Postacute/Long COVID in Pediatrics

Development of a Multidisciplinary Rehabilitation Clinic and Preliminary Case Series

Amanda K. Morrow, MD, Rowena Ng, PhD, Gray Vargas, PhD, Dasal Tenzin Jashar, PhD, Ellen Henning, PhD, Nika Stinson, PT, DPT, and Laura A. Malone, MD, PhD

Abstract: The long-term sequelae after SARS-CoV-2 infections in children is unknown. Guidance is needed on helpful models of care for an emerging subset of pediatric patients with postacute/long COVID who continue to experience persistent symptoms after initial COVID-19 diagnosis. Here, we describe a pediatric multidisciplinary post–COVID-19 rehabilitation clinic model as well as a case series of the initial cohort of patients who presented to this clinic. A consecutive sample of nine patients (pediatric patients <21 yrs of age) who presented to our clinic are included. The most common presenting symptoms were fatigue (8 of 9 patients), headaches (6 of 9), difficulty with schoolwork (6 of 8), "brain fog" (4 of 9), and dizziness/lightheadedness (4 of 9). Most patients had decreased scores on self-reported quality-of-life measures compared with healthy controls. In the patients who participated in neuropsychological testing, a subset demonstrated difficulties with sustained auditory attention and divided attention; however, most of these patients had preexisting attention and/or mood concerns. There were also some who self-reported elevated depression and anxiety symptoms. Pediatric patients with postacute/long COVID may present with a variety of physical, cognitive, and mood symptoms. We present a model of care to address these symptoms through a multidisciplinary rehabilitation approach.

Key Words: Pediatric Rehabilitation, Postacute COVID Syndrome, Long COVID, SARS-CoV-2

(*Am J Phys Med Rehabil* 2021;100:1140–1147)

The COVID-19 pandemic has affected more than 184 million people worldwide, causing almost 4 million deaths. Reports from the American Academy of Pediatrics and Children's Hospital Association state that there are more than 4 million pediatric cases of COVID-19, representing approximately 14.2% of the cases in the United States.[1] These pediatric cases result in hospitalization rates between 0.1% and 1.9% and death in up to 0.03%.[1] Although children with SARS-CoV-2 are typically asymptomatic or present with mild symptoms acutely,[2] there are subpopulations with higher risk of severe presentations.[3] Most publications in the literature that describe pediatric patients focus on acute manifestations of the SARS-CoV-2 infection and hospitalization considerations,[3–10] such as multisystem inflammatory syndrome (MIS-C) or pediatric inflammatory multisystem syndrome.[11–15]

As we learn more about the sequela of SARS-CoV-2 infections, evidence is growing that a cohort of patients continue to have persistent symptoms long after their acute presentations. These patients have been termed "long-haulers" or diagnosed with "long-COVID" or "postacute COVID syndrome."[16–21] Some of the symptoms of postacute/long COVID in adults include fatigue, muscle weakness, shortness of breath, sleep difficulties, anxiety, and depression. Most articles describe these symptoms in adults that were hospitalized during their acute infection,[22–24] but we know that hospitalization rates among children with SARS-CoV-2 infection remain low, which may lead to an underrecognition of this syndrome for pediatric patients. A recent survey study found that 42.6% of pediatric patients experienced at least one persistent symptom more than 60 days from initial infection despite only 4.7% of the patients having been hospitalized.[25] Postacute/long COVID may be a significant concern in the pediatric population even in patients who do not require hospitalization.[25,26] The pathophysiology underlying the symptoms of postacute/long COVID is not yet understood, nor do we know whether certain risk factors predispose children or adults to these syndromes. Given the varied presentations and symptoms, it is possible that postacute/long COVID is multifactorial in nature.

As a result of this need, we have developed a multidisciplinary Pediatric Post COVID-19 Rehabilitation Clinic at the Kennedy Krieger Institute to serve pediatric patients with persistent symptoms after initial COVID-19 infection. Here, we describe the structure of this clinic and clinical approach to this patient population and share a case series of an initial cohort of patients.

CLINIC STRUCTURE

The Post COVID-19 Rehabilitation Clinic provides a multidisciplinary rehabilitation approach that addresses medical, psychosocial, and cognitive concerns with a goal to improve patients' overall functioning to better participate in day-to-day tasks, physical activity, and schooling. Specific symptoms are addressed in the context of additional psychosocial and environmental factors that may affect overall quality of life.

The multidisciplinary team consists of medicine (neurology and pediatric rehabilitation medicine), physical therapy, behavioral psychology, neuropsychology, and social work. Assessments are performed in an outpatient clinical setting, and cases are discussed among team members to provide comprehensive recommendations.

From the Kennedy Krieger Institute, Baltimore, Maryland (AKM, RN, GV, DTJ, EH, NS, LAM); Department of Physical Medicine and Rehabilitation, Johns Hopkins School of Medicine, Baltimore, Maryland (AKM, LAM); Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, Maryland (RN); and Department of Neurology, Johns Hopkins School of Medicine, Baltimore, Maryland (LAM).

All correspondence should be addressed to: Laura A. Malone, MD, PhD, 707 N Broadway, Rm G-04, Baltimore, MD 21205.

Financial disclosure statements have been obtained, and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article.

