

Functional status of children and adolescents with COVID-19 in a reference hospital in southern Brazil

Estado funcional de crianças e adolescentes com COVID-19 em um hospital de referência no sul do Brasil

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Abstract

Introduction: COVID-19 could leave important consequences, including functional decline. **Objective:** Evaluate functional status in pediatric patients hospitalized with COVID-19 and correlate with clinical variables. **Methods:** Prospective and retrospective longitudinal study with patients with COVID-19. Hospitalization data were collected from medical record review and post discharge data were collected by telephone contact. Functional status was evaluated by Functional Status Scale (FSS-Brazil) in three moments (hospital admission, hospital discharge and after hospital discharge). Spearman test was used to correlate continuous variables and the linear model with generalized estimation equations was used to verify differences in the proportion of functional impairment occurrence (FSS-Brazil ≥ 8) at different moments of the study and previous disease presence. **Results:** It was included 232 patients, 56% male, median age of five years old. Seventy (30.2%) patients had post discharge data. The mean global score of FSS-Brazil was 7.3 at hospital admission, 6.8 at discharge hospital and 6.8 after discharge hospital. Functional status was adequate in the three different moments evaluated in 75% of the sample. The ventilatory support needed was not correlated with functional status and the length of hospital stay and oxygen therapy showed weak correlations with functional status. Having no previous disease reduced the risk of functional impairment by 94%. **Conclusion:** The majority of the patients maintained adequate functional status. Absence of previous disease was a protective factor for long term functional impairment.

Keywords: Child. COVID-19. Follow up studies. Functional status. Pediatrics.

Resumo

Introdução: A COVID-19 pode deixar sequelas importantes, como declínio funcional. **Objetivo:** Avaliar a funcionalidade dos pacientes pediátricos internados com COVID-19 e correlacionar com variáveis clínicas. **Métodos:** Estudo longitudinal retrospectivo e prospectivo, com pacientes pediátricos com COVID-19. Os dados de internação hospitalar foram coletados a partir da revisão de prontuários e os dados pós-alta através de contato telefônico. A funcionalidade foi avaliada através da Escala de Estado Funcional Pediátrica (FSS-Brasil) em três momentos (admissão, alta e pós-alta hospitalar). A correlação entre as variáveis contínuas foi avaliada pelo teste de Spearman e utilizou-se o modelo linear com equações de estimação generalizada para verificar as diferenças nas proporções de ocorrência de prejuízo funcional (FSS-Brasil ≥ 8) nos diferentes momentos do estudo e na presença de doenças prévias. **Resultados:** Foram incluídos 232 pacientes, 56% do sexo masculino, mediana de 5 anos de idade. Foram obtidos dados de seguimento pós-alta hospitalar de 70 (30,2%) crianças. O escore global médio da FSS-Brasil foi de 7,3 na admissão, 6,8 na alta e 6,8 após a alta. A funcionalidade apresentou-se adequada nos três momentos de avaliação em 75% da amostra. A necessidade de suporte ventilatório não foi correlacionado com a funcionalidade, e o tempo de internação e oxigenoterapia apresentaram correlações fracas com a funcionalidade. A inexistência de doenças prévias reduziu em 94% o risco de prejuízo funcional. **Conclusão:** A maioria das crianças manteve funcionalidade adequada. Não ter doenças prévias foi um fator de proteção para o prejuízo funcional em longo prazo.

Palavras-chave: Criança. COVID-19. Estudo longitudinal. Estado funcional. Pediatria.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) is a member of the coronavirus family and the causative agent of severe acute respiratory syndrome.¹ The spread of the virus began in December 2019 in Wuhan, China, although it was detected only in January 2020. In March 2020, the World Health Organization (WHO) declared a pandemic resulting from the new coronavirus, which lasted for two years, with persisting challenges such as new strains of the virus and the population's resistance to vaccines.¹

Although the clinical manifestations of coronavirus

disease 2019 (COVID-19) are milder in children than those in adults, and in many cases asymptomatic, due to the extensive spread of the virus, many children were infected.² In Latin America, approximately 47% of children required hospitalization and 12.7% required intensive treatment.³ In Brazil, 41% of children who required hospitalization in an intensive care unit (ICU) had comorbidities, which is considered the only factor associated with the worst severity of COVID-19.⁴

