the second review, neonates were not included in the study. The estimated reported  
213 mortality in these two studies was 0.08% and 0.1% of analyzed patients. Higher morbidity  
214 and mortality ratios were described by the ptbnet COVID-19 study Group who collected data  
215 from 25 European countries during the peak of the pandemic in Europe in April 2020  
216 (Gotzinger et al., 2020). Out of 582 patients, 8% required ICU admission, and 4% required  
217 mechanical ventilation. The case fatality rate was 0.69%, and age younger than 1 month, male  
218 sex, signs or symptoms of lower respiratory tract infections at presentation, and the presence  
219 of pre-existing medical conditions were associated with ICU admission.

220 Another plausible explanation might be that the children who attend day-care, kindergarten,  
221 and school and are frequently exposed to the respiratory viruses, develop some basal level of  
222 the antibodies, which give cross protection against SARS-CoV-2 (Schuez-Havupalo et al.,  
223 2020).

224 In the case of newborns, and very young babies, a part of explanation can be that they are  
225 protected either by antibodies transferred during pregnancy through the placenta from mother  
226 (Jackson and Nazar, 2006; Palmeira et al., 2011, Brodin, 2020). or the compounds, such as  
227 the Lactoferrin, a globular glycoprotein present in the breast milk that have the antimicrobial  
228 and immunomodulatory roles in protecting the newborn from the various infections (Telang  
229 2018), including the necrotizing enterocolitis (Sherman, 2013) and SARS (Lang et al., 2011).

230 A plausible hypothesis for a lower number of positive cases among children is that a high  
231 percentage of them might have been protected by the cross-immunity conferred by infections  
232 with other viruses including human coronaviruses (e.g. Brodin, 2020). Also, the vaccination  
233 against other infectious diseases may stimulate the cross-immunity. The young patients were  
234 probably better protected because of freshly acquired immune memory (Miri et al., 2020). Of  
235 special interest can be the so-called trained immunity caused by vaccinations with live  
236 viruses, such as OPV, anti-measles vaccine, or mycobacteria, including BCG (Netea et al.,  
237 2020; Chumakov et al., 2020). Moreover, the authors also hypothesized that if SARS-CoV-2  
238 will mutate, and the specific vaccine will be weak or ineffective, the OPV may be the only  
239 real solution in the future (Chumakov et al., 2020). In this case, again, recent vaccination  
240 might give a better protective effect.

241 Interestingly, the PCR tests of children included in our study showed that, within the first  
242 three months of the COVID-19 pandemic in Warsaw, the children had significantly higher  
243 risk for RSV or influenza A/B than for SARS-CoV-2 infection. If this bias toward RSV and  
244 influenza A/B infection persists for the next seasonal peak of flu, and respiratory infections,  
245 the physicians in Masovia area should keep in mind that the common flu/respiratory infections

246 are much more frequent than COVID-19. However taking into account the risk of spreading  
247 COVID-19, authorities should perform a routine broad testing for all these viruses. The data  
248 from many countries show that an early detection of SARS-CoV-2 infection is one of the  
249 most effective strategies of pandemic control.

250 In addition, our study did not show any case of the co-infection between SARS-CoV-2  
251 and other viruses tested, or between RSV and Influenza A/B. Reina and Dueñas (2019) showed  
252 that the RSV and influenza co-infection occurred in 4.8% of the total studied RSV cases. It is  
253 possible that the limited number of pediatric patients, which were tested for RSV and Influenza  
254 A/B in our study is responsible for this discrepancy. In contrast, some studies have reported the  
255 presence of coinfections with SARS-CoV-2 and other respiratory tract pathogens, both in  
256 children and adults. In most cases studied, the researchers have reported coinfection with others  
257 than SARS-CoV-2 coronaviruses (HKU1, NL63, 229E, OC43), influenza, and parainfluenza  
258 viruses, RSV, rhinoviruses-enteroviruses, human metapneumoviruses, adenoviruses, and  
259 *Mycoplasma pneumoniae*. Nevertheless, the coinfection rates were low and ranged between  
260 0.1% - 3%, and the studies did not clearly assess whether they influenced the course of infection  
261 with SARS-CoV-2 or not. In general, the clinical course was mild, ending with full recovery  
262 (Nowak et al., 2020; Wee et al., 2020; Blasco et al., 2019).

263 We want to emphasize some limitations of our study. First, the number of examined patients  
264 was not very high. We wanted to present our results as quickly as possible to spread the  
265 information included in this article before the onset of the expected autumn/winter wave of  
266 the pandemic, and for this reason, we have chosen to describe the results of the first 3 months  
267 of the pandemic. It allows to draw conclusions, but further studies should be performed to  
268 verify whether the observed percentage of children vs. adults infections are similar during  
269 the whole period of the pandemic period without the anti-SARS-CoV-2 vaccination.

## 270 **Conclusions**

271 The results of our study are consistent with the previous data showing that SARS-CoV-2  
272 infection in children occurs less often than in the adults. Routine testing for SARS-CoV-2 is  
273 crucial for the control of the pandemic, and discerning between COVID-19 and common  
274 seasonal respiratory infections.

