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ORIGINAL RESEARCH

Effect of COVID-19 on the care of children with neurometabolic disorders

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has disrupted many aspects of life including the management and treatment of patients with neurometabolic disorders. This questionnaire-based study was planned to know the effect of the COVID-19 pandemic on children with neurometabolic disorders and their caregivers, and also to understand the present and future needs of such children.

Methods: This online cross-sectional survey was conducted in the Department of Pediatrics of the Pediatric Neurology Clinic in a tertiary care hospital. Parents and/or primary caregivers of children diagnosed with neurometabolic disorders were contacted telephonically during the pandemic to respond to our questionnaire. Questions were hosted online to know the health and behavioral profile of children with neurometabolic disorders as well as caregivers' burden.

Results: We contacted 50 families of children with neurometabolic disorders. Of these, 40 families responded to our online survey. The underlying diagnoses were biotinidase deficiency ($n = 12$), mitochondrial encephalopathy ($n = 9$), classical homocystinuria ($n = 6$), cobalamin C defect ($n = 6$), maple syrup urine disease ($n = 3$), phenylketonuria ($n = 3$), and citrullinemia ($n = 1$). During the COVID-19 pandemic, parents preferred home therapy for their children. Most of the children (42.5%) could not avail medical services. A significant number of children had no accessibility to doctors (12.5%) and medicine (40%). Nearly half of them (47.5%) lost their follow-ups with their physician or the hospital. Caregivers felt that their quality of life was affected by the COVID-19 pandemic in several ways, but irrespective of that, 30% of the caregivers felt more confident in controlling the problems related to their child's illness.

Conclusion: There was a significant effect of the COVID-19 pandemic on the health of children with neurometabolic disorders and caregivers' quality of life. Survey-based studies can aid in providing an insight into the needs and complex situations of children with neurometabolic disorders and their parents, even when physical assessments are curtailed.

Keywords: COVID-19, neurometabolic disorders, inborn errors of metabolism, caregivers, children, coronavirus.

Background

Coronavirus disease 2019 (COVID-19) is a global pandemic caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). Since the first reports of the disease from Wuhan, China, the understanding of COVID-19 and its management strategies have been evolving [1]. The disease has emerged as a novel, global public health problem that requires strict personal protection measures, sanitization, and social distancing. The disease has affected millions globally, and its impact has been beyond the acute physical illness (long COVID). To prevent the spread of this rapidly growing disease, nationwide lockdowns were instituted by several countries as an emergency measure. The lockdowns reduced the community mobility and subsequently the virus' transmission. At the same time, the lockdown measures also impacted the healthcare services, lifestyle, and mental health of the people due to unprecedented changes around them and disruption of their daily schedule [2].

Although COVID-19 affected a smaller number of children as compared to adults, and that too with milder disease, it impacted children with underlying predisposition significantly. COVID-19 and the measures instituted to limit its spread have significantly affected the care of children with chronic neurological illnesses [3]. Children with pre-existing neurological disorders are particularly vulnerable because the routine requirements of these children are often neglected in such acute health crises. Also, they may be at a higher risk of acquiring severe COVID-19 illness due to their underlying disorder or its medications, such as corticosteroids and immunosuppressants [4]. As an overwhelming number of patients need intensive care, children with pre-existing neurological impairment may not be a priority for intensive care services. The lockdown also resulted in the closure of therapy and day-care centers, curtailed routine health check-up visits, and limited the availability of medications and/or medical foods [5]. The families faced financial, health, and accessibility-related problems. Children with neurometabolic disorder are one such group of chronic neurological disorders where the healthcare needs were affected by COVID-19 and its associated restrictions. Hence, we conducted this study to explore the effect of the COVID-19 pandemic on children with neurometabolic disorders and the quality of life of their caregivers.

Methods

This cross-sectional survey was conducted in the Department of Pediatrics of the Pediatric Neurology Clinic in a tertiary care hospital. Parents and primary caregivers of children diagnosed with neurometabolic disorders and being followed up in the Pediatric Neurology Clinic were contacted telephonically between August 2021 and September 2021 and asked to respond to the survey via Google Forms. The responses of parents who could not access Google were recorded telephonically. Consent was taken before starting the survey, and the study was approved by the Departmental Review Board of the Institute. A pragmatic anonymized survey was developed. The survey included 38 questions. Questions were designed to bring out the difficulties faced by the children with neurometabolic diseases and their parents during COVID-19 and the related lockdowns between March 2020 and March 2021. The questions were based on the management of daily life routine; special therapy utilization; behavioral problems such as irritation, aggressiveness, school avoidance, and withdrawal from activities and friends; stress level; health issues; accessibility to doctors and medicine; healthcare service utilization such as telecommunication; and caregivers' burden in terms of physical, psychosocial, occupational, and economic impact of caring their children.

