

(RESEARCH ARTICLE)



## Cardiac troponin testing in the management of patients infected with Sars-Cov-2

Faralahy Harisolofa Rakotonjafiniarivo <sup>1,\*</sup>, Miora Koloina Ranaivosoa <sup>1</sup>, Lucia Mélanie Ravaoharisoa <sup>2</sup> and Andry Rasamindrakotroka <sup>3</sup>

<sup>1</sup> *Laboratory of Biochemistry of Joseph Ravoahangy Andrianavalona University Hospital Antananarivo, Madagascar.*

<sup>2</sup> *Laboratory of Joseph Ravoahangy Andrianavalona University Hospital Antananarivo, Madagascar.*

<sup>3</sup> *Laboratory of Training and Research in Medical Biology, University of Antananarivo, Madagascar.*

GSC Biological and Pharmaceutical Sciences, 2022, 19(01), 056–060

Publication history: Received on 09 February 2022; revised on 04 April 2022; accepted on 06 April 2022

Article DOI: <https://doi.org/10.30574/gscbps.2022.19.1.0071>

### Abstract

Coronavirus disease 2019 (COVID-19) is a viral zoonosis caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). High sensitive Troponin cardiac (hs-cTn) is a biomarker frequently measured during the management of COVID-19. We conducted a descriptive retrospective study at the Paraclinical Service of Training and Researches in Biochemistry at the University Hospital Center of Joseph Ravoahangy Andrianavalona Madagascar over a period of five months. Our objective was to describe the modalities and the relevance of the prescription of hs-cTn determination within the intensive care units of the hospital. Of the 42 patient files collected in our work, we found a slight male predominance (sex ratio = 1.47) and the average age was 56.8 years. In 18 patients, hs-cTn was positive and among the 19 patients who died as a result of their disease 11 had elevated plasma troponin levels. During COVID 19, troponin assay should be prescribed appropriately to enhance the management of patients in a developing country like Madagascar where the cost of assaying this biomarker remains high

**Keywords:** Biochemistry; COVID-19; Highly sensitive Troponin; Antananarivo

### 1. Introduction

Currently, the world is facing an epidemic caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), the etiological agent of COVID-19 (Coronavirus disease 2019) [1]. The pathophysiology of SARS-CoV-2 is characterised by an overproduction of inflammatory cytokines (IL-6 and TNF- $\alpha$ ) leading to a multi-organ dysfunction syndrome and acutely affecting the cardiovascular system [2]. In addition, pre-existing risk factors may increase the severity of COVID-19 leading to decompensation of underlying cardiac pathologies and the development of new acute complications [3].

The role of cardiac troponin as diagnostic biomarkers of myocardial damage is well established [4]. In Madagascar, this biomarker is frequently prescribed by clinical services in patients with COVID-19.

### 2. Material and methods

This is a retrospective and descriptive study conducted at the Paraclinical Service of Training and Research at the University Hospital of Joseph Ravoahangy Andrianavalona (CHU-JRA) in Antananarivo Madagascar over a period of 5 months (April to August 2021). The data were collected from the medical analysis request forms received by the laboratory and the patients' files at the level of the medical and surgical intensive care units of the CHU-JRA. All test requests involving a first troponinemia determination in patients with COVID-19 in the intensive care units were

\* Corresponding author: Faralahy Harisolofa Rakotonjafiniarivo  
Laboratory of Biochemistry of Joseph Ravoahangy Andrianavalona University Hospital Antananarivo, Madagascar.

included. The parameters studied were gender, age, patient history, chronology of the request, troponinemia positivity and patient outcome

Blood samples were collected in tubes with lithium heparin as anticoagulant. Hypersensitive cardiac troponin I (hs-cTnI) was measured using the VIDAS High sensitive Troponin I kit (bioMérieux SA France) on the VIDAS automated system (bioMérieux SA France) using a ELFA (Enzyme Linked Fluorescent Assay) technology. A sample delivery time of no more than 1 hour and the avoidance of analytical interferences (haemolysis and coagulated samples) were respected

In the Biochemistry laboratory of the CHU-JRA, a positive troponinemia is defined by a hs-cTnI level > 30 ng/L in men and a hs-cTnI level > 14 ng/L in women.

Student's T-test was used to compare the observed results. The difference between two averages was considered significant when  $p < 0.05$ .