ISSN: 0894-9115
DOI: 10.1097/PHM.0000000000001896

Medical

The medical assessment includes evaluations by neurology and pediatric rehabilitation medicine. History and physical examinations are performed including a full neurologic examination and a mobility evaluation. A 10-min standing tolerance test is performed to evaluate for orthostatic intolerance (OI).[27] Information is collected including timing and characterization of initial diagnosis of COVID-19, previous diagnostic workup and treatments, and persistent symptoms. Physicians provide therapeutic recommendations to address specific symptoms while considering how symptoms may be interconnected as part of the postacute/long COVID syndrome. If there are any concerning signs or symptoms that warrant further evaluation, additional diagnostic workup and/or referral to appropriate medical subspecialists is made.

Physical Therapy

Because many patients complain of fatigue and difficulty with physical activity, a formal evaluation is performed by a licensed physical therapist to target therapeutic exercise interventions specific to each patient. Each evaluation includes an assessment for baseline strength using manual muscle testing, range of motion, balance using functional balance grades, and observation of functional mobility and gait. Physical performance and functional capacity are measured using the following measures[28]: time to ascend/descend stairs,[29] 2-min walk test,[30–32] and 30-sec sit to stand.[33]

Behavioral Psychology/Social Work

Given the potential impact of changes in physical symptoms on daily functioning and emotional well-being, a licensed psychologist with specialization in pediatric psychology and a licensed clinical social worker meet with patients and families to support patient and family coping. The social worker discusses family well-being and functioning to ascertain whether additional family support and/or resources could be useful. The psychologist uses a biopsychosocial framework[34] for assessment and intervention, which recognizes the multiple biological, psychological, and social aspects that contribute to the experience of illness. Assessment includes a clinical interview of functioning across a variety of domains including adjustment to medical changes, health-related behaviors (e.g., sleep, appetite, hydration, physical activity), physical symptom management, premorbid mental health concerns, behavioral concerns, and school concerns. In addition to structured measures of mood, anxiety, and quality of life, additional assessment considerations include measures of functional disability (e.g., Functional Disability Inventory[35]) and caregiver perspectives of patients' quality of life (e.g., Pediatric Quality of Life [PedsQL] Inventory–Parent Proxy Report[36]). Consistent with the role of pediatric psychologists in multidisciplinary hospital-based clinics, information is shared with the clinic team to inform broader team recommendations.[37,38] Brief targeted intervention is also provided in clinic including psychoeducation about relevant topics, facilitation of problem solving, and brief cognitive-behavioral or other therapeutic techniques. Interventions are individualized and based on presenting concern. Referrals for ongoing outpatient or more intensive services are also provided as warranted.

Neuropsychology

As part of a multidisciplinary rehabilitation service model, neuropsychological consultation plays an essential role in facilitating treatment and educational planning. A neuropsychological screening protocol was developed to provide a brief assessment of cognitive domains thought to potentially be affected by COVID-19. This was based on previous studies of adults with postacute/long COVID and patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and concussion/mild traumatic brain injury.[39] Our test battery was designed for implementation for either in-person or telehealth (audio-video) visits to accommodate families seeking clinical services from out of town. As suggested by the growing demand for telehealth services,[40] a flexible model of neuropsychological care is considered necessary during this medical crisis. Behavioral screeners were included to determine the need for more in-depth characterization of externalizing/internalizing symptoms. This protocol is administered by neuropsychologists or psychology associates supervised by neuropsychologists. Based on the patient's developmental functioning, presenting concerns, sensory/motor deficits, and behavioral compliance, alternative or additional cognitive measures may be given.

METHODS

Cohort

Detailed in this case series are the first nine patients that presented to our multidisciplinary Pediatric Post COVID-19 Rehabilitation Clinic at the Kennedy Krieger Institute in Baltimore, Maryland. This retrospective medical record review case series was acknowledged by the Johns Hopkins Medicine Institutional Review Board as exempt research. All patients or guardians provided informed written consent for publication of their case. The cohort included patients younger than 21 yrs who were either local or traveled from other states within the United States. Patients were self-referred. Patients were screened by the clinic directors for a history of SARS-CoV-2 infection. They either had a history of a positive COVID-19 test (nucleic acid test [NAT] or serum antibody test) or an acute clinical presentation consistent with COVID-19. Most of the clinical diagnoses also had a known close exposure to COVID-19 before symptom onset. Patients with a clinical diagnosis were included given limited testing availability in the early phases of the pandemic, especially for those with mild symptoms. Initial evaluations were done via an in-person visit with neuropsychological evaluations (in-person or telehealth) completed within a week after the clinic visit based on the family's availability. Given the elevated reports of severe fatigue, this assessment was scheduled on a separate day to avoid overexerting patients with the multiple clinical visits and tests. Formal statistical tests were not completed because of the small sample size. Information presented is meant to be descriptive in nature.

Assessments

Pediatric quality-of-life assessments were completed by the patients on the day of the initial visit. The PedsQL Version 4.0 Generic Short Form is composed of 15 items across 4 dimensions: physical functioning, emotional functioning, social functioning, and school functioning. In addition to a total

score, there are two summary scores: physical, composed of the physical functioning items, and psychosocial, composed of the emotional, social, and school items. The PedsQL Multidimensional Fatigue Scale is composed of 18 items across three dimensions: general fatigue, sleep/rest fatigue, and cognitive fatigue. The Multidimensional Fatigue Scale is reported as total and the three subscale scores. Published normative values from healthy children for the Generic PedsQL Inventory[41] and Multidimensional Fatigue PedsQL Inventory[42] were used for comparison. In past studies, the PedsQL has demonstrated internal consistency, construct validity, and discriminant validity.[41–44]

The standing tolerance test was completed on the day of the initial visit in the same methodology as described by Roma et al.[27] (2018), which is a modification of the passive standing test of Hyatt et al.[45] Briefly, an automated blood pressure cuff (Dynamap) was placed on the right upper limb, recording blood pressure and heart rate (HR) at 1-min intervals throughout the test. As blood pressure and HR were recorded every minute, the patient was also asked about the severity of orthostatic symptoms on a 0- to 10-point scale. The standing tolerance test was stopped early at the request of the patient or in the event of severe presyncope.