The statistical analysis was performed using SPSS software (version 26.0, IBM). Continuous data were presented as mean ± standard deviation, and categorical data were expressed as percentage (%). Z-score test was applied to compare the proportions between two extreme populations (often and never). A p-value of <0.05 was considered statistically significant.

Results

Table 1. Baseline features of children with neurometabolic disorders ($n = 40$)

Variables	**n (%)**
Underlying diagnoses	
• Biotinidase deficiency	• 12 (30%)
• Mitochondrial encephalopathy	• 9 (22.5%)
• Classical homocystinuria	• 6 (15%)
• Cobalamin C defect	• 6 (15%)
• Phenylketonuria	• 3 (7.5%)
• Maple syrup urine disease	• 3 (7.5%)
• Citrullinemia	• 1 (2.5%)
Gender distribution	
• Males	• 23 (57.5%)
• Females	• 17 (42.5%)
Mean age of children (years)	8.9 ± 5.07 years (range: 1.5–21)
Responders	
• Father	• 20 (50%)
• Mother	• 17 (42.5%)
• Grandparents	• 3 (7.5%)
Before lockdown	
• Schooling	• 21 (52.5%)
• Special therapy*	• 9 (22.5%)
COVID-19 infection	
• Children with neurometabolic disorders	• None
• Family members	• 10 (25%)
Effect on health due to COVID-19 and the lockdown	
• Death	• 1 (2.5%)
• Acute worsening	• 2 (5%)
• Without any new adverse effect on health	• 37 (92%)

*Physiotherapy, speech therapy.

We identified and contacted 50 families of children with neurometabolic disorders, who were previously being followed up in the Pediatric Neurology Clinic and their care was discontinued due to the lockdown. Among these, 40 families responded to the online survey. The baseline features are presented in Table 1. Notably, none of the children contracted COVID-19 illness during the study period even though one-fifth of the family members were affected. Before COVID-19, all children were in static health conditions without any major crisis or deterioration based on their underlying diagnosis. During the COVID-19 pandemic, due to the non-availability of medicines, 9 (22.5%) children with neurometabolic disorders had to stop their treatment, and deterioration in health was observed in 2 (5%) cases [biotinidase deficiency: 1 (8.3%) and MSUD: 1 (33.3%)]. One child with cobalamin C defect succumbed to death due to metabolic crisis at a local hospital, and the parents/caregivers were unable to access the doctor at the tertiary care hospital during COVID-19. Other 37 (92%) children with neurometabolic disorders did not report any adverse events. Figure 1 emphasizes the impact of COVID-19 on the management of these children and the measures taken by the parents during the lockdown to continue their care. Parents of three (7.5%) children (with biotinidase deficiency, MSUD, and mitochondrial encephalopathy each) faced more difficulty in maintaining the routine of their children during the COVID-19 pandemic. These parents did not have accessibility to medicines due to which they had to stop the treatment of their children, leading to the worsening of their health conditions. Overall, the care of children worsened in terms of difficulty

Figure 1. Effect of the COVID-19 lockdown on the care of children and measures adopted by parents.

