

Review Article

The Main Associated Symptoms Related to COVID-19 (Coronavirus Disease 2019) Among Pediatric Patients

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Abstract

Context: Findings have been perceived that only fewer children face COVID-19 and among infected, they have fewer violent signs. Being less severity among children could be significant for meditating therapeutics for high-risk adults and the elderly.

Evidence Acquisition: This study reviewed the main associated symptoms related to COVID-19 such as epidemiologic, laboratory-related, and therapeutic aspects among pediatric patients. In this narrative review, the most recent reproduced data on pediatric patients' clinical revelation with COVID-19 have been considered and reviewed.

Results: All ages of pediatric patients were susceptible against the COVID-19. There wasn't any significant sex difference. Asymptomatic, mild, or moderate signs were reported in more than 90% of all patients. Although pediatric patients clinical appearance of COVID-19 was commonly less severe compare to adult patients, young pediatric patients, exclusively infants, were vulnerable to infection.

Conclusion: It is important that clinicians must be informed of possible clinical manifestations of pediatric patients' COVID-19 cases to avoid neglecting or overdiagnosis of patients. As well as, this review provided strong documents of human-to-human transmission.

KeyWords: Epidemiological Aspects of COVID-19, Laboratory Tests, Therapeutic Aspects of COVID-19, Pediatric patients

1. Context

Coronaviruses (CoVs), belonged to the family *Coronaviridae*, is a zoonotic single-stranded RNA viruses. A variety of animals (including cattle, companion birds, and animals) can be infected by CoVs, with the potency to cause rigid cardiovascular, respiratory, enteric, and neurologic disease. [1-8] CoVs frequently cause symptoms of respiratory and gastrointestinal diseases, ranging from the common cold to syndrome related to severe acute respiratory distress (ARDS), coagulopathy, pneumonia,

bronchitis, multi-organ failure, and even death in humans. Also, human coronaviruses (HCoVs) are related to some diseases such as asthma, cystic fibrosis, and chronic obstructive pulmonary disease. [9-11]

In January 2020, in more than 170 countries, COVID-19 has been widespread with rather than 500 000 cases. Only scant initial data on the burden of COVID-19 in pediatric patients was reported because the preliminary data focused on severe respiratory manifestations in adults. Dong

et al, reported more than 2000 pediatric patients with COVID-19. Virologically, almost 4% had asymptomatic infection. Almost, this rate certainly understated asymptomatic infection true rate. Because many pediatric patients who were asymptomatic were unlikely to be tested. Otherwise, among pediatric patients who were symptomatic, only 5% had dyspnea or hypoxemia, and merely 0.6% proceeded to ARDS or multiorgan system dysfunction. In different studies has been reported that preschool-aged pediatric patients and infants were the same as older pediatric patients to have severe clinical manifestations (12-16). This review considered the main finding of COVID-19 among pediatric patients according to epidemiologic, laboratory-related, and therapeutic aspects.

2. Evidence Acquisition

In this narrative review, the most recent reproduced information on common sign and Covid-19 symptoms in pediatric patients and the idea that the coronavirus may have asymptomatic infection have been reviewed. Advancement in the understanding was so important because many pediatric patients who were asymptomatic were unlikely to be tested and neglected. Epidemiologically, this situation is so important because the importance of pediatric patients' roles in transmitting of infections remains uncertain.

3. Results

The Main Epidemiologic Aspect of COVID 19

This review provided strong documents about human-to-human infections transmission related to Covid -19. Covid-19 manifestations in pediatric patients were different ranging from a common cold, bronchitis, pneumonia, ADRS, multi-organ failure, and even death. Other members of coronaviruses family such as SARS-CoV, MERS-CoV and SARS-CoV-2 seemed to less effect on pediatric patients. Comparing

to adults, they caused diseases with fewer symptoms, and lower case-fatality rates. Introductory, evidence proposed that pediatric patients were just the same as adults as of being infected with SARS-CoV-2 .They were less presumably to be symptomatic or expand vigorous symptoms. Compared with adults, pediatric patients more frequently have gastrointestinal symptoms. In most pediatric patients with SARS-CoV, fever occurs, but the case for novel CoVs isn't present. Many pediatric patients affected by MERS-CoV were without any symptoms. Most of the time, adults more often had a nosocomial exhibition; in contrast, the most of pediatric patients with novel CoVs have been proven indoor contact, frequently showing symptoms formerly them. This review summarizes epidemiologic, clinical, and diagnostic findings, with a focus on pediatric patients. [17]