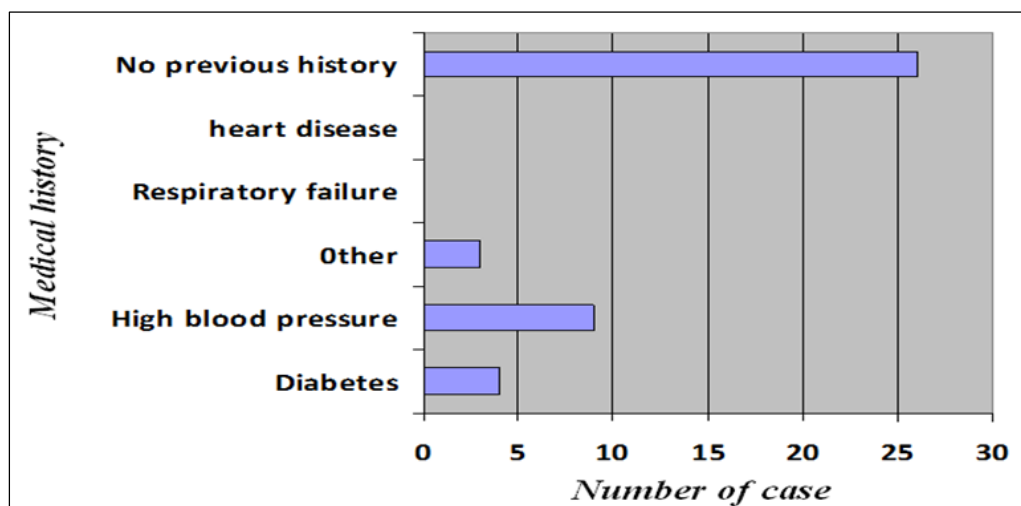
Data processing was performed using Microsoft Office Excel 2007® and Epi Info 7®.

### 3. Results

Our study included 42 patients records with a male predominance (N=25) with a sex ratio = 1.47. The average age was 56.8 years with extremes of 18 to 95 years. Twenty-six patients had no particular medical history, 9 were hypertensive and 4 diabetic (figure 1). Troponin measurements were requested in 14 patients on the day of admission to the intensive care unit (figure2).

The hs-cTnI was positive in 18 patients (42.8%) including 12 women (figure3) and the increase of troponin level was major (> 3 times the positivity threshold) for 13 patients (Table 1).

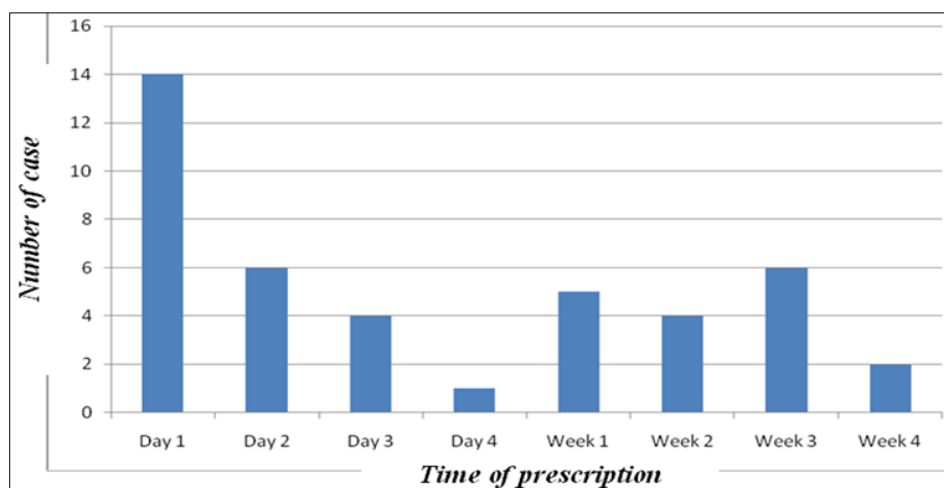
As for the patients included in our study, 19 died, 11 of them among the patients with a positive troponinemia. Comparison of the means by the T-Student test showed no significant difference ( $p > 0.05$ ).



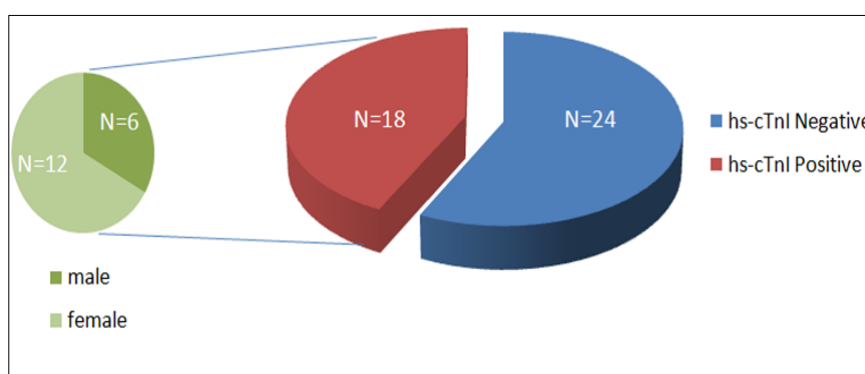
**Figure 1** Medical history in the patients' medical records

