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Childhood Studies Apr.2022

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 manifestations of COVID-19 or 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.

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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 nonspecific 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 79.39% (95% CI: 73.94%- 84.37%), 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

Childhood Studies Apr.2022

plots, chi- square, and I- square tests. According to the recommendations of Cochrane Handbook of Systematic Reviews and meta- analysis, chi-square p- value less than0.05 denote significant heterogeneity while I-square values show no important heterogeneity between0% 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 (1) Prevalence of COVID-19 respiratory manifestations in pediatric patients					
N.	Manifestation	Total Sample	N.	Manifestation	Total Sample
		Size (%)			Size (%)
1	Fever	820 (34.54%)	10	Serous Effusion	13 (0.55%)
2	Cough	561(23.63%)	11	Tachypnea	12 (0.51%)
3	Rhinorrhea	273(11.50%)	12	Chest Pain	9 (0.38%)
4	Respiratory Symptoms	237 (9.98%)	13	Status Asthmaticus	3(0.13%)
	Not Specified				
5	Dyspnea	192(8.09%)	14	Cyanosis	2 (0.08%)
6	Sore Throat	98(4.13%)	15	Sub- Pleural	2(0.08%)
				Thickenings	
7	Respiratory Distress	32(1.35%)	16	Otitis Media	1 (0.04%)
8	Expectoration	25(1.05%)	17	Orthopnea	1 (0.04%)
9	Pneumonia	17(0.72%)			
Table (2) Prevalence of COVID-19 extra-respiratory manifestations in pediatric patients.					

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N.	Manifestation	Total Sample	N.	Manifestation	Total Sample
		Size (%)			Size (%)
1	Asymptomatic	423 (17.82%)	26	Renal Failure	26 (1.10%)
2	Pallor	2 (0.08%)	27	Renal Manifestations	2 (0.08%)
				Not Specified	
3	Rash	156(6.57%)	28	Lymphadenopathy	45 (1.9%)
4	Mottled Skin	4 (0.17%)	29	Conjunctivitis	139(5.86%)
5	Skin Desquamation	7 (0.29%)	30	Irritability	23 (0.97%)
6	Abdominal Pain	161 (6.78%)	31	Altered Mental Status	51 (2.15%)
7	Nausea/Vomiting	19 (8.38%)	32	Drowsiness/ Dizziness	89 (3.75%)
8	Diarrhea	205 (8.64%)	33	Mood Deflection	7 (0.29%)
9	Anosmia	51 (2.15%)	34	Headache	40 (1.68%)
10	Mucous Membrane	17 (0 72%)	35	Hypotonia	6 (0 25%)
10	Changes	17 (0.7270)	55	Trypotoma	0 (0.2570)
11	Lips And Oral Cavity	73 (3.07%)	36	Hypertonia	1 (0.04%)
	Changes				
12	Poor Feeding/	5 (0.21%)	37	Neck Stiffness	22 (0.93%)
	Decrease Appetite				
13	Intussusception	284 (11.96%)	38	Paroxysmal Episodes	1 (0.04%)
14	Hematemesis	1 (0.04%)	39	Diplopia	2 (0.08%)
15	Constipation	7 (0.29%)	40	Neurological	
				Symptoms Not	40 (1.68%)
				Specified	

N.	Manifestation	Total Sample Size (%)	N.	Manifestation	Total Sample Size (%)
16	Melena	2 (0.08%)	41	Multi- Organ Dysfunction Syndrome	2 (0.08%)
17	GIT* Symptoms Not Specified	145 (6.11%)	42	Pediatric Multisystem Inflammatory Syndrome	178 (7.50%)
18	Tachycardia	1 (0.04%)	43	Complete Kawasaki's Disease	43 (1.81%)
19	Hypertension	1 (0.04%)	44	Arthralgia/ Arthritis	6 (0.25%)
20	Heart Failure	3 (0.13%)	45	Myalgia	33 (1.39%)
21	Myocarditis	19 (0.80%)	46	Malaise	1 (0.04%)
22	Femoral Artery Thrombosis	1 (0.04%)	47	Febrile Seizures	20 (0.84%)
23	Dic**	2 (0.08%)	48	Metabolic Involvement	2 (0.08%)
24	Pain In Lower Limp	1 (0.04%)	49	Shock	89 (3.75%)
25	Oliguria	1 (0.04%)	50	Bilateral Bulbar Conjunctival Injection	17 (0.72%)

*GIT: GastoIntestinal Tract ** DIC: Disseminated Intravascular Coagulopathy.

Thirty- two neurological complications were reported in the pool of studies included in these studies of a total number of 2374 patient as studies groups (shown in table 2).