There are not many distributed archives including the clinical and chest CT discoveries of COVID-19 pneumonia in pediatric patients. As indicated by past examinations, there was a male-overwhelmed propensity and scarcely any cases happened in pediatric patients for COVID-19 pneumonia. There was some clinical beginning manifestations qualities that were accounted for in pediatric patients including fever, cough, and fatigue, without other microbe contamination report (negative for *Chlamydia pneumonia*, respiratory syncytial virus, *Mycoplasma pneumonia*, *Coxsackie* virus B, *Adenovirus*, flu A, flu B, and human parainfluenza virus). The blood test was vague. Lab test demonstrated increased/ normal C-responsive protein, decreased/normal blood leukocyte check, increased/normal lymphocyte count, reased/decreased/normal lymphocyte proportion, decreased/normal neutrophil proportion. CT documents were normal, single pure, single consolidation, multiple consolidations or ground-glass opacity (GGO). Different findings were with or without pleural emission and

without Lymphadenopathy. The pulmonary involvement in pediatric patient with COVID-19 was gentle with a central GGO or union. With COVID-19 epidemic and clinical features with or without lab affirmation, CT was the methodology of decision for early finding, seriousness appraisal, and convenient helpful impacts' assessment. For screening in pediatric patients versus chest CT, the introduction history and clinical indications were more useful. The CT documents in pediatric patients were different (from normal appearances to a few lesions injuries) including ground-glass haziness or lung consolidation. The introduction history and clinical side effects could be more useful for the screening, despite the fact that the pediatric patients' chest CT imaging highlights with COVID-19 pneumonia were vague. It was accounted for that HCoV's can be segregated from 4% to 6% of hospitalized pediatric patients with intense respiratory tract infections and from 8% of pediatric patients in a wandering setting. [18-21]

The most regularly influenced of pediatric patients who have risk are younger than 3 and pediatric patients with coronary illness. Most people seroconvert to HCoV's during adolescence, reinfections later in life are normal. There wasn't any reduction in the relative of HCoV's infection prevalence with age increment, rather than other respiratory tract infections such as RSV respiratory syncytial virus. [22-27]

Compared with pediatric patients coinfecting with other respiratory viruses, pediatric patients with respiratory virus (HCoV) symptoms more likely suffered ongoing disease. [28] Normal flowing HCoV's in pediatric patients can cause regular cold manifestations, for example, fever, pharyngitis, rhinitis, laryngitis, otitis, and cerebral pain, yet additionally pneumonia, wheezing, bronchitis, bronchiolitis. Gastrointestinal manifestations are more normal in pediatric patients contrasted with grown-ups, with up to 57% of cases. In an

investigation containing pediatric patients and adults' sore throat, myalgia, fatigue, and headache were more normal in patients with HCoV compare to patients with RSV. Different indications were more regular in the last mentioned people (such as fever, cough and dyspnea). Few patients with HCoV's had fever compare to those patients contaminated with RSV or flu. [29-31]

Human Covid NL63 was types of Covid that was distinguished in late 2004 of children with bronchiolitis in the Netherlands. In pediatric patients, HCoV-NL63 has been related with febrile seizures, asthma intensifications, conjunctivitis and croup. Human Covid HKU1 (HCoV-HKU1) is a types of Covid which started from infected mice. In people, infection brings about an upper respiratory malady with side effects of the regular cold, however can progress to pneumonia and bronchiolitis. It was first found in January 2005 in two patients in Hong Kong. Resulting research uncovered it has worldwide dispersion and prior beginning. In pediatric patients, HCoV-HKU1 has been related with febrile seizures. The identification of HCoV in child CSF with intense dispersed encephalomyelitis or in adults CSF with numerous sclerosis was reported, yet uncommon instances of neurologic infections have likewise been proven. [32-34]