Table 1 details the recommended neuropsychological screening battery as a function of patient's age. Importantly, a semiflexible battery approach was adopted across cases.

RESULTS

Table 2 reports demographic information and symptoms for patients in our clinic. Our patients varied in age between 4 and 18 yrs, with 6 of 9 patients being adolescents. Only one patient was hospitalized during the acute illness and was

TABLE 1. Outpatient neuropsychological screening protocol applied through traditional in-person and novel telehealth assessment models

Cognitive Constructs	3–4 yrs	5–7 yrs	8–15 yrs	16–17 yrs	18+ yrs
Verbal skills	DAS-II Naming Vocabulary	DAS-II Naming Vocabulary (5–6 yrs) or WASI-II Vocabulary (6+ yrs)	WASI-II Vocabulary	WASI-II Vocabulary	WASI-II Vocabulary
Nonverbal reasoning	DAS-II Matrices	DAS-II Matrices (5–6 yrs) or WASI-II Matrix Reasoning (6+ yrs)	WASI-II Matrix Reasoning	WASI-II Matrix Reasoning	WASI-II Matrix Reasoning
Working memory	DAS-II: Digits Forward	DAS-II: Digits Forward	WISC-V: Digit Span	WAIS-IV Digit Span	WAIS-IV Digit Span
Attention	—	TEA-Ch Score (6+ yrs)	TEA-Ch Score and Score DT	CMS Sequences (16 yrs), BTA (17 yrs)	TEA Elevator Counting and Elevator Counting With Distractions
Processing speed	—	NEPSY-II Inhibition–Naming	Oral SDMT	Oral SDMT	Oral SDMT
Executive function	—	NEPSY-II Inhibition and Switching	DKEFS Verbal Fluency	DKEFS Verbal Fluency	DKEFS Verbal Fluency
Verbal memory	—	ChAMP List	ChAMP List	ChAMP List	CVLT-3
Performance validity indicator	—	MVP Verbal	MVP Verbal	MVP Verbal	MVP Verbal

Questionnaires (Caregiver-Report)	3–4 yrs	5–7 yrs	8–15 yrs	16–17 yrs	18+ yrs
Psychosocial and behavior	Conners Early Childhood (2.5+ yrs)	Conners Early Childhood (5 yrs), CBRS (6+ yrs)	CBRS	CBRS	BASC-3, CAARS
Executive functioning	BRIEF-P	BRIEF-P/BRIEF-2	BRIEF-2	BRIEF-2	BRIEF-2/BRIEF-A
Behavioral screeners	—	ADHD-RS-5 (5+ yrs), VBRS ODD/CD (6+ yrs), RCADS–Anxiety, Depression, OCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), VBRS ODD/CD (6+ yrs), RCADS–Anxiety, Depression, OCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), VBRS ODD/CD (6+ yrs), RCADS–Anxiety, Depression, OCD subscales (6+ yrs)	ADHD-RS-5 (5+ yrs), VBRS ODD/CD (6+ yrs), RCADS–Anxiety, Depression, OCD subscales (6+ yrs)

Questionnaires (Self-report)	3–4 yrs	5–7 yrs	8–15 yrs	16–17 yrs	18+ yrs
Anxiety	—	RCMAS-2 (6–7 yrs), MASC-2 (8+ yrs)	RCMAS-2 (6–7 yrs), MASC-2 (8+ yrs)	RCMAS-2 (6–7 yrs), MASC-2 (8+ yrs)	BAI
Depression	—	CDI-2 (7–17 yrs), BDI-2 (17+ yrs)	CDI-2 (7–17 yrs), BDI-2 (17+ yrs)	CDI-2 (7–17 yrs), BDI-2 (17+ yrs)	BDI-2

ADHD-RS-V, ADHD Rating Scale; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BASC-3, Behavior Assessment System for Children, Third Edition; BRIEF-A, Behavior Rating Inventory of Executive Function Adult; BRIEF-P, Behavior Rating Inventory of Executive Function Preschool; BRIEF-2, Behavior Rating Inventory of Executive Function 2nd Edition; BTA, Brief Test of Attention; CVLT-3, California Verbal Learning Test, Third Edition; ChAMP, Child and Adolescent Memory Profile; CDI-2, Children's Depression Inventory, Second Edition; CMS, Children's Memory Scale; CAARS, Conners Adult ADHD Rating Scales; CBRS, Conners Behavior Rating Scale; DKEFS, Delis Kaplan Executive Function System; DAS-II, Differential Abilities Scale, Second Edition; NEPSY-II, Developmental Neuropsychological Assessment; MVP, Memory Validity Profile; MASC-2, Multidimensional Anxiety Scale for Children, Second Edition; RCADS, Revised Children's Anxiety and Depression Scale; RCMAS-2, Revised Children's Manifest Anxiety Scale, Second Edition; SDMT, Symbol Digits Modalities Test; TEA-Ch, Test of Everyday Attention for Children; VBRS ODD/CD, Vanderbilt Behavior Rating Scale Oppositional Defiant and Conduct Problems; WASI-II, Wechsler Abbreviated Scale of Intelligence, Second Edition; WAIS-IV, Wechsler Adult Intelligence Scale, Fourth Edition; WISC-V, Wechsler Intelligence Scale for Children, Fifth Edition.