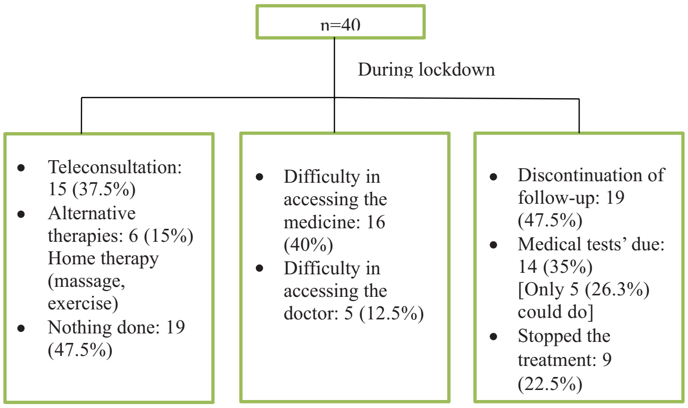
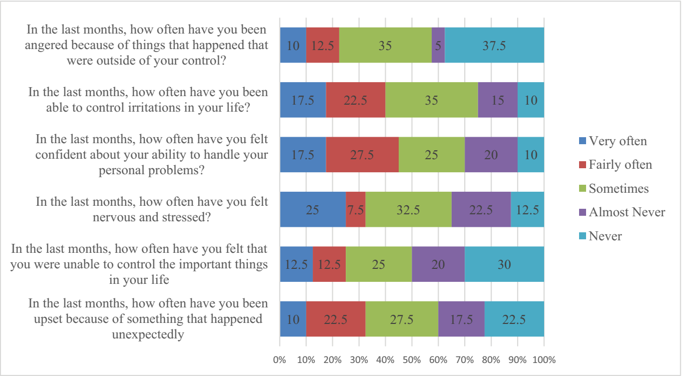


Figure 2. Parental responses regarding the care of their children with neurometabolic disorders.



in accessing the medicines and doctors and discontinuation of follow-up.

Parental perception of the burden and quality of life

Overall, 40% ($n = 16$) of the families faced a financial crisis during the lockdown. This directly or indirectly affected the care of their households and children, especially the affected ones. Figure 2 shows the emotional response of parents with regard to the care of their children with neurometabolic disorders. Majority of the parents felt more confident in controlling their anger (37.5%) and important things (30%) in life related to their child's illness. Table 2 shows the comparison of parental responses as a reflection of caregiver burden felt by the parents regarding their child's illness. Caregivers' quality of life had impacted during the COVID-19 pandemic, but a significant number of caregivers were able to control the important things in their life.

Discussion

The needs of children with neurometabolic disorders are multifaceted. These children need not only continuation of medical therapy but also regular follow-ups with often repeated investigations to prevent neurological deterioration or metabolic decompensations [4, 5]. The COVID-19 pandemic has impacted the care of these children both in the acute phase and in the long term. International patient's organizations such as EURORDIS and NORD revealed that SARS-CoV-2 had detrimental effects

Table 2. Comparison of parental responses as a reflection of caregiver burden felt by the parents regarding their child's illness

	Responses			
Questions	**Often (very often + often)**	**Never (almost never + never)**	**Z-value (two-tailed)**	**p-value**
How often have you been angered because of things that happened that were outside of your control?	9 (22.5%)	17 (42.5%)	−1.9096	0.561
How often have you been able to control irritations in your life?	16 (40%)	10 (25%)	1.4322	0.152
How often have you felt confident about your ability to handle your personal problems?	18 (45%)	12 (30%)	1.3856	0.164
How often have you felt nervous and stressed?	13 (32.5%)	14 (35%)	−0.2364	0.810
How often have you felt that you were unable to control the important things in your life?	10 (25%)	20 (50%)	**−2.3094**	**0.021***
How often have you been upset because of something that happened unexpectedly?	13 (32.5%)	16 (40%)	−0.6977	0.483

Bold represents significant, $p < 0.05^*$, $p < 0.01^{**}$, $p < 0.001^{***}$, and ns for $p > 0.05$.

on the rare disease community worldwide [6, 7]. The COVID-19 pandemic has led to medication shortages, interruption of care, and closed hospitals and has significant concern regarding its impact on the present and future management of rare diseases [8]. Our study highlights that none of the children in our cohort experienced COVID-19 illness, probably as a result of the lockdown and cautious measures by the parents. Yet, the disruption of their routine and care was significant. The parents had to resort to additional measures to ensure the continuum of care, including availing of telemedicine consultation and home therapies like massage and exercises. Literature also suggests that home therapies were an alternate taken up by the parents of patients with lysosomal storage disorder. Parents had anxiety and fear of the ongoing pandemic, so they avoided visits to the hospital and adopted home therapies as an alternate [9]. Disruption of daily routines including schooling and visits for special therapies was significant in our study. This was partly due to the lockdown but also due to the fear of exposure to COVID-19 infection. During the COVID-19 lockdown, cases of delayed access to hospital care due to COVID fear were reported from Italy [8, 9]. We also found that the cost and non-availability of medicines for children with neurometabolic disorder contributed to discontinuation of treatment in nearly one-fourth of our cases, resulting in worsening of their health. During the COVID-19 lockdown, a -51.2% decline in pharmacy mobility was observed across India [2]. The results of our study are in line with a two MetabERN survey-based study done on IEM patients to check the impact of COVID-19. The patient organizers found that $>50\%$ of IEM patients had discontinuation of care due to not getting medicine on time and lost follow-ups [10, 11]. Although we did not study the impact of COVID-19 on the diagnosis of neurometabolic disorders, studies have shown that newer diagnosis of IEM was delayed because of disruption in the number of working days in the hospitals during COVID. A study from Brazil reported a 34% reduction in the diagnosis of new IEM patients from period 1 (March 1, 2019, to February 29, 2020) to period 2 (March 1, 2020, to February 28, 2021) [12]. Thus, information regarding the needs of children with neurometabolic disorders during emergencies such as COVID-19 is crucial to ensure their well-being, and our study adds to this data.