Pediatric patients who were influenced by extreme intense respiratory condition related Covid (SARS-CoV) milder infection compare with adults, without deaths have been reported. In pediatric patients with SARS-CoV disease, some manifestation were accounted for as following : fever (91%–100%), cough (43%–80%), dyspnea (10%–14%), myalgia (10%–40%), sore throat (5%–30%), rhinitis (33%–60%), headache (14%–40%) and, less generally, vomiting (20%), diarrhea (10%), abdominal pain (10%), and febrile seizures (10%). Absolutely, 30% of pediatric patients infected by SARS-CoV had a nosocomial contact and 50%–80% had

other relatives who were infected. More often, pediatric patients recuperate rapidly from a SARS-CoV infection. Some anomalies on CT eg. ground-glass pacifications with air trapping can endure for a while. [35-38]

Middle East respiratory syndrome (MERS) is a viral respiratory malady brought about by a novel Covid (MERS- CoV), which was first distinguished in Saudi Arabia in 2012. A low extent (0.1%–4%) of MERS-CoV has been accounted for in pediatric patients. None of MERS-CoV tested positive was accounted for in a huge case arrangement of pediatric patients with intense respiratory tract disease who introduced to a tertiary emergency clinic in Saudi Arabia during the MERS-CoV scourge (2012–2013). Two different investigations were performed on pediatric patients infected with MERS-CoV, with a mean age of 7-10 years, 42% of pediatric patients were asymptomatic. In the other investigation of pediatric patients, 14% experienced cough and breath shortness, 28% from diarrhea and vomiting, and 57% from fever. 28% of pediatric patients required oxygen supplementation and 14% mechanical ventilation. Household (32%) was the principle of MERS-CoV disease wellsprings in pediatric patients and different contacts (23%), trailed by nosocomial transmission (19%). Based on Chinese Centers for Disease Control and Prevention reports, pediatric patients were less regularly influenced by SARS-CoV-2, and just 2% were in people under 19 years old. Underlying disease was not reported the pediatric patients: 9% were asymptomatic, 65% had regular respiratory side effects, and 26% had mellow malady. The most well-known manifestations were cough (38%) and fever (50%). In any case, at times, fever introduction was with low to direct or even without any headache, fever, cough, rhinitis, fatigue, and diarrhea. In most cases poor feeding, dyspnea, and cyanosis was reported; however the numbers were not determined. Just 44% of

infants were accounted for to have fever. Most infected pediatric patients with SARS-CoV-2 recuperated two weeks after the beginning of indications and no death had been accounted for by February 2020. [39-41]

Some extraordinary and non-specific laboratory findings were accounted for from pediatric patients with novel CoVs during Covid illness of 2019 (Covid-19). The WBC was normal or diminished with diminished neutrophil as well as lymphocyte counts. CRP and procalcitonin levels were regularly typical. Thrombocytopenia maybe happened. It was reported that in serious cases, lactate dehydrogenase levels, liver enzymes, d-dimers, and abnormal coagulation have been raised. [42-47]

The most well-known blood findings of the COVID-19 were thrombocytopenia (32.8%), lymphopenia (75.9%), leukopenia (31.1%), with raised AST (aspartate aminotransferase) (24.6%), CK (creatinine kinase) (14.7%), lactate dehydrogenase (45.9%), ALT (alanine aminotransferase) (22.4%), and CRP (C-responsive protein). There is likewise a proposal that lymphopenia because of diminishes in T cells (both CD4+ and CD8+) may be a basic factor related with COVID-19 seriousness and fatality. [48-51]

Laboratory-related Aspect of COVID 19

All presumed cases are to be accounted for to region and state reconnaissance officials. Favored analytic test for SARS-CoV-2 RNA is RT-PCR (reverse transcriptase polymerase chain reaction). For epidemiological purposes, next generation sequencing was used to recognize SARS-CoV-2 strains and transformations. Initial 7–10 days of disease, rapid serology kits which affirmed for clinical use, may not show positive results but for several weeks following contamination, results remain positive. Nasopharyngeal and oropharyngeal swab are favored samples for children not

accepting mechanical ventilation upper respiratory tract specimen; these ought to be transferred in VTM (viral transport media) on ice. In precisely for ventilated children, BAL (bronchoalveolar lavage) or endotracheal suction would be the favored specimen. These must be gathered into VTM and transported in the cold chain. Sputum specimen ought to be stayed away from in view of aerosol generation risk. In an indicative child, the viral load is relied upon to be high. Single test utilizing upper respiratory tract specimen such as nasopharyngeal and oropharyngeal swab ought to have the option to distinguish practically all the cases. All indicative children who have embraced global travel over the most recent 14 days or all hospitalized kids with serious intense respiratory sickness, for example, fever and cough as well as fatigue or asymptomatic direct. Between day 5 and day 14 after contacting, high-risks contacts of an affirmed case ought to be tested. [52-57]

