APPLICATION FOR IRB APPROVAL OF RETROSPECTIVE STUDIES
(NOT FOR POSTGRADUATE THESIS OR MEDICAL STUDENT OR ALLIED HEALTH OR NURSING STUDENT PROJECT RELATED)

CHRISTIAN MEDICAL COLLEGE, VELLORE

2. Acronym, if any: DIPS (Delayed Inflammatory Pulmonary Syndrome)
3. (i) Is this project related to “Artificial intelligence or Machine Learning”? (No)
   (ii) Is the MoU with the collaborating institutions approved by the:
       a. Internal IT committee? NA
       b. CMC Legal cell? NA
       (Note: Please attach the approval copy along with the IRB application)
4. Name and Designation of Principal Investigator (s) / Co investigator(s) / Co - author(s)

   Address for communication (including telephone and fax numbers and email id, employment number):

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Contact person for scientific queries if different from Principal investigator  
(Including telephone and fax numbers and email id, employment number):

Dr Binila Chacko (Professor, Medical Intensive Care Unit, CMC Hospital)

5. Source/s of Monetary or Material Support

Internal Fluid Research Grant : NA
External : NA
6. **Contributions of each of the author/investigators(s):**

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<thead>
<tr>
<th>Author(s)</th>
<th>Responsibilities</th>
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<tr>
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<td>Research and Study design</td>
</tr>
<tr>
<td>Dr. Prithviraj</td>
<td>✓</td>
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<tr>
<td>Dr. Dhanoop</td>
<td>✓</td>
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<tr>
<td>Dr. Binila</td>
<td>✓</td>
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<td>Dr. JV Peter</td>
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<td>Dr. Mohan</td>
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<td>Dr. Jonathan</td>
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<td>Dr. Balamugesh</td>
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<td>Dr. Richa</td>
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<td>Dr. George MV</td>
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7. **Sites of the study (including departments where the study was done):**

Department of Medical Intensive Care, CMC Hospital: MICU, MHDU, STICU

8. **Brief Summary (in 250 words):**

While COVID-19 may affect multiple organ systems, symptoms are most often located in the respiratory tract (1). Classically, mortality attributable to COVID-19 infection occurs mainly through the development of viral pneumonia-induced acute respiratory distress syndrome (ARDS). (2) However, a recently recognized consequence of COVID-19 infection appears to be the development of a multi-system inflammatory syndrome, characterized by a dysregulated host immune response causing widespread organ dysfunction, that is not attributable to, and usually follows the period of viremia. (3) This entity was first described in a pediatric population and is termed MIS-C (Multisystem Inflammatory Syndrome- Children). (4) A similar phenomenon was subsequently reported in adults during the second wave of the pandemic in 2021. (3) Of note is the fact that this description encompassed a predominantly extrapulmonary syndrome, (5) with cardiac and gastrointestinal being the most common systems affected.

The case definition for MIS-A that has been proposed by the CDC is as follows (5): A patient aged ≥21 years hospitalized for ≥24 hours, or with an illness resulting in death, who meets the following
clinical and laboratory criteria. The patient should not have a more likely alternative diagnosis for the illness (e.g., bacterial sepsis, exacerbation of a chronic medical condition).

I. Clinical Criteria: Subjective fever or documented fever (≥38.0°C) for ≥24 hours prior to hospitalization or within the first THREE days of hospitalization* and at least THREE of the following clinical criteria occurring prior to hospitalization or within the first THREE days of hospitalization*. At least ONE must be a primary clinical criterion.
   A. Primary clinical criteria
      1. Severe cardiac illness: Includes myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new-onset right or left ventricular dysfunction (LVEF<50%), 2nd/3rd degree A-V block, or ventricular tachycardia. (Note: cardiac arrest alone does not meet this criterion)
      2. Rash AND non-purulent conjunctivitis
   B. Secondary clinical criteria
      1. New-onset neurologic signs and symptoms Includes encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome)
      2. Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy)
      3. Abdominal pain, vomiting, or diarrhoea
      4. Thrombocytopenia (platelet count <150,000/ microliter)

II. Laboratory evidence: The presence of laboratory evidence of inflammation AND SARS-CoV-2 infection.
   A. Elevated levels of at least TWO of the following: C-reactive protein, ferritin, IL-6, erythrocyte sedimentation rate, procalcitonin
   B. A positive SARS-CoV-2 test for current or recent infection by RT-PCR, serology, or antigen detection

NOTE: *These criteria must be met by the end of hospital day 3, where the date of hospital admission is hospital day 0.

