COVID-19 IN IMMUNOSUPPRESSED CHILDREN

July 1st 2020

STUDY PROTOCOL

Introduction

Viral infections are frequent in children and have the potential for greater severity in immunosuppressed patients, especially in the pediatric age group. At the moment, Brazil is facing the effects of a pandemic of severe acute respiratory infection caused by a new coronavirus, called SARS-CoV-2, whose clinical presentation in the pediatric immunosuppressed patients is still unknown and needs to be urgently studied. Some reports in the world literature describe less impact on the transplanted pediatric population, as well as on immunosuppressed patients.

Objectives

Primary objective: Describe the clinical characteristics and the seroconversion profile (IgM / IgG) by the new coronavirus (SARS-CoV-2) in pediatric renal or liver transplant and in oncologic patients during the 2020 pandemic.

Secondary objectives:

- Describe the prevalence and incidence of seropositivity - IgM and IgG for Coronavirus in immunosuppressed transplanted or oncohematological patients;
- Among patients with flu syndrome, describe the percentage of positive PCR-RT for the new Coronavirus;
- In children with positive results (PCR-RT or immunoglobulins), describe the clinical-evolutionary spectrum associated with the infection;
- In an exploratory way, investigate the association between clinical, laboratory and radiological image variables in the presentation and outcomes;
- Describe the profile of viral shedding.

Study Design

Multicenter, observational, longitudinal, descriptive study, part retrospective and part prospective, with exploratory analytical component.

Study Period

Retrospective data collection: 06/30/2020 to 10/30/2020.
Prospective data collection: 06/30/2020 to 02/28/2021.
End of the study: 06/30/2021.

Inclusion criteria (eligibility)

Patients from 0 to 18 years of age, kidney or liver transplant recipients, on regular outpatient follow-up at the Hospital Estadual da Criança and, in the case of kidney transplant recipients, also at the Hospital Federal de Bonsucesso, both with a functioning graft and using immunosuppression.
Patients from 0 to 18 years of age with oncohematological diseases on regular outpatient follow-up at the Hospital Estadual da Criança.

Exclusion criteria (non-eligible patients)
Patients whose parents refuse to sign the Informed Consent Form (ICF) will be excluded.

Loss criteria (patients excluded after entering the study)
Patients who withdraw consent to participate; Loss of follow-up; Patients who have not made available the results of laboratory tests for viral detection until the data analysis period; Patients transferred to other services during treatment; Deaths not related to COVID-19 (for these patients data until death will be used).

Variables to be measured
- Demographic data (initials, record, age, sex, race / ethnicity, weight, height, BMI).
- Epidemiological data:
    - For kidney transplant patients: time of transplant, in years and complete months; primary kidney disease; presence and time of onset of respiratory symptoms, in days; presence of risk factors or comorbidities; current immunosuppression (drugs and doses); serum level of calcineurin inhibitor on the day of collection; previous vaccination for Influenza; previous viral infections; date of the last episode of rejection treated.
    - For liver transplant patients: time of transplant, in years and complete months; primary liver disease; presence and time of onset of respiratory symptoms, in days; presence of risk factors or comorbidities; current immunosuppression (drugs and doses); serum level of calcineurin inhibitor on the day of collection; previous vaccination for Influenza; previous viral infections; date of the last episode of rejection treated.
    - For oncohematological patients: time of diagnosis, in years and complete months; primary oncohematological disease; treatment received for the oncohematological disease; presence and time of onset of respiratory symptoms, in days; presence of risk factors or comorbidities; current immunosuppression (drugs and doses); serum level of calcineurin inhibitor on the day of collection; previous vaccination for Influenza; previous viral infections.

- Clinics visit / hospitalization data: clinical picture: syndromic diagnosis / signs and symptoms; initial image exam: chest X-ray and / or chest CT; Treatment performed: antiviral, antibiotic, corticoid (reason / dose / time); respiratory support (oxygen therapy only / Non-Invasive Ventilation / High Flow Nasal Cannula / invasive mechanical pulmonary ventilation / ECMO - time of use (days); days free of oxygen therapy, Non-Invasive Ventilation and invasive mechanical pulmonary ventilation .
- Diagnosis of SARS-CoV-2 infection: rapid test for Covid-19 in the blood: IgM / IgG; rapid test for Covid-19 in nasopharyngeal or tracheal secretion.
- Outcomes: Asymptomatic; Symptomatic home treatment; Symptomatic need for hospitalization in an open unit; Symptomatic need for hospitalization in a closed unit; Death.

In patients admitted to the PICU - Final clinical diagnosis: SARI, SARS, ARDS; destination: discharge from the ICU / transfer to another hospital / death; length of stay in the ICU, in days.

Definitions used in the study

• SARI – Severe Acute Respiratory Infecction - like any acute respiratory condition (up to 10 days of evolution) that has a clinical indication for admission to a pediatric intensive care unit.

• SARS – Severe Acute Respiratory Syndrome - a form of severe acute respiratory infection, leading to acute respiratory distress, characterized by fever, difficult breathing, pulmonary radiological changes, associated with infection by respiratory viruses.

• ARDS – Acute Respiratory Distress Syndrome - a form of acute respiratory failure characterized by hypoxemia and need for ventilatory support, according to the international consensus definition.

• Confirmed case of SARS-CoV-2 infection - any positive result for SARS-CoV-2, performed using the Polymerase Chain Reaction (PCR) technique and / or immunofluorescence method on material harvested using swab or nasopharyngeal aspirate or tracheal aspirate or positive IgM / IgG serology at any time during the study.

Risks and benefits

The study will not involve any additional intervention or clinical risk for the participants and their families. The risks involved may be related to breach of data confidentiality, but the researchers are committed to taking all measures to maintain confidentiality in the study environment. There are also risks related to the venipuncture necessary to obtain the blood sample that will be used for the measurement of immunoglobulins. However, the collection will be made by the same puncture that is already required for routine exams collection and these risks will be minimized through blood collection by trained and experienced personnel.

On the other hand, the results of the present study may bring direct benefits to the participants, since it will be able to identify and differentiate patients who have proven to have had asymptomatic Coronavirus infection and who have acquired immunity against this virus. This fact may represent a lower burden, both for the individual and for society, as it can mean protection against future infections by Coronavirus.

Statistics and data analysis

The sample size will be determined by convenience, corresponding to the number of participants included while the study is admitting new participants to the cohort. All eligible participants who had a sample collected for measurement of Immunoglobulin or PCR-RT for coronavirus will have their data analyzed. Categorical variables will be described as proportions and will be compared, when relevant, using the chi-square test or Fisher's exact test. Continuous variables will be described as mean and standard deviation or as median and interquartile range, depending on the distribution characteristic. Comparisons involving continuous variables will be performed, when pertinent and exploratory, using the Student's t-test for parametric data and through the Mann-Whitney test or ANOVA for non-parametric data. Logistic regression models can be performed to assess independent associations between prognostic factors and outcomes, association between individual characteristics and severity, as well as length of hospital stay, length of stay in the hospital and in the PICU and mortality. In all analyzes, the level of significance (alpha) will be set at 5%.