When viral RNA degree being underneath the constraint of test identification, COVID-19 false negatives results happen. Best example types are assortment techniques and testing stages include on SARS2-CoV detection. It could help clarify why SARS-CoV-2 tests were negative when the patient has clinical symptoms. Microbiology dogma directs that good specimen assortment prompts exact outcomes from the lab. Nasopharyngeal swabs are the favored specimen type for COVID-19 according to CDC. CDC permit taking oropharyngeal swab for gathering samples. It is controversial on saliva using to diagnose COVID-19 disease. Generally, it was proven that a patient who is contaminated with SARS-CoV-2 high viral load may have contradictory results. LOD means the limit of detection. LOD of a RT-PCR test describes the RNA base measurement that will distinguish 95 out of 100 times. About patients contaminated with SARS-CoV-2 without test positive, a high false-negative outcome will prompt. If

the LOD for a test is excessively low, it means the test will recognize viral RNA smallest measurement, prompting false-positive test outcomes. Individuals with SARS-CoV-2 will be positive rather than negative. Clinically, RNA specialty identified in an individual is critical. The target LOD for a precise test is simply that craftsmanship. [58]

So, for NAT; blood and stool samples collecting at disease later periods increase the positive results whether being the inaccessible of lower respiratory tract specimens. Volume expanding raise identification affectability. Placing samples in guanidine salt reagents inactivate virus and protect RNA. In addition, setting appropriate positive, and negative controls to gain great outcomes; at the same time enhancing human RNase P quality to avoid false-negative results. For immune response assay, assorted measures focusing on various antigens, and gathering paired samples are needed. [59]

Therapeutic Aspects of COVID 19

For the flu, on potential bacterial-SARS-CoV-2 co-infection treatment was focused. This suggestion has been applied in COVID-19 treatment which accounted for SARS-CoV-2 infection in China. Being insufficient data, NIH recommend for empiric broad-spectrum antibiotic therapy in the absence of another indication in severe or critical illness, and patients with COVID-19. In the guidelines of Infectious Diseases Society of America this issue has been ignored. Conversely, the Surviving Sepsis Campaign specialists utilize empiric antimicrobials/antibacterial therapy in ventilated patients with COVID-19 and respiratory distress. in spite of the fact that they are with a low degree of proof-dependent on the information extrapolated from past examinations on different sorts of viral types of pneumonia, especially flu. Empiric antimicrobials therapy in Taiwan and Canada for treating all presumable bacteria causing respiratory disease and

sepsis. The decision ought to be founded on the clinical conclusion, susceptibility tests, and local epidemiology. In UK, antibiotics should just be offered to patients with suspected or affirmed COVID-19, if the probable reason is bacterial agent. When the patients are at high risks group whether the agent is bacteria or virus it stays hazy. Especially, oral doxycycline is favored against *M. pneumonia* and *S. aureus*. In China country, for COVID-19 patients with suspected co-bacterial infection azithromycin, amoxicillin, and fluoroquinolones was suggested for mild cases however wide range anti-infection covering all potential microbes was recommended for serious cases. In light of the restricted information of the current work, it stays indistinct which antimicrobial operators ought to be experimentally recommended in patients with suspected COVID-19. To prevent antimicrobial resistance rising due to = inappropriate antibiotic utilization for viral pneumonia, antimicrobial susceptibility testing should be done. [60-69]

4. Conclusion

Within the sight of COVID-19, clinicians must know about the conceivable clinical indications of pediatric patients' COVID-19 cases to abstain from neglecting or overdiagnosis of patients.

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Conflict of Interest

The authors declare no conflict of interest.

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