diagnosed with MIS-C. He is the youngest patient presented here, and his symptoms had mostly resolved by the time when he was seen in our clinic. The remainder of the patients were children and adolescents in the community with relatively mild acute illnesses who developed persistent symptoms after their acute COVID-19 infection. We ascertained patients' primary complaints through an intake questionnaire and clinical interview on the initial visit where patients/parents described symptoms in their own words (Table 2). Postacute/long COVID symptoms were varied, but we saw most patients complaining of fatigue (8 of 9) and headaches (6 of 9). Patients also described cognitive difficulties or "brain fog" (4 of 9), school concerns (6 of 8), and dizziness/lightheadedness (4 of 9). Only three patients reported cardiopulmonary complaints as one of their postacute symptoms or most important concern at the visit; however, on review of systems, a majority of our patients (5 of 9) did have at least one persistent cardiopulmonary symptom at the time of initial clinic visit. Reported symptoms included chest pain/pressure/tightness (4/5), palpitations (2/5), and shortness of breath (4/5). Of the five patients with persistent symptoms, workup by other providers before presentation in our clinic included electrocardiogram (3 of 5), chest radiograph (4 of 5), echocardiogram (1 of 5), cardiac enzymes (1 of 5), Holter monitor (1 of 5), cardiac stress test (1 of 5), pulmonary function test (1 of 5), and peak flow meter (1 of 5). All testing was reportedly normal with the exception of one patient with

TABLE 2. Patient characteristics

Patient Number	Age	Sex	Preexisting Conditions	COVID-19 Diagnosis Details	Acute Hospitalization	Time Since COVID-19 Diagnosis	Postacute Symptoms	Most Important Concern	School Concerns
1	18 yrs	F	Type 1 diabetes, anxiety, depression	Clinical diagnosis with known exposure	N	8 mos	Fatigue, muscle weakness, dizziness, headaches, difficulty concentrating, OI, nonepileptic seizures	Nonepileptic seizures	N
2	12 yrs	F	None	Clinical diagnosis with known exposure	N	2 mos	Panic attacks, trouble focusing and prioritizing ("brain fog"), abnormal movements, fatigue	"Brain fog" and mental health	Y
3	4 yrs	M	Speech delay	COVID-19 NAT+	Y (MIS-C)	4 mos	None	Developmental delays and spells concerning for seizure	N/A
4	15 yrs	F	Anxiety, asthma, seasonal allergies	COVID-19 NAT+	N	7 mos	Trouble breathing, dizziness, fatigue, lung pain, parosmia, anxiety	Mental health/ anxiety	Y
5	17 yrs	F	Dyslexia, seasonal allergies	Clinical diagnosis	N	11 mos	Brain fog, functional neurological disorder, headaches, fatigue, cognitive issues, pain, deconditioning, OI	Autonomic dysfunction	Y
6	15 yrs	F	None	COVID-19 NAT+	N	7 mos	Fatigue, shortness of breath, headaches, OI	Fatigue and shortness of breath	Y
7	9 yrs	M	Eosinophilic esophagitis, speech delay (resolved)	Clinical diagnosis with known exposure	N	11 mos	Headaches, fatigue, anxiety, sensory issues, "brain fog," lymphadenopathy	Headaches and "brain fog"	Y
8	13 yrs	F	Sensory processing disorder, vitiligo, fructose malabsorption, scoliosis	COVID-19 antibody+	N	12 mos	Abdominal pain, fatigue, myalgias, headaches, facial flushing, rashes/hives	Abdominal pain	N
9	9 yrs	M	Migraine, multiple concussions, sensory integration disorder	COVID-19 NAT+	N	3 mos	Headaches, chest pain/ tightness, fatigue, diarrhea, sore throat, swollen glands, deconditioning	Chest tightness/ pain	Y

Patient demographic information and details on the acute COVID-19 diagnosis and illness along with presenting symptoms are described. If patients reported declining school performance (e.g., grades) and/or difficulty completing schoolwork, they are described as having school concerns in the table. Note that only one patient described was hospitalized with MIS-C, and this child had no postacute concerns but rather an evaluation was completed for preexisting developmental delays. He was also the youngest patient seen in clinic and therefore some more subtle complaints may have been missed.

N/A, not applicable; N, no; Y, yes.

peak flow meter measurement who had an improvement in peak flow after bronchodilator use. Of note, these five patients did not include the one patient with a history of MIS-C (patient 3) as this patient had complete resolution of all cardiopulmonary symptoms at the time of our clinic evaluation. Patient 3 did have previous abnormal chest imaging and echocardiograms related to his MIS-C diagnosis.

We report testing and questionnaire results from the patients in Table 3. The standing tolerance test results are reported as symptom progression and HR changes from supine to standing to screen for postural orthostatic tachycardia syndrome (POTS). Criteria for a diagnosis of POTS for patients younger than 20 yrs requires worsening of orthostatic symptoms and a HR increase of ≥40 beats per minute (bpm) or an upright HR of at least 120 bpm,[27] although more recent studies have recommended using an HR increase of ≥30 bpm as a cutoff.[46] Six of seven of our patients who completed the standing tolerance test experienced symptoms and >30 bpm change in HR with two of the patients with a >40-bpm change. Any patient that was close to meeting the diagnostic criteria was referred to a POTS specialist for diagnosis and management. In addition, we assessed how the constellation of symptoms children were experiencing affected their quality of life. We found that most patients reported substantial impact on their quality of life, as assessed by the self-report PedsQL Core and Fatigue questionnaires (Table 3). Healthy control published data are reported for comparison on the self-report core scale (n = 5480)[41] and fatigue scale (n = 52).[42]

