Radiological Manifestation of Neurological Complications in COVID-19 pediatric patients admitted in ICU : Retrospective observational study

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Abstract

Background: Early in the COVID 19 pandemic, the most severely affected with the highest mortality were older adults. By contrast, children were a minority of cases and most of them were mildly affected or asymptomatic. As the pandemic progressed, Increasing reports of children developing pediatric multi system inflammatory syndrome temporally associated with COVID-19(MIS-C) suggest that, children may be at high risk of a secondary neurological complications

Objectives: the purpose of the study was for understanding the neuroimaging manifestations of COVID-19 in pediatric population.

Patients and methods: In this prospective observational study 80 patients with past or present history of COVID-19 infection who presented with neurologic/ neuropsychiatric symptoms between April 2021 and May 2022. Medical records with a special emphasis on CT/MRI were reviewed regarding the intra cranial neurological complication

Results: We reported findings in 80 patients with neuro-COVID .The study had (36 %) of patients represented by convulsions, then dizziness(22.5%), vertigo, nausea& vomiting (25.2%), headache (16.3%). The most common diagnosis was encephalitis in 23 cases, cerebral edema & ADEM by 18 & 17 cases respectively. 11 cases show vasculitis/lacunar infarcts, 7 were normal, 3 cases with PRES and 1 case with venous thrombosis. Regarding the outcome 7 patients died (8.7%), 24 patients (30%) suffered from different disabilities. Unremarkable CT findings were found in the majority of cases (75 cases) while the remaining cases (5 cases) showed patchy ill-defined areas of hypodensity that was correlated with MRI and clinical manifestations and diagnosed as encephalitis (3 cases), diffuse cerebral edema manifested as loss of gyral pattern and ventricular effacement (2 cases).

Conclusion : Neurological findings of Cerebral Mucormycosis significantly vary from mild to fatal complication , neurological imaging study showed be enrolled within the protocol of COVID-19 work up, mainly MR

Keywords: MRI; CT; Brain; COVID 19; Infarction; Thrombosis

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Introduction

The severe acute respiratory syndrome, caused by corona virus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) was initially identified in Wuhan, China, in December 2019 and has since spread around the globe. (Hacohen et al., 2020) Earlier in the pandemic, elderlies with serious comorbidities were the most severely affected and had the greatest morbidity rates. Children, on the other hand, were a minority of instances, 80% of them slightly completely were just or asymptomatic. (Lindan et al., 2021)

It became obvious as the pandemic spread that additional systemic manifestations, such as neurological manifestations, may appear in along with respiratory contribution.(Niazkar et al., 2020.)

Children become at a greater risk of inflammatory secondary condition а regardless of having a typical mild acute infection, according to growing reports of children developing systematic inflammatory responses necessitating intensive care (labelled pediatric MIS-C) and another group of children with a Kawasaki-like condition. (Verdoni et al., 2020)

Severe neurologic consequences include cerebrovascular the following: events (micro or macro-hemorrhages and ischemic strokes), encephalopathies, neurodegenerati ve diseases, Meningoencephalitis, immunemediated or infectious issues (acute disseminated encephalomyelitis, Guillainsyndrome, encephalomyelitis), Barre seizures, and signs of neuropsychiatric illness (such as psychosis and mood disorders), Transverse myelitis, cytotoxic injuries in the callosal splenium, and acute disseminated encephalomyelitis (ADEM). (Orman et al., 2021)

Those neural consequences were documented to arise as primary neurological

illnesses in the acute or subacute phase as well as MIS-C complications in the delayed phase, which commonly occurs weeks following the COVID-19 infection. In all of the phases, ADEM and myelitis were evident; encephalitis and thrombo-ischemic conditions were found in the acute and subacute phase; and splenial injuries were mostly seen in the delayed phase (Lindan et al., 2021; Ray et al., 2021) . The purpose of the study was to increase awareness and comprehension of COVID-19's neuroimaging complication in pediatric populations.

Patients and methods

Patients

Prospective single-center observational research was carried out at a university hospital's tertiary care facility. From April 2021 to May 2022, 80 patients who had a prior or current history of the usual COVID-19 infection and had neurologic or neuropsychiatric manifestations.

Demographic information (Age and gender), concomitant diseases history, a comprehensive clinical and neurological examination, and laboratory results were all performed (**Fig.S1**).