In addition to the damage associated with the disease itself, the need for hospitalization in this age group, especially for long periods, can cause functional losses^{5,6} which can affect the child's performance in the dimensions of physical, cognitive, emotional, and social health, which can affect their quality of life.⁷ Oliveira et al.⁸ found the presence of new morbidities after hospital discharge in 11.5% of children who required ICU admission. Pinto et al.⁹ reported that < 10% of children achieved functional gains within three years after hospital discharge. Little data on the functional status of pediatric patients with COVID-19 have been published. Casassola et al.¹⁰ observed that approximately 45% of children with COVID-19 had adequate functional status within the first 24 hours of hospital admission. Furthermore, studies have observed that functional impairment after hospital discharge is associated with the need for readmission.¹¹⁻¹³

In this context, the effect of COVID-19 on the functional status of hospitalized children is of fundamental importance, as studies regarding this topic are still scarce. Therefore, the present study aimed to evaluate the functional status of pediatric patients hospitalized for COVID-19 during hospitalization, discharge, and post-discharge. Furthermore, this study aimed to verify possible correlations between the functional status after hospital discharge and presence of previous illnesses, length of stay, need for intensive therapy, use of ventilatory support, and oxygen therapy, as well as associated factors such as the presence of previous illnesses and functional impairment after hospital discharge.

Methods

This retrospective and prospective longitudinal study was conducted at Hospital de Clínicas de Porto Alegre (HCPA). This project was approved by the HCPA Ethics and Research Committee (approval number

35890820.7.1001.5327). This study is part of a project entitled NUTRICOVID on a subsample of pediatric patients and was conducted in accordance with the General Personal Data Protection Law (GDPL)¹⁴ for research on human beings during the COVID-19 pandemic.

The sample consisted of pediatric patients with a record of hospitalization at the HCPA who had a positive reverse transcriptase reaction, followed by (RT-PCR), for COVID-19. Patients of both sexes were included, from the age of one month to 18 years 11 months and 29 full days, who were hospitalized from March 2020 to March 2022. Patients with a hospital stay of < 24 hours, institutionalized children, pregnant women, and medical records with restricted access were excluded.

The data were obtained in two stages. First, the data from electronic hospital records were reviewed and collected. Second, corresponding data collection via telephone interviews with the patients' family members/guardians occurred between six and 18 months after hospital discharge. A Research Electronic Data Capture (RedCap) platform was used to collect and store data from the two developed questionnaires. Questionnaire 1 was used to collect data from medical records (step 1), and questionnaire 2 was used to collect data via telephone interviews (step 2).

Questionnaire 1 collected personal and demographic data, including the presence of previous illnesses (according to medical diagnosis reported in the medical record), reason for hospitalization, symptoms, total hospitalization time, need and length of stay in the pediatric ICU (PICU), need for oxygen therapy, non-invasive and invasive mechanical ventilation, period of use, and assessment of functional status using the Functional Status Scale (FSS-Brazil) at the time of admission and discharge from the hospital.

Questionnaire 2 collected sociodemographic data, health service follow-up, and clinical aspects, such as loss of smell/taste and gastrointestinal symptoms, COVID-19 reinfection, and hospital readmission. Additionally, a new functional status assessment was performed using FSS-Brazil. Three telephone contact attempts were made with each patient at different times and on different days to reduce losses to follow-up.

Functional status assessment was performed by trained researchers through the application of the FSS-Brazil at the time of admission, discharge, and post-discharge, and was scored based on the evolution

of all health professionals involved and the parents' reports/responsibilities. Patients admitted to the PICU underwent the FSS-Brazil performed by the physiotherapists responsible for the unit. For the post-discharge application, researchers were trained to apply a standardized telephone script based on a previous study.⁹ The FSS-Brazil is a functional status assessment instrument already translated and validated for the Brazilian population,¹⁵ consisting of six domains: mental status, sensory, communication, motor function, eating, and respiration. In each domain, the score ranges from 1 (adequate) to 6 (very severe dysfunction), with an overall score between 6 and 30. The final classification was as follows: 6 - 7 points, adequate function; 8 - 9 points, mild dysfunction; 10 - 15 points, moderate dysfunction; 16 - 21 points, severe dysfunction; and > 21 points, very severe dysfunction.¹⁶

The database was built on the REDCap platform and exported to the Statistical Package for Social Science (SPSS) version 22.0 for Windows for analysis. Continuous variables are described as means and standard deviations or medians and interquartile ranges, and categorical variables as absolute and relative frequencies. The Shapiro-Wilk normality test was performed, and non-parametric tests were used for data with abnormal distribution.