Table 4 provides an overview of the testing results for the neuropsychological evaluations. Of note, one patient could not complete testing because of scheduling difficulties and interstate telepsychological practice regulations. The neuropsychological screening battery was not administered to two of the remaining eight patients referred for testing because of difficulty engaging in testing or developmental level. Testing was discontinued for one patient shortly after the session began because of significant anxiety and mood regulation difficulties. Most patients who participated in neuropsychological testing presented with intact verbal ability, visual reasoning, executive functioning (including working memory), processing speed, and verbal memory. Half or more of these patients exhibited difficulties with sustained auditory attention and divided attention, and many had elevated parent and self-report of inattention and psychiatric symptoms. However, it is important to note that the majority of these patients had preexisting attention, mood, and/or anxiety concerns. Therefore, the impairments observed on testing and symptoms reported on rating scales cannot be directly attributed to the long-term effects of COVID-19 alone. These results are currently presented qualitatively because of sample size. It is expected that a larger

TABLE 3. Results of standing tolerance test and PedsQL self-report questionnaires

Patient Number	Standing Tolerance Test (Changes Reported From Supine to Standing)	PedsQL Core			PedsQL Fatigue			
		Total	Physical Subscale	Psychosocial Subscale	Total	General Subscale	Sleep/Rest Subscale	Cognitive Subscale
1	Worse symptoms (dizziness) HR increase 36 bpm	51.1	21.9	66.7	25	20.8	16.7	37.5
2	Worse symptoms (headache and dizziness) HR increase 35 bpm	58.7	56.3	60	56.9	50	70.8	50
3	—	—	—	—	—	—	—	—
4	Worse symptoms (dizziness and fatigue) HR increase 33 bpm	48.9	31.3	58.3	36.1	37.5	4.2	66.7
5	N/A previously diagnosed with POTS via tilt-table test	18.5	0	28.3	26.4	4.2	41.7	33.3
6	Worse symptoms (weakness and headache) HR increase 51 bpm	55.4	43.8	61.7	43.1	33.3	25	70.8
7	Worse symptoms (dizziness, headache, fatigue, blurry vision) HR increase 32 bpm	—	—	—	—	—	—	—
8	Stable symptoms HR increase 29 bpm	85.9	81.3	88.3	88.9	91.7	95.8	79.2
9	Worse symptoms (headache and fatigue) HR increase 44 bpm	52.2	31.3	63.3	—	—	—	—
Healthy subjects (published data[41,42])		83.8 ± 12.7	87.5 ± 13.5	81.9 ± 14.1	80.5 ± 13.3	85.3 ± 15	75 ± 18.8	81.1 ± 17.4

The norms for healthy subjects from published data are reported for the PedsQL questionnaires for comparison. For analysis, items are reverse scored and linearly transformed to a 0- to 100- point scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0). Higher values on the PedsQL represent better health-related quality of life. Of note, patient 3 was too young to complete the self-report questionnaire. Because of a clerical error, patient 7 did not receive questionnaires to fill out during initial evaluation and patient 9 only received one of the questionnaires for which there are missing data.

TABLE 4. Neuropsychological and psychosocial functioning of initial clinical cohort evaluated through the pediatric post–COVID-19 rehabilitation clinic

Cognitive Domain	Patients With Impaired Performance
Verbal skills	0 of 4
Nonverbal reasoning	0 of 4
Working memory	0 of 5
Attention	
Sustained auditory attention	3 of 5
Divided attention	2 of 4
Processing speed	0 of 5
Executive functioning	0 of 5
Verbal memory	0 of 5
Validity	0 of 5

CBRS Caregiver-Report Inventories	Patients With Elevated Symptoms
ADHD predominantly inattentive	4 of 4
ADHD predominantly hyperactive/impulsive	1 of 4
Major depressive disorder	3 of 4
Generalized anxiety disorder	3 of 4
Perfectionistic/compulsive behaviors	2 of 4
Physical symptoms	4 of 4

Self-report Inventories	Patients With Elevated Symptoms
CDI-2 low mood composite	2 of 4
MASC-2 anxiety composite	2 of 4

Area of Concern	Patients With Difficulties Before COVID-19 Illness
Attention/hyperactivity/impulsivity	5 of 8
Mood and/or anxiety concerns	6 of 8
Neurodevelopmental concerns	3 of 8[a]

Impairment on performance-based cognitive measures are defined as scaled score <6, standard score <80, *t* score <37, *z* score <−1.33, or percentile <9th. Elevated symptoms on caregiver- or self-report inventories are defined as *t* score >65. Pre–COVID-19 behavioral and cognitive concerns represent areas of difficulty that patients displayed before the viral infection, based on caregiver and/or self-report.

[a] Neurodevelopmental concerns include developmental delays. Two reported speech/language delays and one reported motor delays paired with early sensory processing concerns.

CBRS, Conners Behavior Rating Scale; CDI-2, Children's Depression Inventory, Second Edition; MASC-2, Multidimensional Anxiety Scale for Children, Second Edition.

sample size will be established in the future as additional patients are evaluated, which will allow for quantitative analysis.

