


was isolated in ocular secretions (Loon et al., 2004). Other coronaviruses have been found to cause viral conjunctivitis in humans (Li et al., 2020).

**Conclusion:**

In conclusion, we reviewed the current literature on pediatric patients with coexisting severe neurological manifestations and SARS-CoV-2 infections. Though severe neurological symptoms are not typical with coexisting severe neurological manifestations and SARS-CoV-2 infections. Though severe neurological symptoms are not typical, many of these patients were unaware of COVID-19 exposure and positivity upon arrival to the hospital, so testing is warranted to prevent infectious spread.

**References:**

23. Verdoni, L; Mazza, A; Gervasoni, A; Martelli, L; Ruggeri, M; Ciuffreda, M; Bonanomi, E; D’Antiga, L (2020): An outbreak of severe Kawasaki- like disease at the Italian epicentre of the SARS-
through PubMed, Medscape and Google scholar search between 2020 to the end of 2021. A total number of 381 studies were examined then checked and overlapping citations were removed from them the pool of 38 studies focused on manifestations and neurological complications.

In the current study regarding COVID-19 manifestations in pediatric patients, our results showed that 67 manifestations were reported in the pool of studies included in these studies of a total number of 2374 patient as a study.

The current study was supported by the Systematic Review and Meta-Analysis by Panda et.al. (2021) aimed to provide a pooled estimate of neurological complications in children with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. The study included 21 studies/case series and five case reports (3707 patients) fulfilled the eligibility criteria and were included in this systematic review, from a total of 460 records. Headache, myalgia and fatigue were predominant non-specific neurological manifestations, presenting altogether in 16.7% cases.

As well the meta analysis by Wang et al. (2021) included Seventy- one articles involving 11,671 children. Based on the clinical characteristics of the existing paediatric cases, children with COVID-19 can be divided into five clinical types: asymptomatic, mild, common, severe, and critically severe infections. Most COVID-19 positive children were in the mild category. Fever and cough were the most common clinical symptoms in adults. A meta analysis of adults from 43 studies involving 3,600 patients were included. Among these patients, fever (83.3% [95% CI, 78.4%- 87.7%]), cough (60.3% [95% CI, 54.2%- 66.3%]), and fatigue (38.0% [95% CI, 29.8%- 46.5%]) were the most common clinical symptoms. Compared with adults, this study found that the incidence of fever among children was 55.8% (50.3%- 61.3%), the incidence of respiratory symptoms was 56.8% (50.9%- 62.5%), and the incidence of chest tightness was 6.1% (3.9%- 8.6%).

The Systematic Review and Meta-Analysis by Nazari et al. (2021) selected 64 studies with 11,687 patients, the study showed that the most common manifestations were fever 79.3% (95% CI: 73.9%- 84.3%), cough 54.77% (95%CI: 49.10%- 60.38%), fatigue 32.39% (95% CI: 26.78%- 38.0%), dyspnea 28.47% (95% CI: 21.49%- 35.99%), chest tightness 23.83% (95% CI: 17.84%- 29.82%), and shortness of breath 20.42% (95% CI: 13.28%- 28.85%). The highest incidence rate among CNS symptoms of COVID-19 patients was for headache (8.69% with 95% CI: 6.76%- 10.82%), followed by dizziness (5.94%, 95%CI: 3.66%- 8.22%), and impaired consciousness (1.90% with 95% CI: 1.0%- 2.79%).

Vakili et al. (2021) in their meta-analysis revealed that Anorexia was also another symptom observed in 28.9% (95% CI: 19.9- 38.8; I²= 96.3%) of patients. This loss of appetite can have different reasons.

As Kinnaird et al. (2018) reported that altered taste sensitivity could disturb taste processing in anorexia nervosa; appetite loss can have different reasons, such as gustatory dysfunction. Alternatively, it can be a result of the immune responses of the patient. The role of a dysfunctional immune system has been proved in both COVID-19 and anorexia nervosa (AN) (DeSarbo et al., 2020).

Regarding the Prevalence of myalgia in pediatric patients infected by COVID-19 by meta-analysis we found Five studies were analyzed with total sample size 143 (24.5%), heterogeneity test showed Q= 5.9526 of significant value P= 0.2027, publication bias of significant value P= 0.4272 by Egger’s test and P= 0.3272 by Begg’s test. This was in agreement with the meta-analysis by Vitalakumar et al. (2021) as they reported that myalgia was reported with pooled proportion of 21.4% (18.8–24.1).