The Spearman's test was used to test for correlations between continuous variables. The Mann-Whitney U test was used to compare FSS-Brazil and categorical data. The linear model with generalized estimation equations with binary outcome, modeled through the logit link function, was used to verify the differences in the proportions of occurrence of functional impairment (FSS-Brazil ≥ 8)¹⁶ at different time points (admission, discharge, and post-discharge) and in the presence of previous illnesses, adjusting for age and sex. Differences were considered statistically significant at $p < 0.05$.

Results

Of the 337 patients diagnosed with COVID-19, 105 were excluded due to hospitalization < 24 hours ($n = 54$), pregnancy ($n = 19$), or institutionalization ($n = 2$). Furthermore, 30 patients refused to participate because of disagreements with the GDPL. A total of 232 children were included in the study. The median age of the cohort was five years and 56% of the patients were boys.

COVID-19 symptoms were prevalent in 189 (81.5%) patients. Deaths (including other causes) were recorded in 6% of the assessed population (n = 14), 8 of which occurred during hospitalization and 6 after hospital discharge. Of the total number of hospitalized patients, follow-up data were obtained for 70 (30.2%) children via telephone contact after hospital discharge (Figure 1). Table 1 shows the clinical characteristics of the patients.

Figure 2 shows the functional status classification according to the FSS-Brazil at different time points (admission, discharge, and post-discharge). Adequate functional status was most prevalent at the three assessment time points, although approximately 13% and 19% of the children had some degree of functional impairment at hospital discharge and post-discharge, respectively.

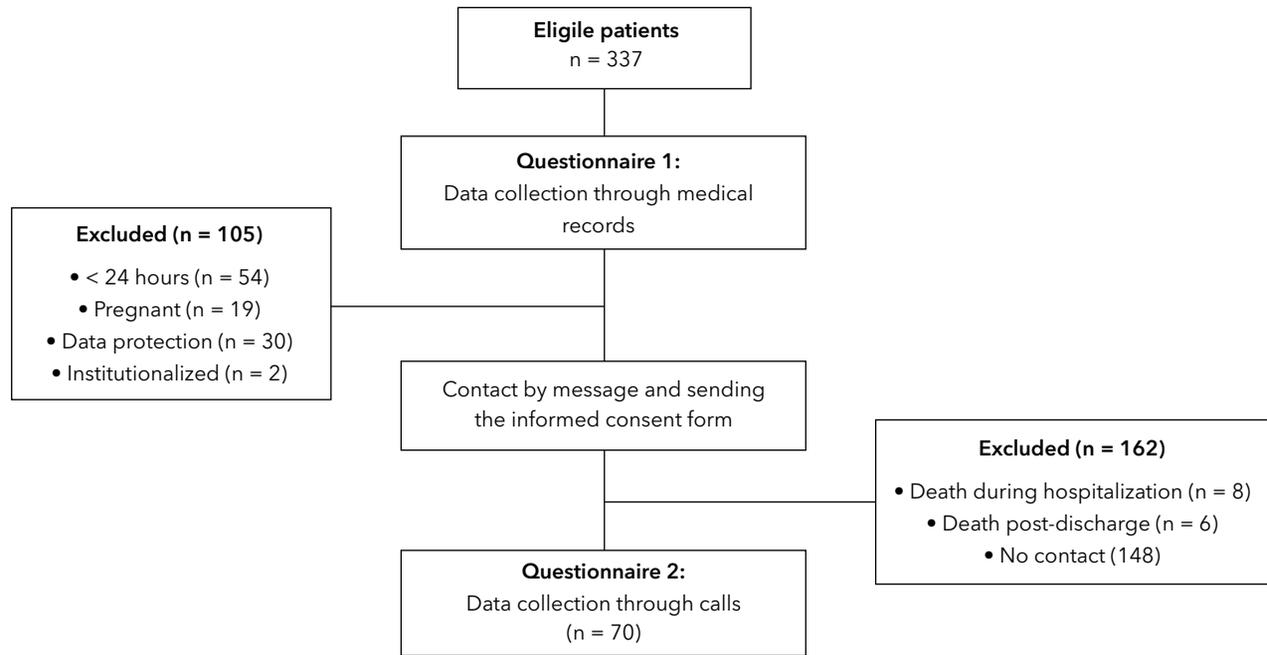


Figure 1 - Flowchart of patients. Rio Grande do Sul, Brazil.