According to the above criteria, organ involvement in the form of declining pulmonary function cannot be considered withing the ambit of MIS-A. However, in our experience of managing patients with severe COVID-19 during the second wave, we encountered several patients who had survived the infective complications of the virus, only to develop a relapse in the respiratory distress, which could not be attributed to superadded infections or fluid overload. Unlike a fibrotic phase of ARDS which forms a continuum with the primary insult itself, this phenomenon seems to affect those who had successfully suppressed the viremia and virus-related tissue damage but gone on to develop a pro-inflammatory state causing predominantly pulmonary manifestations. Since the CDC definition of MIS-A does not include a pulmonary decompensation, as shown above, the phenomenon observed here appears to be a novel observation. We seek to describe the clinical and laboratory characteristics of this entity from a retrospective review of cases admitted in the Medical ICU during the second wave of the pandemic, along with clinical outcomes and caveats during management.

References:


9. Provide the date range of the chart review: (if this is a retrospective chart review, the end date should antedate the IRB submission date): 31/03/2021 to 02/11/2021.

The IRB application should be made when the study is started, rather than when it is completed

10. Objectives of the study: (Primary endpoints of study, listed and numbered individually)

   - To describe the clinical and laboratory profile of patients noted to have a post COVID pulmonary hyperinflammation syndrome
   - To investigate for predictors developing pulmonary hyperinflammation
   - To describe outcomes and management caveats encountered in the management of patients with COVID related pulmonary hyperinflammation syndrome.

11. Confidentiality of data:

   a) Describe how data (both paper and electronic) will be stored to safe-guard Confidentiality: password protected computer

   b) Specify as to who will have access to harvested patient data:

      - Dr Prithviraj Bose
• Dr Binila Chacko

c) Clarify as to how harvested patient data will be stored and how it will be destroyed when no longer needed: The data will be stored in an electronic form and maintained on the password protected department computer for as long as it is needed.

12. Avoidance of conflict regarding ownership of the data: NA
13. Name of statisticians involved in the analysis.
14. Informed Consent:

In view of the retrospective nature of the study and the large number of COVID-19 patients admitted in the ICU, resulting in deidentification of patient information, informed consent waiver is being sought from the institutional review board.

15. Signature of Principal Investigator(s) / Co-investigator(s) / Co-author(s):

I/We give my/our consent to be a Co-Investigator and provide my/our expertise to the project. I/We have approved this version of the protocol and have contributed substantially to its development. This study is purely retrospective without any prospective component. It does not involve analysis of novel therapy. (Signatures attached)

16. Approval of Head of the Department:

(Not necessarily a coauthor / co investigator in this study)

Please list below all additional documents that are being submitted along with this application including all appendices.

Notes for filling in this form

1. The application is required for Research Committee Approval.

3. Submission procedure
   - Project proposal
   - Curriculum Vitae(s) **(Only Soft copy)**
   - Signatures by all investigators, the Guide and the Head of the Department/Unit need to be scanned.

   **Applications submitted after the due date for the Silver IRB will not be entertained.**

   **IMPORTANT:**

   **Clearance for the study will be given only after the ratification in the Silver Institutional Review Board meeting.**

   **The Investigators need not have to represent for the Silver Institutional Review Board for presentation.**

Completed application with all supporting documents (Hard and Soft copy) should be submitted to

**Institutional Review Board (IRB)**  
Christian Medical College  
Office of Research, 1st Floor, Carman Block, Bagayam, Vellore 632 002 India.  
E-mail: research@cmcvellore.ac.in.  
Tel: 0416 -2284294, Fax: 0416 – 2262788.

**HOSPITAL CAMPUS:**  
ASHA Building 1st floor, Curriculum Office,  
Tel: 0416-3075645

**Hours for submission:**  
8.00 am to 5.00 pm (Monday – Friday)  
8.00 am to 12.00 pm (Saturday)

**Hours for submission in Hospital Campus (ASHA Building 1st Floor, Curriculum office)**  
8.00 am to 4.00 pm (Monday – Friday)  
8.00 am to 11.00 am (Saturday)