Also, Collantes et al. (2021) showed that myalgia was reported with pooled proportion of 20%, the random effect modeling analysis was (0.21; 0.18- 0.25; I²= 85%). Furthermore, Favas et al. (2020) revealed that myalgia was reported with pooled proportion of (19.3%; 95% CI 15.1-23.6).

Neurological consequences of COVID-19 may precipitate the development of dysarthria, and for patients with preexisting dysarthria, speech may worsen with additional neurological insult and/or peripheral changes. Dysarthria results from a wide range of neurological etiologies that cause damage to the speech motor control system. Dysarthria can result from deficits to any or all of the five primary subsystems that are key to speech production: respiratory, laryngeal, velopharyngeal, orofacial, and prosodic. (Sevitz et al., 2021).

In the current study the prevalence of progressive difficulty to walk in pediatric patients infected by COVID-19 was reported by 3 studies with total sample size 9 (78.4%), heterogeneity test showed Q= 3.1540 of significant value P= 0.2066, publication bias of significant value P= 0.8922 by Egger’s test and P= 1.0000 by Begg’s test.

Abdel- Mannan et al. (2020) reported that all the children with COVID-19 were complicated by difficulty to walk while 50% was reported by Krueger et al., 2021. The sample sizes of these studies were very low resulting in statistical weakness, their results should by confirmed with studies with larger sample size.

In the current study the prevalence of muscle weakness in pediatric patients infected by COVID-19 by meta-analysis was reported by 3 studies with total sample size 18 (42.5%), heterogeneity test showed Q= 2.2988 of significant value P= 0.3168, publication bias of significant value P= 0.0927 by Egger’s test and P= 0.1172 by Begg’s test.

It is theorized that individuals with severe COVID-19 infection may have increased probability of developing neurological manifestations such as disturbances in consciousness, skeletal muscle injury, including acute stroke (Mao et al., 2020).

Coronaviruses can cause severe ocular disease in animals, including anterior uveitis, retinitis, vasculitis, and optic neuritis in feline and murine species. However, ocular manifestations in humans are typically mild and rare (Seah et al., 2020), although there are increasing numbers of associated ocular findings in patients positive for the COVID-19. There are no described ocular manifestations of Middle East respiratory syndrome (MERS) or SARS, though, as previously stated, SARS- CoV...
plots, chi-square, and I² square tests. According to the recommendations of Cochrane Handbook of Systematic Reviews and meta-analysis, chi-square p-value less than 0.05 denote significant heterogeneity while I² square values show no important heterogeneity between 0% and 40%, moderate heterogeneity from 30% to 60%, substantial heterogeneity from 50% to 100%.

Evidence of publication bias: Evidence of publication bias had been sought using the funnel plot tests (Begg’s test and Egger’s test).

Results:

The data was collected by online search through PubMed, Medscape and Google scholar search between December 2020 to October 2021. A total number of 381 studies were examined then checked and overlapping citations were removed from them the pool of 38 studies focused on manifestations and neurological complications.

Sixty seven manifestations were reported in the pool of studies included in this studies of a total number of 2374 patient as studies groups (shown in table (1)& (2)). Fever is found to be the most common reported COVID-19 manifestations in pediatric patients (34.54%) followed by cough (23.63%).

Table (2) ‐ prevalence of COVID-19 respiratory manifestations in pediatric patients

<table>
<thead>
<tr>
<th>N.</th>
<th>Manifestation</th>
<th>Total Sample Size (%)</th>
<th>N.</th>
<th>Manifestation</th>
<th>Total Sample Size (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fever</td>
<td>820 (34.54%)</td>
<td>10</td>
<td>Serous Effusion</td>
<td>13 (0.55%)</td>
</tr>
<tr>
<td>2</td>
<td>Cough</td>
<td>561 (23.63%)</td>
<td>11</td>
<td>Tachypnea</td>
<td>12 (0.51%)</td>
</tr>
<tr>
<td>3</td>
<td>Rhinorrhea</td>
<td>273 (11.50%)</td>
<td>10</td>
<td>Chest Pain</td>
<td>9 (0.38%)</td>
</tr>
<tr>
<td>4</td>
<td>Respiratory Symptoms Not Specified</td>
<td>237 (9.98%)</td>
<td>13</td>
<td>Status Asthmaticus</td>
<td>30 (1.30%)</td>
</tr>
<tr>
<td>5</td>
<td>Dyspnea</td>
<td>192 (8.09%)</td>
<td>14</td>
<td>Cynosis</td>
<td>2 (0.08%)</td>
</tr>
<tr>
<td>6</td>
<td>Sore Throat</td>
<td>98 (4.36%)</td>
<td>15</td>
<td>Sub-Pleural Thickening</td>
<td>20 (0.88%)</td>
</tr>
<tr>
<td>7</td>
<td>Respiratory Distress</td>
<td>32 (1.35%)</td>
<td>16</td>
<td>Otitis Media</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>8</td>
<td>Expectoration</td>
<td>25 (1.05%)</td>
<td>17</td>
<td>Orthopnea</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>9</td>
<td>Pneumonia</td>
<td>17 (0.72%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table (2) ‐ prevalence of COVID-19 extra-respiratory manifestations in pediatric patients.