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

Table (2) Prevalence of COVID-19 neurological complications in pediatric patients

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 \geq 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 ~12.500000 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", "Corona Virus", "(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.
- [⊥] 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.

Study procedure: The study started by searching articles using the key words ("neurological", "neurology", "complications", "manifestations", "COVID-19", "Coronavirus" and "(SARS)- CoV- 2").

Screening:

Unique citations were imported into an Excel sheet. The screening was conducted in two steps: title and abstract screening, followed by a fulltexts 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.

Data Extraction:

Data entry and processing were carried out using a standardized Excel sheet and reviewers extracted the data from the included studies. The extracted data included the following domains:

- 1. Summary characteristics of the included studies.
- 2. Baseline characteristics of studied populations.
- 3. Study outcomes.

Direct Meta analysis:

The authors performed all statistical analyses using MedCalc software package Full version 20.014 (MedCalc, 2018).

Assessment of Heterogeneity:

The authors assessed heterogeneity by visual inspection of the forest

Manifestations and neurological complications of COVID 19 in pediatric patients:

A Meta-Analysis study

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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 studies 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.

در اسة الأعر اض والمضاعفات العصبية لدى مرضى الاطفال المصابين بفير وس كوفيد ١٩: در اسة تحليل ميتا

مقدمة: لقد دمر العالم الأعراض الخطيرة والممينة فى بعض الأحيان الناجمة عن فيروس كورونا البشرى، ومتلازمة الجهاز التنفسى الحادة الوخيمة (سارس)-كوفيد-٢، ومرض فيروس كورونا المصاحب ٢٠١٩ (كوفيد- ١٩) على الرغم من أن أعراض كوفيد- ١٩ هى فى الأساس رئوية (حمى، سعال جاف، والتعب، والالتهاب الرئوي)، فقد وجد بشكل متزايد أن العديد من الأعضاء قد تتأثر، بما فى ذلك المخ، مع مضاعفات فى الجهاز العصبى تصل إلى ٣٦% من المرضى. الهدف: الهدف من هذه الدراسه هو تحديد الاعراض والمضاعفات العصبية لـــكوفيد ٩٩ لدى مرضى الأطفال.

نوع الدراسة وتصيبها: دراسة تحليل مينا تأسيس ممارسات قائمة على الأدلة باستخدام التحليل المينا. ستجرى هذه الدراسة على قاعدة بيانات محوسبة سابقة مصرية و عالمية، ومؤلفون يعملون فى مجال البحث، وبرامج مؤتمرات، ومقالات مراجعة، ومجلات بحث يدوية ذات صلة، وتقارير حالة تشمل التورط العصبى فى مرضى الأطفال المصابين بفيروس كوفيد ١٩. تم استرجاع المقالات ذات الصلة (التى تم الحكم عليها على أساس العنوان والملخص) للحصول على تقييم أكثر تفصيلا وتم البحث فى ببليوغر افيات المقالات ذات الصلة بحثا عن مراجع إضافية. تتضمن الدراسة جميع الدراسات المنشورة وتقارير الحالة حول اصابة الجهاز العصبى فى الكوفيد ١٩ والمرضى الأطفال من سن ، إلى ١٨ عاما.

النتيجة: تم الإبلاغ عن ٣٣ مضاعفة عصبية فى مجموعة الدراسات المشمولة فى هذه الدراسات لعدد لجمالى قدره ٢٣٧٤ مريضا كمجموعات دراسات وتم استخلاصها وتحليلها بواسطة برنامج ميد كالك. لم تكن هناك بيانات كافية للتحليل التلوى فى ٢٠ مضاعفات عصبية، وأظهرت ثلاث مضاعفات عصبية تغايرية معنوية. عدم التجانس غير الملحوظ وتحيز النشر.

الخلاصة: فى الختام، قمنا بمراجعة الأدبيات الحالية حول مرضى الأطفال الذين يتعايشون مع مظاهر عصبية شديدة وعدوى سارس كو ف٢. على الرغم من أن الأعراض العصبية الحادة ليست مظاهر نموذجية ل كوفيد ١٩، إلا أن هذه المراجعة تجمع نتائج عدد من الحالات المصابة باضطرابات عصبية تهدد الحياة. بالإضافة إلى ذلك، لم يكن العديد من هؤلاء المرضى على دراية بالتعرض لكوفيد ١٩ والإيجابية عند وصولهم إلى المستشفى، لذلك فإن الاختبار له ما يبرره لمنع انتشار العدوى.

الكلمات المفتاحية: كوفيد ١٩، سارس كو ف٢، الأمراض العصبية، الأطفال، المضاعفات.