**Table 1** Distribution of cases in patients with high hs-cTnI levels

Stage of elevation in male patients	Number of case	Stage of elevation in female patients	Number of case
30 – 60 ng/mL	2	14 – 60 ng/mL	4
60 – 90 ng/mL	0	60 – 90 ng/mL	1
> 90 ng/mL	4	> 90 ng/mL	7



**Figure 2** Prescription time in relation to the patient's hospital admission



**Figure 3** Distribution of patients according to troponin test results

#### 4. Discussion

There is great heterogeneity in the demographics of COVID-19 patients. Our study shows a male predominance with a sex ratio of 1.12 which is close to a study performed in China [5] and in Italy [6] in 2020. At the genetic level, vulnerability markers have been identified on the ACE2 (Angiotensin Converting Enzyme 2) gene, which codes for the cellular receptor of the virus [7] and is located on the X chromosome, which could explain the gender differences in susceptibility, with an increase in morbidity and mortality in men [8].

The average age of the patients was 56.8 years. The resuscitation services of the CHU-JRA mainly take care of adult patients. Studies conducted by Chinese teams suggest that children and adults are equally susceptible to SARS-CoV-2 infection [9, 10], while other research highlights that children <18 years of age are less likely to develop the infection [11, 12]. Advanced age itself is a risk factor for the severity of COVID-19 [13].

Regarding comorbidities, 9 patients were hypertensive and 4 were diabetic. Certain comorbidities such as hypertension and diabetes are associated with a high expression of ACE2 receptors and a higher release of protein convertase that favours the entry of the virus into host cells [14].

In clinical practice, cardiac troponin I (cTnI) is measured in suspected acute coronary syndrome [2].

In the present study, the chronology of the request for troponin testing showed that 14 requests were made as soon as the patients were admitted to the intensive care unit. This early request may be justified by the fact that the troponin assay was prescribed to detect a myocardial complication of SARS-CoV-2 infection. ACE2 is highly expressed on the surface of myocardial cells and alveolar cells and the binding of the protein S (Spike) of SARS-CoV-2 to ACE2 facilitates

entry of the virus into these myocardial cells [15]. A.Maino *et al.* described an association between the severity of infection and elevated Troponin at hospital admission [16]. The lack of financial resources and the fact that health care is not free in a underdeveloping country such as Madagascar and this situation may be an obstacle to the performance of this troponin testing on admission.

Biological examination showed that 42.8% (N=18) of the 42 patients in this study had elevated cTnI. Furthermore, cardiac injury defined by elevated hs-cTnI was significantly related to biomarkers of inflammation (IL-6 (Interleukin 6) and CRP (C - reactive protein), hyperferritinemia and leukocytosis), showing a significant correlation between myocardial injury and inflammatory hyperactivity triggered by SARS-CoV-2 [2]. Apart from ischemic myocardial injury, and in view of the abundance of ACE2 in myocardial cells [15], other studies have suggested that myocarditis may explain an increase in hypersensitive troponins through the description of cases of fulminant myocarditis secondary to SARS-CoV-2 [17,18].

Of the patients with elevated hs-cTnI, 13 (72.2%) had values greater than 3 times the threshold for positivity. A US study has shown that higher plasma troponin elevation is predictive of a bad prognosis in patients infected with SARS-CoV-2[19].

In our study, the outcome was fatal in 19 patients, 11 (57.9%) of whom had elevated hs-cTnI. Heart disease is an important cause of death in patients infected with SARS-CoV-2 and occurs as a result of different mechanisms of myocardial aggression such as direct myocardial damage by viral action, systemic inflammatory responses, destabilized coronary plaque and aggravated hypoxia [20]. Our study was performed in patients admitted to intensive care units and according to the literature, cardiac Troponin level increase is commonly observed in critically ill COVID-19 patients and myocardial injury is strongly associated with in-hospital mortality [21].

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## 5. Conclusion

Myocardial involvement may be observed in patients during SARS-CoV-2 infection and may be predictive of a worse prognosis. Laboratory testing for hs-cTnI should be performed early and targeted because it can assist in the management of these patients with COVID-19.

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## Compliance with ethical standards

### *Acknowledgments*

We would like to thank all the staff of the laboratory of University Hospital of Ravoahangy Andrianavalona. Similarly, we would like to express our gratitude to the director of establishment for authorizing us to carry out this study.

### *Disclosure of conflict of interest*

The author declares no conflict of interest.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study

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