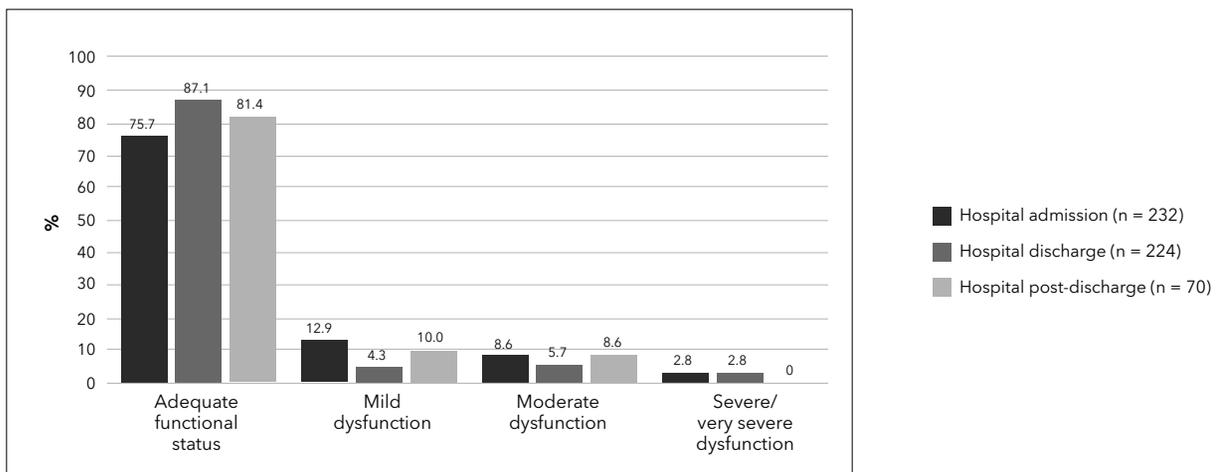


Figure 2 - Classification of functional status according to the Functional Status Scale (FSS-Brazil) at the different moments evaluated in the study (admission, hospital discharge and post-hospital discharge) of children and adolescents hospitalized for COVID-19. Rio Grande do Sul, Brazil.

Table 1 - Sociodemographic and clinical characteristics of the total sample and post-hospital discharge of children and adolescents hospitalized for COVID-19. Rio Grande do Sul, Brazil.

Variables	Total sample (n = 232)	Post-hospital discharge sample (n = 70)
Sex (male)	130 (56.0)	42 (60.0)
Age (years)		
≤ 2	96 (41.4)	24 (34.3)
2 - 5	22 (9.5)	8 (11.4)
5 - 10	43 (18.5)	19 (27.1)
≥ 10	71 (30.6)	19 (27.1)
Previous illnesses	141 (60.8)	45 (64.3)
Respiratory	28 (12.1)	10 (14.3)
Neurological/ neuromuscular	26 (11.2)	10 (14.3)
Neoplasm	25 (10.8)	4 (5.7)
Gastrointestinal	23 (9.9)	6 (8.6)
Congenital/genetic defects	22 (9.5)	0 (0.0)
Hematological/Immunological	20 (8.6)	8 (11.4)
Metabolic	15 (6.5)	5 (7.1)
Cardiovascular	11 (4.7)	4 (5.7)
Renal/urological	10 (4.3)	4 (5.7)
Global score FSS-Brazil		
Admission	7.3 ± 2.4	7.5 ± 2.9
Discharge	6.8 ± 2.1	6.9 ± 2.7
Post hospital discharge (n = 70)	6.9 ± 1.9	6.9 ± 1.9
Symptomatic patient for COVID-19	189 (81.5)	59 (84.3)
Fever	141 (60.8)	49 (70.0)
Cough	83 (35.8)	21 (30.0)
Shourtness of breath	55 (23.7)	16 (22.9)
Runny nose	39 (16.9)	10 (14.3)
Vomiting	35 (15.1)	11 (15.7)
Diarrhea	30 (12.9)	8 (11.4)
Headache	23 (9.9)	7 (10.0)
Others*	42 (18.1)	18 (25.7)
Oxygen therapy	87 (37.5)	24 (34.3)
Oxygen therapy time (days)	3 (3.0)	3 (4.0)
Invasive mechanical ventilation	24 (10.3)	4 (5.7)
Invasive mechanical ventilation time (days)	5 (8.0)	4 (11.0)
No invasive mechanical ventilation	8 (3.4)	3 (4.3)
Need for intensive care unit	50 (21.5)	11 (15.7)
Total length of stay (days)	6 (12.8)	5 (9.0)