<table>
<thead>
<tr>
<th>N.</th>
<th>Manifestation</th>
<th>Total Sample Size (%)</th>
<th>N.</th>
<th>Manifestation</th>
<th>Total Sample Size (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Seizures</td>
<td>32 (1.35%)</td>
<td>17</td>
<td>Neurological Complications Not Specified</td>
<td>3 (0.13%)</td>
</tr>
<tr>
<td>2</td>
<td>Meningism</td>
<td>23 (0.97%)</td>
<td>18</td>
<td>Brain Hemorrhage</td>
<td>3 (0.13%)</td>
</tr>
<tr>
<td>3</td>
<td>Meningitis/ Encephalitis</td>
<td>20 (0.84%)</td>
<td>19</td>
<td>Acute Brain Dysfunction</td>
<td>2 (0.08%)</td>
</tr>
<tr>
<td>4</td>
<td>Cranial Nerve Palsy</td>
<td>16 (0.67%)</td>
<td>20</td>
<td>Hallucinations</td>
<td>2 (0.08%)</td>
</tr>
<tr>
<td>5</td>
<td>Vertigo</td>
<td>15 (0.63%)</td>
<td>21</td>
<td>Aphasia</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>6</td>
<td>Vision Changes</td>
<td>15 (0.63%)</td>
<td>22</td>
<td>Hyperreflexicity</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>7</td>
<td>Encephalopathy</td>
<td>8 (0.34%)</td>
<td>23</td>
<td>Hypersexuality</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>8</td>
<td>Dysarthria</td>
<td>8 (0.34%)</td>
<td>24</td>
<td>Dysphonia</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>9</td>
<td>Muscle Weakness</td>
<td>7 (0.29%)</td>
<td>25</td>
<td>Dysphagia</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>10</td>
<td>Progressive Difficulty To Walk</td>
<td>7 (0.29%)</td>
<td>26</td>
<td>Ruptured Cerebral Pseudoneurysm</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>11</td>
<td>Status Epilepticus</td>
<td>4 (0.17%)</td>
<td>27</td>
<td>Disorganization</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>12</td>
<td>Gait Instability</td>
<td>4 (0.17%)</td>
<td>28</td>
<td>Quadraparesis</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>13</td>
<td>Paresthesia</td>
<td>4 (0.17%)</td>
<td>29</td>
<td>Photophobia</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>14</td>
<td>Ataxia</td>
<td>3 (0.13%)</td>
<td>30</td>
<td>Ophthalmoplegia</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>15</td>
<td>Sleep Disorder</td>
<td>3 (0.13%)</td>
<td>31</td>
<td>GBS</td>
<td>1 (0.04%)</td>
</tr>
<tr>
<td>16</td>
<td>Papuliodema</td>
<td>3 (0.13%)</td>
<td>32</td>
<td>Central Apnea</td>
<td>1 (0.04%)</td>
</tr>
</tbody>
</table>

Discussion:

Children of all ages can get COVID-19 (WHO, 2021). Although children typically have a lower risk of exposure and are tested less frequently than adults, the incidence in children is similar to that in adults (Dawood et al., 2022). In studies where children and adolescents were tested for acute or past severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections without respect to symptoms, the rates of infection in children ≥5 years were similar to or greater than those in adults (Hobb et al., 2021).

The main aim of this study was to identify manifestations of covid in pediatric patients and to identify neurological complications of Covid in pediatric patients.

This was meta-analysis study. The data was collected by online search...
**Introduction:**

The world is devastated by serious and sometimes fatal symptoms caused by human coronavirus, Severe Acute Respiratory Syndrome (SARS)-CoV-2, and the associated coronavirus disease 2019 (COVID-19) although COVID-19 symptoms are primarily pulmonary (fever, dry cough, fatigue, pneumonia), it is increasingly found that multiple organ systems may be affected, including the brain, with neurological involvement affecting up to ~36% of patients (Stafstrom & Jantzie, 2020).