DISCUSSION

Here, we describe the multidisciplinary clinic structure, presenting symptoms and concerns, and preliminary results from standardized assessments from patients and families in our Pediatric Post COVID-19 Rehabilitation Clinic at the Kennedy Krieger Institute. We are finding that there is a subset of pediatric patients with mild acute COVID-19 illness that present with persistent or exacerbated symptoms after their acute illness. Our small case series demonstrates that patient symptoms are varied but many complain of fatigue, headaches, cognitive difficulties, and OI. On neuropsychological testing, patients are demonstrating impaired performance primarily with attention as opposed to other domains, such as executive functioning or working memory, which has been reported in the adult literature.[39,47] Elevated anxiety and depression symptoms are also commonly reported. It is also important to note that many of the patients in our cohort had a history of attention and/or mood concerns, although none of the patients reported taking medications to address these concerns before their COVID-19 diagnosis. Therefore, it is possible that these anxiety, attention, and/or mood concerns are not directly related to disease mechanisms associated with COVID-19. Furthermore, the stressors related to COVID-19, such as isolation and virtual schooling, could also have triggered or exacerbated mood and anxiety concerns. In addition, for some, we have found that the reported postacute/long COVID symptoms are significantly affecting their quality of life.

There are minimal to no data on how to optimally treat postacute/long COVID in children. Our management strategies are based on other chronic conditions with overlapping symptoms, including ME/CFS, OI/POTS, and concussion/mild traumatic brain injury. We consider medical, physical, behavioral, environmental, and educational interventions that may be helpful. Below are examples of our approach to some of the most common complaints seen in our clinic.

Fatigue

Causes of fatigue are multifactorial and other known medical causes of fatigue are considered. Timing and characterization of fatigue are determined as patients with ME/CFS often describe fatigue as disabling, worse after physical activity, and not improved with sleep.[48] Sleep disturbances are addressed through environmental and behavioral interventions to improve sleep hygiene. Additional treatment options to improve fatigue are discussed including cognitive behavioral therapy and graded exercise therapy, which have been studied in patients with ME/CFS.[49] Subsymptom threshold aerobic exercise has also been shown to be beneficial in patients with persistent symptoms after concussion/mild traumatic brain injury.[50]

Orthostatic Intolerance

Orthostatic intolerance is an abnormal autonomic response with symptoms developing in an upright posture that improve in the supine position.[51] In patients with complaints of dizziness or lightheadedness or who experience symptoms with the standing tolerance test consistent with OI or POTS, initial recommendations include increasing dietary intake of fluids and salt, compression garments, physical countermeasure maneuvers such as leg crossing and muscle pumping, and exercise training with the goal of expanding blood volume.[51,52] A daily routine including maintaining a regular sleep schedule and management of stress and/or anxiety is also important.[53] The Levine Protocol[52] and CHOP Modified Dallas Protocol[54] are examples of exercise protocols developed for

OI/POTS. They involve starting with horizontal exercise and slowly increasing duration and intensity of exercise while incorporating upright positioning as tolerated.[52] Referrals to outpatient physical therapy may be made to supervise an individualized graded exercise program and help with reconditioning and symptom management.

Headaches

Characterization of headaches is made based on patient history. Additional brain imaging may be performed if there are any abnormal findings on neurologic examination or if there is concern for secondary causes of headache.[55] Lifestyle modifications are recommended including adequate hydration, avoidance of triggers, optimizing sleep patterns, eating regular meals, stress management, and maintaining physical activity,[55,56] which overlap with some of the previously mentioned recommendations for ME/CFS and OI/POTS. If needed, additional pharmacologic management may be recommended including preventative and abortive medications with education to prevent rebound headaches from overuse of abortive agents.[55]

Cognitive Dysfunction

Targeted neuropsychological testing is performed to identify any areas of cognitive weakness, mood, and behavioral factors in need of further evaluation/treatment. Recommendations are given to optimize day-to-day cognitive functioning and school participation and performance and to address mood or behavioral difficulties as necessary. Similar to approaches outlining return to school after concussion/mild traumatic brain injury,[57] our team may recommend a gradual transition back to learning with the potential need for temporary academic adjustments or environmental accommodations if symptoms are exacerbated in the school setting. Examples of adjustments include planned rest breaks, increased test taking time, and/or limiting amount of homework assignments as patients are building up their tolerance for academic activity. If there are concerns for ADHD, appropriate treatment recommendations are made including behavioral therapy and medication management.[58]

Mood/Psychological Symptoms

Patients are screened for comorbid mood and psychological symptoms, which may exacerbate other symptoms and limit recovery potential. Anxiety and depressive symptoms commonly co-occur in patients with ME/CFS,[58] OI/POTS,[53] and concussion.[59] For mood/affective symptoms, initial symptoms are addressed by our psychologist in clinic and patients may be referred for outpatient psychotherapy for additional coping and support as well as psychiatry if needed for medication management of significant mood symptoms.

Limitations

There are several limitations to our study including its retrospective and descriptive nature. Given the small sample size, statistical analyses could not be performed. Patients were self-referred to our clinic, which may have resulted in selection bias. We were unable to estimate the prevalence of developing postacute/long COVID in children after SARS-CoV-2 infection because we only had data available for those presenting to our clinic. Future studies are needed to address this important question. Only one of our patients was hospitalized for initial infection, and at this time, we were unable to draw any conclusions regarding long-term implications for patients with more serious infections requiring hospitalization versus those with mild initial symptoms. We decided to include patients with a clinical diagnosis in this case series given limited testing availability in the early phases of the pandemic, especially for those with mild symptoms. Because we included patients both with a positive COVID-19 test and those with a suspicion of COVID-19 diagnosis based on clinical history, we were unable to confirm that all of the reported symptoms and clinical courses were due exclusively to SARS-CoV-2. There is also missing data for some patients who did not complete questionnaires or fully participate in neuropsychological testing. Future studies with larger sample sizes will hopefully be able to address some of these limitations.