Caring for a person with neurological illness causes physical, psychological, social, and economic difficulties for their caregivers. Our study also assessed this aspect among the families. As the study was in the form of an online survey, we could not use standardized detailed tools requiring additional time and/or visits. Our study shows that during the COVID-19 lockdown, one-third of the caregivers felt more confident in controlling the important things in their life. The families were staying together, which was a source of strength to handle the things related to their child's illness. Despite this, difficulties in accessing the medicine and doctor, discontinuation of treatment, fear of going to the hospital for their children's follow-up, and financial crisis made them upset and stressed sometimes and affected their quality of life and social functioning.

It is important to assess the caregivers' burden during stressful times like COVID-19 because such situations cause compromise of caregiver needs, well-being, and quality of life. A cross-sectional study from France done on 1000 caregivers of neurological patients revealed that the lockdown had a negative impact on the behavior, social interaction, and morale of caregivers. They felt lack of help and support [13]. This, in turn, affects the care of their children. Literature shows that caregivers were more worried about the health of their children because of lack of proper therapeutic service support, finances, and illness. They found telemedicine more beneficial as it avoids long journeys and saves money as well [14, 15].

Our study was limited by the smaller number of patients and the absence of any standardized scales to assess caregiver burden and quality of life. The questionnaire could not be validated. However, neurometabolic diseases are rare conditions, and our single-center-based study captures their felt needs. Survey-based studies play an important role in the rapid assessment of the current and future needs of patients with rare diseases during emergency situations like COVID-19.

Conclusion

Our study highlights the problems faced by children with neurometabolic disorders and their parents during the COVID-19 pandemic. Parents of patients with neurometabolic disorders such as biotinidase deficiency, mitochondrial encephalopathy, classical homocystinuria, cobalamin C defect, maple syrup urine disease, phenylketonuria, and citrullinemia preferred home therapy for their children. Nearly half of the patients with neurometabolic disorders lost their follow-ups, could not avail medical services, or had no accessibility to medicines. Caregivers felt that the COVID-19 pandemic affected their quality of life in several ways, but irrespective of that, one-third felt more confident in being able to control the problems related to their child's illness. Survey-based studies can aid in providing an insight into the needs and complex situations of children with neurometabolic disorders and their parents, even when physical assessments are curtailed. Organization of responses from different surveys can help in prioritizing the actions of healthcare systems to minimize the impact of pandemics or similar prolonged lockdown conditions on patients with rare diseases.

Abbreviations

COVID-19 – *coronavirus disease 2019*; BTD – biotinidase deficiency; ME – mitochondrial encephalopathy; CHCU – classical homocystinuria; Cbl-C – Cobalamin C defect; PKU – phenylketonuria; MSUD – maple syrup urine disease; Cit – citrullinemia; SPSS – Statistical Package for the Social Sciences; PO – patient's organizations; EURORDIS – The European Organisation for Rare Diseases; NORD – National Organization for Rare Disorders; MetabERN – The European Reference Network for Hereditary Metabolic Diseases; IEM – inborn errors of metabolism.

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Competing interests

The author(s) declare that they have no competing interests.

Authors' Contributions

Yashu Sharma contributed to conception, study design, data collection, and result analysis.

Gunjan Didwal contributed to conception and data collection.

Rajdeep Kaur contributed to data collection, result analysis, and review of the manuscript.

Savita Verma Attri contributed to the analysis of results and revised the final manuscript.

Arushi Gahlot Saini contributed to the conception, study design, and analysis of results and revised the final manuscript.

Naveen Sankhyan contributed to the analysis of results and revised the final manuscript.

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