275

276

## 277 **Declarations:**

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## 281 **Conflicts of interest/Competing interests**

282 The authors declare no conflict of interest.

## 283 **Availability of data and material**

284 All data and material is freely available.



285 **Ethical Approval**

286 No ethical approval was obtained because this study did not involve a clinical  
287 evaluation, did not involve laboratory animals and invasive procedures.

288 **Authors` contributions**

289 EK, AL, SL, MK and JZK designed the study. AZ, MW, DK performed tests, MK and JZK  
290 wrote the manuscript, EK, AZ, MW, DK, EP, KB, AL, SL, CK, AH and JZK analysed  
291 results, AL and SL performed the statistical analysis, EK, AZ, MW, DK, EP, AL, SL, CK,  
292 AH, MK and JZK edited the manuscript.

293

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297

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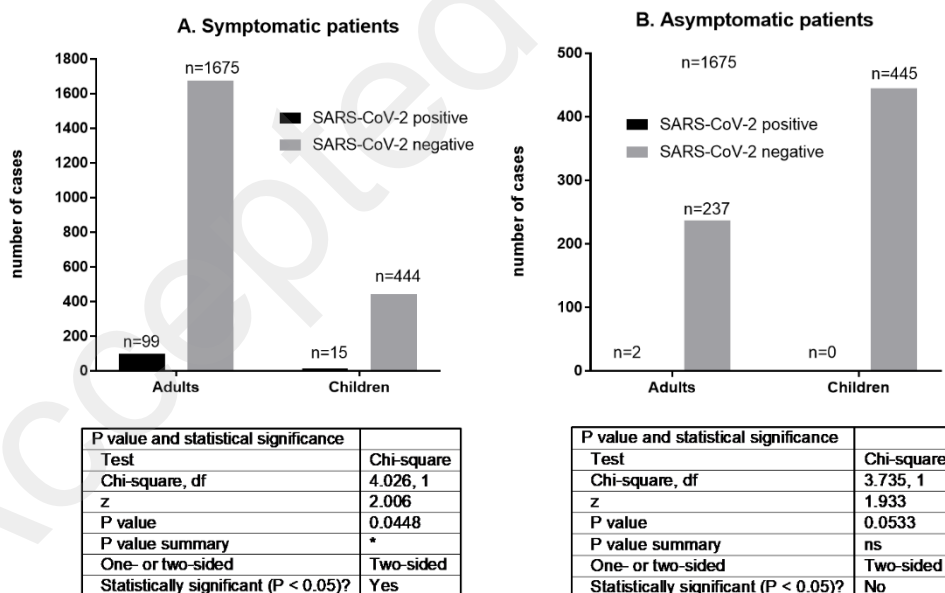
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417 **Visualistaion of figures and their legends**

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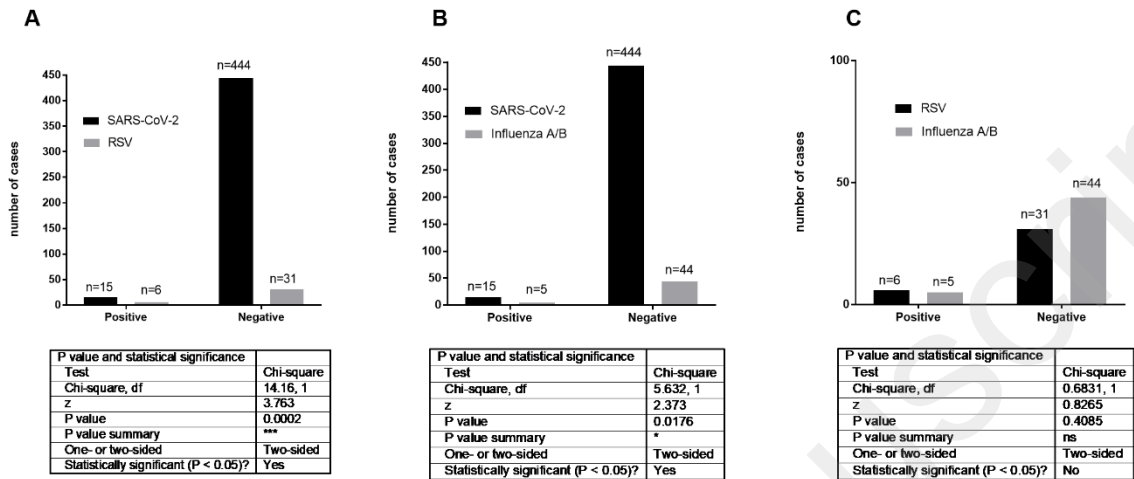
420 Fig. 1

421 The statistical analysis by chi-square test of the results obtained in: A – symptomatic patients,  
 422 B – asyptomaptic patients.

423

424 Fig. 2

425



426

427 The statistical analysis by chi-square test of the results obtained in: A – SARS-CoV-2 vs.  
428 RSV tests; B – SARS-CoV-2 vs. influenza A/B; C- RSV vs. influenza A/B.