Despite all the scientific community’s and health workers’ effort, by September 5, 2020, approximately 26 million cases of the COVID-19 have been confirmed worldwide, resulting in more than 870,000 deaths worldwide. While the number of confirmed, cases is duplicated within a few weeks, it reached ~12,500,000 COVID-19 cases in Africa by September 5, 2020 (Soltani et al., 2021).

It appears that children are less frequently infected and less severely affected by COVID-19, unlike other respiratory diseases (Carsetti et al., 2020). However, due to the outrageous number of infected children, some fatal cases are being reported, associated with extrapulmonary complications, pointing to a need of medical and scientific attention (Walker et al., 2020). In addition, the recently described multisystem inflammatory syndrome-children (MIS-C), raises the fears that COVID-19 or its complications also affect children (Verdoni et al., 2020).

Neurological symptoms such as sudden loss of smell and taste were reported in a huge number of COVID-19 patients. Viral infections have been found as a cause of sensorineural hearing loss through damage of inner ear structures or by precipitating inflammatory responses which then lead to this damage so COVID-19 should be taken into consideration in patients presented with sudden hearing loss (Abdel Rhman and Abdel Wahid, 2020).

**Patients & Methods:**

This study is a meta analysis type conducted on a previously international computerized databases, review articles, hand searching relevant journal, case reports which are including neurological involvement in COVID-19 pediatric patients. All studies were listed by citation, title, authors and abstract and with basic information. The authors searched using the All Fields for the terms "Neurological", "Neurology", "Complications", "Manifestations", "COVID-19", "Coronavirus" and "(SARS)-CoV-2".

**Study Identification And Eligibility Criteria:**

Following the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and meta analysis (PRISMA) statement, searching databases published up to study years.

- **Inclusion Criteria:** The study reviewed all published studies and case reports about neurological involvement in COVID-19 Pediatric patients (0-18) years globally.
- **Exclusion criteria:** Adults, if data cannot be extracted and if only abstract is available.
- **Ethical and legal consideration:** The study proposal was approved by the scientific ethical committee of the faculty of Postgraduate Childhood Studies and it was conducted according to the guidelines of Helsinki.

**Study Tools:**

Primary data was reanalyzed statistically and processed data was compared. Secondary data was analyzed for detection of Impact of COVID-19 on pediatrics patients with neurological complications.

**Screening:**

Unique citations were imported into an Excel sheet. The screening was conducted in two steps: title and abstract screening, followed by a full-texts screening of potentially eligible records.

**Statistical Considerations:**

PRISMA flow chart was produced based on the search results and the inclusion/exclusion criteria. To facilitate the assessment of possible risk of bias of each study, information was collected using the funnel plot tests (Begg’s test and Egger’s test) for assessing the risk of bias.

**Data analysis:**

Statistical analysis was done in the following factors; geographic area (Asia, Africa, Europe, United States), study size (≤50 versus >50 patients), clinical severity complications and outcomes of pediatric patients with COVID-19 infection. With Applying previous consideration included papers reached 38 papers.

![Figure (1) PRISMA flow diagram for study selection.](image-url)
**Manifestations and neurological complications of COVID-19 in pediatric patients:**

A Meta-Analysis study

**Summary**

**Background:** Knowledge about neurological complications of COVID-19 in children is limited due to the paucity of data in the existing literature. Some systematic reviews are available describing overall clinical features of COVID-19 in children and neurological complications of COVID-19 in adults.

**Objectives:** To identify manifestations and neurological complications of COVID-19 in pediatric patients.

**Methods:** This study is a meta-analysis type conducted on a previously international computerized databases, review articles, hand searching relevant journal, case reports which are including neurological involvement in COVID-19 pediatric patients.

**Result:** Sixty-seven manifestations and thirty-two neurological complications were reported in the pool of studies included in this study of a total number of 2374 patient as studies groups. Fever is found to be the most common reported COVID-19 manifestations in pediatric patients (34.54%) followed by cough (23.63%).

**Conclusion:** In conclusion, we reviewed the current literature on pediatric patients with coexisting severe neurological manifestations and SARS-CoV-2 infections. Though severe neurological symptoms are not typical manifestations of COVID-19 or multisystem inflammatory syndrome- children (MIS-C), this review compiles the findings of a number of cases with life-threatening neurological disorders. In addition, many of these patients were unaware of COVID-19 exposure and positivity upon arrival to the hospital, so testing is warranted to prevent infectious spread.

**Keywords:** COVID-19, SARS-CoV-2 Infections, Neurological, Pediatric, Complications.