CONCLUSIONS

Children with postacute/long COVID may complain of a variety of physical, cognitive, and mood symptoms that impact their overall quality of life and participation in activities. As active research is being pursued to better understand the etiology and mechanisms of disease, our Pediatric Post COVID-19 Rehabilitation Clinic offers a multidisciplinary approach to patient care as we continue to learn more about this condition. Future studies are needed to better characterize the symptoms, clinical course, and syndrome prognosis in addition to guiding personalized treatment recommendations.

ACKNOWLEDGMENTS

The authors thank our patients and clinical staff (our nurse, Sherri Clark, social worker, Bridget Fulford, and clinic coordinators, Sharon Ramos and La'Kendra Davis) for their help in the care of these patients.

REFERENCES

1. Children and COVID-19: state-level data report. Available at: http://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/. Accessed January 25, 2021
2. Dong Y, Mo X, Hu Y, et al: Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;145:e20200702
3. Cruz AT, Zeichner SL: COVID-19 in children: initial characterization of the pediatric disease. *Pediatrics* 2020;145:e20200834
4. Frontera JA, Sabadia S, Lalchan R, et al: A prospective study of neurologic disorders in hospitalized patients with COVID-19 in New York City. *Neurology* 2021;96:e575–86
5. Kim Y, Walser SA, Asghar SJ, et al: A comprehensive review of neurologic manifestations of COVID-19 and management of pre-existing neurologic disorders in children. *J Child Neurol* 2021;36:324–30
6. Lee-Archer P, von Ungern-Sternberg BS: Pediatric anesthetic implications of COVID-19-a review of current literature. *Paediatr Anaesth* 2020;30:136–41
7. Mehta NS, Mytton OT, Mullins EWS, et al: SARS-CoV-2 (COVID-19): what do we know about children? A systematic review. *Clin Infect Dis* 2020;71:2469–79
8. Tsankov BK, Allaire JM, Irvine MA, et al: Severe COVID-19 infection and pediatric comorbidities: a systematic review and meta-analysis. *Int J Infect Dis* 2021;103:246–56
9. Yasuhara J, Kuno T, Takagi H, et al: Clinical characteristics of COVID-19 in children: a systematic review. *Pediatr Pulmonol* 2020;55:2565–75
10. Badal S, Thapa Bajgain K, Badal S, et al: Prevalence, clinical characteristics, and outcomes of pediatric COVID-19: a systematic review and meta-analysis. *J Clin Virol* 2021;135:104715
11. Abdel-Mannan O, Eyre M, Löbel U, et al: Neurologic and radiographic findings associated with COVID-19 infection in children. *JAMA Neurol*. 2020;77:1440–5
12. Lin J, Lawson EC, Verma S, et al: Cytotoxic lesion of the corpus callosum in an adolescent with multisystem inflammatory syndrome and SARS-CoV-2 infection. *AJNR Am J Neuroradiol* 2020;41:2017–9