429

430

### 431 Supplementary Materials 1

432 Age strata in the four groups of patients studied:

433

434 1. symptomatic pediatric patients (n = 459): 0-5 years: 37.6%; 5-10 years: 29.1%; 10-15  
435 years: 29.1%; 15-18 years: 4.2%

436

437 2. symptomatic adult patients (n = 1774): 18-30 years: 26.0%; 30-40 years: 21.0%; 40-50  
438 years: 27.5%; 50-60 years: 7.5%; 60-70 years: 10.5%; 80 and more years: 7.5%.

439

440 3. asymptomatic children (n = 445): 0-5 years: 45.0%; 5-10 years: 25.0%; 10-15 years:  
441 17.5%; 15-18 years: 12.5%

442

443 4. asymptomatic adults (n = 239): 18-30 years: 24.0%; 30-40 years: 15.0%; 40-50 years:  
444 26.5%; 50-60 years: 17.5%; 60-70 years: 8.5%; 80 and more years: 8.5%.

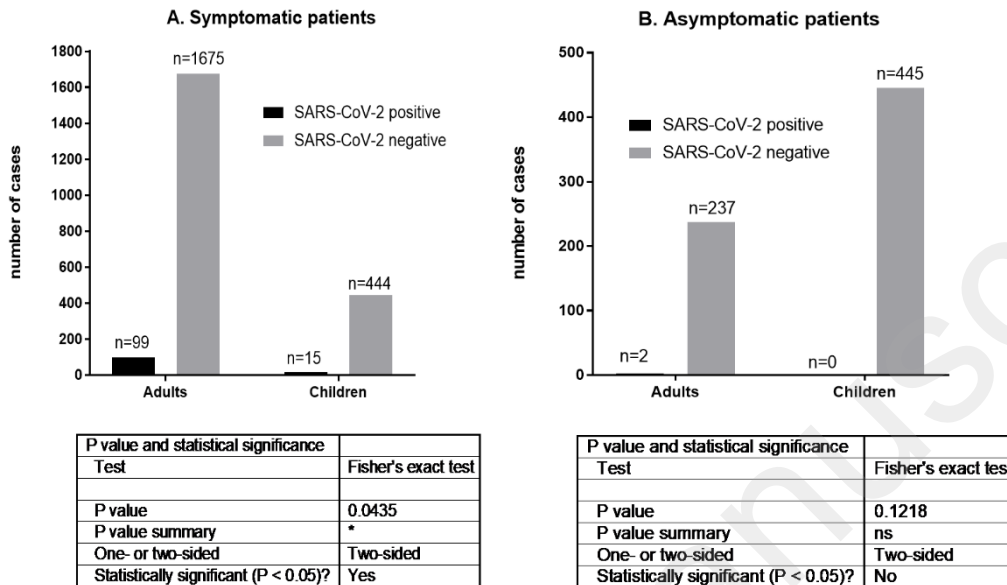
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### 446 Supplementary Materials 2

447

448 Fig. 1 Suppl. Materials

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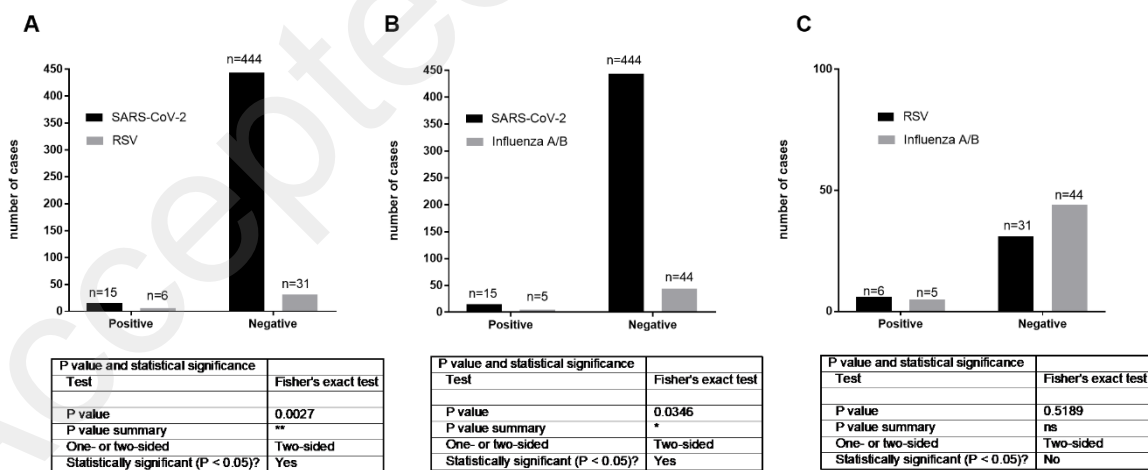


450

451 The statistical analysis by Fisher test of the results obtained in: A – symptomatic patients, B –  
452 asymptomatic patients.

453

454 Fig. 2 Suppl. Materials



455

456 The statistical analysis by Fisher test of the results obtained in: A – SARS-CoV-2 vs. RSV  
457 tests; B – SARS-CoV-2 vs. influenza A/B; C- RSV vs. influenza A/B.

458

459