Note: Data expressed in n (%), except for the global score FSS-Brazil (mean ± standard deviation) and oxygen therapy time, invasive mechanical ventilation time and total length of stay [median (interquartile range)]. FSS-Brazil = Functional Status Scale. *Body pain, sore throat, tiredness, nausea.

Children with previous illnesses had worse global functional scores than previously healthy children, both at admission and hospital discharge. Patients who required PICU admission and oxygen therapy had worse global functional scores only on hospital admission. Among children who did or did not require invasive mechanical ventilation (IMV), the functional status was similar at the three evaluated time points (Table 2).

The length of hospital stay was positively but weakly correlated with the FSS-Brazil score at admission ($p < 0.001$; $r = 0.247$) and discharge ($p < 0.004$; $r = 0.190$). The oxygen therapy time was also positively and weakly correlated with the FSS-Brazil global score ($p < 0.001$;

$r = 0.317$); however, this was observed only at the time of hospital admission, suggesting that the greater the functional impairment, the longer the oxygen therapy time. The other correlations between age, length of hospital stay, oxygen therapy, and the FSS-Brazil score were not significant at any evaluated time points.

Table 3 compares the occurrence of some degree of functional impairment (FSS-Brazil ≥ 8) between different moments (admission, discharge, and post-discharge) and the presence of previous illnesses. Children without a previous illness had 94% protection against the risk of experiencing some degree of functional impairment after hospital discharge.

Table 2 - Median global score of the Functional Status Scale (FSS-Brazil) according to variables related to hospital admission and previous illnesses at different times of the study of children and adolescents hospitalized for COVID-19. Rio Grande do Sul, Brazil

Variables		Admission		Discharge		Post-discharge	
		M	p-value*	M	p-value*	M	p-value*
Previous illnesses	Yes	6 (6 - 8)	< 0.001	6 (6 - 7)	< 0.001	6 (6 - 8)	0.065
	No	6 (6 - 7)		6 (6 - 6)		6 (6 - 6)	
PICU admission	Yes	7 (6 - 10)	< 0.001	6 (6 - 7)	0.127	6 (6 - 6)	0.134
	No	6 (6 - 7)		6 (6 - 6)		6 (6 - 7)	
Oxygen therapy	Yes	7 (6 - 9)	< 0.001	6 (6 - 6)	0.495	6 (6 - 6)	0.179
	No	6 (6 - 7)		6 (6 - 6)		6 (6 - 7)	
Invasive mechanical ventilation	Yes	7 (6 - 9)	0.241	6 (6 - 8)	0.412	6 (6 - 6)	0.364
	No	6 (6 - 7)		6 (6 - 6)		6 (6 - 6)	

Note: PICU = pediatric intensive care unit; M = median (25th percentile-75th percentile). *Mann-Whitney U test.

Table 3 - Difference in the proportions of occurrence of some degree of functional impairment (FSS-Brazil ≥ 8) according to the functional assessment at different times of the study and previous illnesses of children and adolescents hospitalized for COVID-19. Rio Grande do Sul, Brazil

Variables		%	p-value*	OR# (IC95%)
Time of functional assessment	Post-hospital discharge	8	0.007	1
	Hospital discharge	5		0.61 (0.31 - 1.18)
	Admission	11		1.49 (0.72 - 3.09)
Previous illnesses	Yes	25	< 0.001	1
	No	2		0.06 (0.01 - 0.26)

Note: FSS-Brazil = Functional Status Scale; OR = odds ratio; 95%CI = 95% confidence interval; *p-value of the effect test of the Wald chi-square model. #Adjusted for sex and age.