The local ethics commission granted its ethical clearance.No.36264

Inclusion criteria

- Patients younger than 18 years
- Patients with aberrant results from neuroimaging on CT or MRI who have physical or laboratory indications of infection with SARS-CoV-2
- Patient admitted to ICU

Exclusion criteria

- Adult patients
- Patients with previous neurocognitive disorders.
- Patients had no history of COVID

Methods

A 1.5 T MR scanner was used for the MRI (Signa;16 channel, Excite, GE Healthcare,

Milwaukee, WI, USA). The following MR sequence parameters were used: images with T1 weight variables (TR:360 ms, TE: 9 ms), and the image's T2-weighted variables (TR:6672 ms, TE: 147 ms), FLAIR (TR: 7432, TE: 118.6, inversion time (TI): 2200). B value 1000 diffusion-weighted images. testing using a head coil. 22 x 18 mm field of view (FOV), 310 x 620 matrix, 3 mm slice thickness, and 0.4 mm slice gap. A number of instances involve CT imaging

Post contrast series: were obtained 20–30 s after intravenous administration of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) & administrated in 30 cases only

40 cases need anesthesia by chloral hydrate (50:75 mg/kg /dose before procedure by 30:60 minutes can be repeated if needed after 30 minutes if necessary)

CT used were GE optima with slice thickness 5mm, interval 5mm , 120kv & 400 ml AMP

Analysis and interpretation of images: The images were jointly evaluated by two

radiologists. The first reader, S.N, possessed thirteen years of interpreting expertise, while the second, F.Y, possessed a period of twelve years. Information on demographics, comorbidities, neurological symptoms, relevant investigations & treatments, were retrieved.

Statistical analysis

The statistical expressions used to characterize the data were mean, range, frequency (number of instances), and

percentage.

Results

In this research, eighty individuals were included. Their ages varied from 1 to 18, with a mean of 10.45 years, they were 43 boys (53.7%) and 37 girls (46.3%), no substantially statistical variation was detected among them (p>0.05). The most presenting symptom common were convulsions (36 %), then dizziness (22.5%), vertigo, nausea& vomiting (25.2%),headache (16.3%), (Table.1).

Age groups	Number of patients	Percentage
1-5 years	8	1%
5-10 years	24	3%
10-15 years	38	47.5%
15-18 years	10	12.5%
Total	80	100%

 Table 1. Demographic data of the participants

Regarding the co-morbidities, gastroenteritis was found in 29 patients (36.2%),chest infection in 25 patients(31.3%), myocarditis in 7 patients (8.7%), cardiomyopathy in 5 patients (6.3%) while no co-morbidities was found in the remaining 14 cases(17.5%). Regarding the patient's outcome 7 patients died (8.7%) while 24 patients (30%) suffered from different disabilities including epilepsy visual loss ,hearing loss ,cerebral palsy and

cerebellar affection ,in the rest of the patients 49 (61.3 %) were normal at time of discharge but follow up of patients wasn't available.

Unremarkable CT findings were found in the majority of cases (75 cases) while the remaining cases (5 cases) showed patchy ill defined areas of hypodensity that was correlated with MRI and clinical manifestations and diagnosed as encephalitis (3 cases), diffuse cerebral edema manifested as loss of gyral pattern and ventricular effacement (2 cases). (Table.2).

The most prevalent MRI results encountered in this study were described in (**Table.3**).

Table 2.01 minuings of COVID patients.			
CT findings	Number	Percentage	
Unremarkable study	75	93.7%	
patchy ill defined areas of	3	3.7%	
hypodensity			
diffuse cerebral edema	2	2.6%	

 Table 2 .CT findings of COVID patients:

MRI findings	Number	Percentage %
bilateral or unilateral patchy	23	28.8
cortical & subcortical areas of		
abnormal signal (clinically		
diagnosed as Encephalitis)		
Cerebral edema	18	22.5
ADEM	17	21.3
Vasculitis /Lacunar infarction	11	13.7
Normal MRI	7	8.7
PRES	3	3.8
Venous thrombosis	1	1.2
Total	80	100%

 Table 3 .MRI manifestations of COVID

In the current study the most common findings was either bilateral or unilateral patchy cortical & subcortical areas of abnormal signal (low T1SI ,high T2WI and FLAIR SI), patchy pattern of enhancement & in post contrast ,some lesions show hemorrhagic changes and they were diagnosed as encephalitis (23 cases ---38.8%)(Fig. 1), cerebral edema (18 cases ----22.5%) either diffuse and appeared as effacement of cortical sulci and compression on the ventricular system or localized as areas of abnormal low T1 ,high T2 and

FLAIR signal ,some show diffusion restriction but no enhancement, ADEM (17 cases ----21.3) (Fig.2) appeared as subcortical areas of high T2 and FIAIR signal some show enhancement & diffusion restriction , vascultis/lacunar infarcts (11---13.7) (Fig.3), normal radiological findings were recognized in 7 cases (8.7), PRES were noted in 3 cases ---3.8 % as cortical and subcortical patches of abnormal low T1WI and high T2WI with no significant enhancement or restricted diffusion & venous thrombosis noted in 1 case 1.2% (Fig. 4).