13. Whittaker E, Bamford A, Kenny J, et al: Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *JAMA* 2020; 324:259–69
14. Zou H, Lu J, Liu J, et al: Characteristics of pediatric multi-system inflammatory syndrome (PMIS) associated with COVID-19: a meta-analysis and insights into pathogenesis. *Int J Infect Dis*. 2021;102:319–26
15. Minocha PK, Phoon CKL, Verma S, et al: Cardiac findings in pediatric patients with multisystem inflammatory syndrome in children associated with COVID-19. *Clin Pediatr (Phila)* 2021;60:119–26
16. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, et al: More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Sci Rep* 2021;11:16144
17. Mendelson M, Nel J, Blumberg L, et al: Long-COVID: an evolving problem with an extensive impact. *S Afr Med J* 2020;111:10–2
18. Marshall M: The lasting misery of coronavirus long-haulers. *Nature* 2020;585:339–41
19. Dani M, Dirksen A, Taraborrelli P, et al: Autonomic dysfunction in 'long COVID': rationale, physiology and management strategies. *Clin Med (Lond)* 2021;21:e63–7
20. Nath A: Long-haul COVID. *Neurology* 2020;95:559–60
21. Logue JK, Franko NM, McCulloch DJ, et al: Sequelae in adults at 6 months after COVID-19 infection. *JAMA Netw Open* 2021;4:e210830
22. Huang C, Huang L, Wang Y, et al: 6-Month consequences of COVID-19 in patients discharged from hospital: a cohort study. *The Lancet* 2021;397:220–32
23. Bellan M, Soddu D, Balbo PE, et al: Respiratory and psychophysical sequelae among patients with COVID-19 four months after hospital discharge. *JAMA Netw Open* 2021;4:e2036142
24. Nalbandian A, Sehgal K, Gupta A, et al: Post-acute COVID-19 syndrome. *Nat Med* 2021; 27:601–15
25. Buonsenso D, Munblit D, De Rose C, et al: Preliminary evidence on long COVID in children. *Acta Paediatr* 2021;110:2208–11
26. Brackel CLH, Lap CR, Buddingh EP, et al: Pediatric long-COVID: an overlooked phenomenon? *Pediatr Pulmonol* 2021;56:2495–502
27. Roma M, Marden CL, Rowe PC: Passive standing tests for the office diagnosis of postural tachycardia syndrome: new methodological considerations. *Fatigue Biomed Health Behav* 2018;6:179–92
28. Moore JL, Potter K, Blankshain K, et al: A core set of outcome measures for adults with neurologic conditions undergoing rehabilitation: a clinical practice guideline. *J Neurol Phys Ther* 2018;42:174–220
29. Zaino CA, Marchese VG, Westcott SL: Timed up and down stairs test: preliminary reliability and validity of a new measure of functional mobility. *Pediatr Phys Ther* 2004;16:90–8
30. Bohannon RW, Wang YC, Bubela D, et al: Normative two-minute walk test distances for boys and girls 3 to 17 years of age. *Phys Occup Ther Pediatr* 2018;38:39–45
31. Bohannon RW, Wang YC, Gershon RC: Two-minute walk test performance by adults 18 to 85 years: normative values, reliability, and responsiveness. *Arch Phys Med Rehabil* 2015;96:472–7
32. Pin TW, Choi HL: Reliability, validity, and norms of the 2-min walk test in children with and without neuromuscular disorders aged 6-12. *Disabil Rehabil* 2018;40:1266–72
33. Gurses HN, Zeren M, Denizoglu Kulli H, et al: The relationship of sit-to-stand tests with 6-minute walk test in healthy young adults. *Medicine (Baltimore)* 2018;97:e9489
34. Engel GL: The clinical application of the biopsychosocial model. *Am J Psychiatry* 1980; 137:535–44
35. Walker LS, Greene JW: The functional disability inventory: measuring a neglected dimension of child health status. *J Pediatr Psychol* 1991;16:39–58
36. Varni JW, Limbers CA, Burwinkle TM: Parent proxy-report of their children's health-related quality of life: an analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL 4.0 Generic Core Scales. *Health Qual Life Outcomes* 2007;5:2
37. Lassen S, Wu Y, Roberts M: Common presenting concerns and settings for pediatric psychology practice, in: *Clinical Practice of Pediatric Psychology.* New York, NY, Guilford Press, 2014:17–31
38. Conroy C, Logan DE: Pediatric multidisciplinary and interdisciplinary teams and interventions, in: *Clinical Practice of Pediatric Psychology.* New York, NY, Guilford Press, 2014:93–108
39. Graham EL, Clark JR, Orban ZS, et al: Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers". *Ann Clin Transl Neurol* 2021; 8:1073–85
40. Rametta SC, Fridinger SE, Gonzalez AK, et al: Analyzing 2,589 child neurology telehealth encounters necessitated by the COVID-19 pandemic. *Neurology* 2020;95:e1257–66
41. Varni JW, Limbers CA, Burwinkle TM: Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL 4.0 Generic Core Scales. *Health Qual Life Outcomes* 2007;5:43
42. Varni JW, Burwinkle TM, Szer IS: The PedsQL Multidimensional Fatigue Scale in pediatric rheumatology: reliability and validity. *J Rheumatol* 2004;31:2494–500
43. Smith SE, Vargas G, Cucchiara AJ, et al: Hemiparesis and epilepsy are associated with worse reported health status following unilateral stroke in children. *Pediatr Neurol* 2015;52:428–34
44. Chan KS, Mangione-Smith R, Burwinkle TM, et al: The PedsQL: reliability and validity of the short-form generic core scales and asthma module. *Med Care* 2005;43:256–65
45. Hyatt KH, Jacobson LB, Schneider VS: Comparison of 70 degrees tilt, LBNP, and passive standing as measures of orthostatic tolerance. *Aviat Space Environ Med* 1975;46:801–8
46. Boris JR, Huang J, Bernadzikowski T: Orthostatic heart rate does not predict symptomatic burden in pediatric patients with chronic orthostatic intolerance. *Clin Auton Res* 2020; 30:19–28
47. Jaywant A, Vanderlind WM, Alexopoulos GS, et al: Frequency and profile of objective cognitive deficits in hospitalized patients recovering from COVID-19. *Neuropsychopharmacol* 2021:1–6. doi:10.1038/s41386-021-00978-8
48. Crawley E: The epidemiology of chronic fatigue syndrome/myalgic encephalitis in children. *Arch Dis Child* 2014;99:171–4
49. White PD, Goldsmith KA, Johnson AL, et al: Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *Lancet* 2011;377:823–36
50. Leddy JJ, Haider MN, Ellis MJ, et al: Early subthreshold aerobic exercise for sport-related concussion: a randomized clinical trial. *JAMA Pediatr* 2019;173:319–25
51. Stewart JM, Boris JR, Chelimsky G, et al: Pediatric disorders of orthostatic intolerance. *Pediatrics* 2018;141:e20171673
52. Fu Q, Levine BD: Exercise and non-pharmacological treatment of POTS. *Auton Neurosci* 2018;215:20–7
53. Anderson JW, Lambert EA, Sari CI, et al: Cognitive function, health-related quality of life, and symptoms of depression and anxiety sensitivity are impaired in patients with the postural orthostatic tachycardia syndrome (POTS). *Front Physiol* 2014;5:230
54. CHOP Modified Dallas Protocol. Available at: http://www.dynainc.org/docs/chop_modified_dallas_pots_exercise_program.pdf. Accessed August 20, 2021
55. Langdon R, DiSabella MT: Pediatric headache: an overview. *Curr Probl Pediatr Adolesc Health Care* 2017;47:44–65
56. Oskoui M, Pringsheim T, Billinghurst L, et al: Practice guideline update summary: pharmacologic treatment for pediatric migraine prevention: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2019;93:500–9
57. Halstead ME, McAvoy K, Devore CD, et al: Returning to learning following a concussion. *Pediatrics* 2013;132:948–57
58. Bould H, Lewis G, Emond A, et al: Depression and anxiety in children with CFS/ME: cause or effect? *Arch Dis Child* 2011;96:211–4
59. Yrondi A, Brauge D, LeMen J, et al: Depression and sports-related concussion: a systematic review. *Presse Med* 2017;46:890–902