Discussion

The results of the present study demonstrate that most children with COVID-19 who required hospitalization showed functional improvements at hospital discharge. After hospital discharge, approximately 19% of children showed some degree of functional impairment. The absence of previous illnesses was a protective factor associated with some degree of functional impairment during the long-term follow-up.

Most children with COVID-19 presented with adequate functional status at hospital discharge and post-discharge, corroborating previous studies in which most patients returned to their functional state prior to hospitalization at the time of hospital discharge.^{8,17} However, other studies have observed that a significant number of children did not return to their previous functional status in the long term after hospital discharge.^{18,19} The difference between the findings can be explained by the different time points in the long term in which functional status was assessed. Furthermore, all the patients in the aforementioned studies were discharged from the PICU.

In the present study, children and adolescents who required hospitalization in the PICU and oxygen therapy had worse functional status only at the time of admission. Pollack et al.¹⁷ observed that children had a greater functional deficit after discharge from the PICU; however, they improved until hospital discharge. Cassassola et al.¹⁰ observed worse functional status during the hospital admission of children with COVID-19 among those who required oxygen therapy, corroborating the findings of the present study.

Regarding the need for IMV, functional status was similar in the three evaluated time points among children who did or did not require invasive ventilatory support, which differs from previous studies that found an association between the need and longer duration of IMV and worse functional outcomes in the long-term.^{8,13} Furthermore, in a pediatric population with COVID-19, a previous study also demonstrated worse functional status among those who required IMV.¹⁰ The divergence between the present study and others can be explained by the fact that only 10% (n = 24/232) of the patients included in this study required IMV, and identifying a difference between the groups was not possible.

Verifying the association between previous illnesses and functional status revealed that not having a previous

illness was a protective factor against functional impairment. A recent study demonstrated that patients with complex chronic conditions have a global FSS-Brazil score of 14.9 at the time of admission to the PICU, with a slight improvement at PICU discharge (12.0), although the functional classification remained at moderate dysfunction.²⁰ Choi et al.²¹ observed that children with previous illnesses showed greater COVID-19 severity and a higher mortality rate compared to those without previous illnesses. Children with previous illnesses could already have previous functional changes and develop COVID-19 in its most severe form, further affecting their long-term functional status, although this remains debatable.

The present study had some limitations. Sample loss during follow-up after hospital discharge was high (70%), although this is a limitation of the long-term follow-up study design. However, analyses were performed to compare the possible discrepancies between the two groups (those who continued follow-up vs. those who were lost to follow-up). Furthermore, assessing functional status or verifying functional changes before hospitalization was not possible. As this was a retrospective study based on medical records and telephone calls, the FSS-Brazil score was performed using only this information, without direct observation of the patients, although the data obtained through medical records and telephone contacts followed strict protocols and supplied all items for scoring. Additionally, face-to-face evaluation became unfeasible because during the pandemic, restrictions had been implemented on contact between patients and researchers in a hospital environment.

Notably, the strengths of this study must be highlighted which include the evaluation of a large number of children with COVID-19 from a reference center for COVID-19 treatment in southern Brazil. Furthermore, the follow-up in this study allowed functional assessment over time, which, to the best of our knowledge, has not yet been evaluated in this population.

Conclusion

In this study, most children with COVID-19 who required hospitalization showed functional improvements at hospital discharge. The correlations between the clinical variables and functional status, although

significant, were not clinically relevant. However, the absence of a previous disease was an important factor in reducing functional impairment in this population. Studies with larger sample sizes, especially long-term studies, are necessary to identify possible functional deficits and associated factors.

Authors' contributions

LSM, CWS, KZ, VLB, and JLL were responsible for study preparation and design. LSM, CWS, BH, and JLL interpreted and analyzed the results. LSM, CWS, and JLL wrote the manuscript. All authors have reviewed and approved the final version of the manuscript.

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