Fig 1.Axial a)T1, b)T2, C)FLAIR &d) post contrast respectively show Bilateral patchy areas of aberrant intensity of signal in both the cortical and subcortical parts of the frontal lobes. of gyral FLAIR with low signal in T1 and strong signal in T2WI and patchy pattern of enhancement in post contrast study and mild enhancement of the overlying meninges. The lesions seen at right frontal regions show hemorrhagic changes, (encephalitis).



Fig. 2.:A &B) Axial FLAIR demonstrates multiple bilateral patches in occipito-parietal areas with cortical and subcortical locations show aberrant signal intensity., high signal intensity (ADEM).



Fig.3. A) & B) axial FLAIR of the brain shows white matter patches of abnormal high SI (vasculitis)



Fig 4 a), B) & C) axial T1 , T2 & FLAIR respectively show loss of right transverse signal void with abnormal high SI within D) MRV shows non opacified right transverse & sigmoid sinuses venous thrombosis

Discussion

Earlier on in the pandemic of COVID-19, children appeared to be less affected by the illness than adults were, usually exhibiting no symptoms or very minor ones , as the pandemic spread, more severe cases appeared. (Lindan et al., 2021)

In the current study, the most common presenting symptom was convulsions (36%), followed by dizziness(22.5%) then vertigo, nausea& vomiting (25.2%) and headache (16.3%).

In the study conducted by Beril Dilber et all ,The most prevalent reporting manifestations was a headache and found in 88 out of 382 patients(23%),13 of them were hospitalized ,while seizures were detected in 18 patients only (4.7%). (**Dilber et al.**, **2021a**)

Our study is consistent with the research done by Mohammad Kurd et all & also with the study of james et all , both described convulsions as the main presenting symptom of neuro-covid in pediatric age group. (**Kurd et al., 2021**)

Most of the patients were between 10- 15 years old , this comes in concordance with Beril diber who found that the majority of patients aged between 10 -17 years old (34.2%) .(**Dilber et al., 2021**).

Also in study done by Antoon et all, the most affected age group by neurological complications was between 12-18 years old.

(Antoon et al., 2022a)

In this study The most common MRI findings encountered in this study were either bilateral or unilateral patchy cortical & subcortical areas of abnormal signal (clinically diagnosed as encephalitis)

64 (34%) of the 187 kids included in Govil-Dalela & Sivaswamy's meta-analysis using MIS-C had symptoms that may have been meningitis or encephalitis, which is in agreement with our study . (Govil-Dalela & Sivaswamy, 2021)

O'loughlin et al., performed a study 43 children and the results were as on following : (12 individuals) with acute hemorrhagic or ischemic strokes. (15)individuals) with severe encephalopathy, (8 individuals) with ADEM and Acute Central Nervous System Infection, (4 individuals) with Guillain-Barre syndrome, (4 individuals) with acute fulminant cerebral edema and (20 individuals) with MIS-C.(O'loughlin et al., 2021)

In a research by Palabiyik et al, the most prevalent finding was reversible splenial lesions syndrome (RESLES) appeared as an oval area of temporary diffusion restriction. In 43% of the instances, it was noted and were absent from the follow up studies after initiation of treatment . Other findings were acute hemorrhagic necrotizing encephalomyelitis, ADEM-like lesions & Guillain-Barrie syndrome.(Palabiyik et al., 2021)

In the study of COVID-19 and Acute Neurologic sequences in Children , deaths were reported in 1.8% of patients (19 out of 97 patient) while in our study it was in 8.7% of patients)(**Stafstrom, 2022**), while in a study of long term effects of COVID depression, anxiety, impaired cognition, malaise, headache, joint and muscular pain, and sleep difficulties were found .(**Antoon et al., 2022b**)

Conclusion: neurological findings of COVID significantly vary from mild to fatal complication , neurological imaging study showed be enrolled within the protocol of COVID work up, mainly MR **Study limitation**

Study limitation

In this study several patients suffered from various disabilities at time of discharge but lack of long term follow up was one of the limitations of this study.

Abbreviation list

• COVID-19-----Coronavirus disease 2019,

- SARS-CoV-2-----severe acute respiratory syndrome corona virus 2
- MIS-C -----pediatric multi system inflammatory syndrome temporally associated with COVID-19
- ACE2-----angiotensin-converting enzyme 2
- CNS-----central nervous system
- ADEM -----acute disseminated encephalomyelitis

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80 patients with past or present history of COVID-19 infection who presented with neurologic/ neuropsychiatric symptoms between April 2021 and May 2022.

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Fig.S1. Study flowchart