ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Level of high sensitivity troponin I and its correlation with hemodialysis vintage – A pilot study

Saloni Malik[1], Manisha Naithani[2], Anissa Atif Mirza[3], Sharon Kandari[4], Suman KM[5], Gaurav Shekhar Sharma[6]

[1]Senior Demonstrator, Department of Biochemistry, University College of Medical Sciences, New Delhi, [2,3]Professor, [5]MSc Medical Student, Department of Biochemistry, [4]Associate Professor, Department of Nephrology, All India Institute of Medical Sciences, Rishikesh, [6]Associate Professor, Department of Nephrology, SGRRIM & HS and SMI Hospital, Dehradun, Uttarakhand, India

Submission: 13-06-2024 Revision: 25-07-2024 Publication: 01-10-2024

ABSTRACT

Background: Renal replacement therapy (RRT) is advised in end-stage renal disease, the last stage of chronic kidney disease (CKD). RRT includes maintenance hemodialysis (MHD)/peritoneal dialysis/renal transplant. The requirement for MHD is annually escalating in India. It is important to note that over 80% of patients receiving MHD have at least one cardiac disease at the time of dialysis initiation, such as ischemic heart disease, congestive cardiac failure, and arrhythmias. **Aims and Objectives:** The present study aimed to study high-sensitivity cardiac troponin I (hs-cTnI) serum level as a marker of cardiovascular injury in patients receiving MHD. It was an attempt to envisage a correlation between serum hs-cTnI and hemodialysis (HD) vintage (duration since initiation of dialysis till date). **Materials and Methods:** We enrolled 40 patients. Group 1 included those who had received MHD for ≤24 months, and Group 2 included those who had received MHD for more than 24 months. **Results:** We found no significant difference between the two groups' clinical characteristics and demographic features. The pre-and post-HD serum hs-cTnI values of all patients were recorded. The serum hs-cTnI levels were found to be elevated in 34 out of 40 patients' post-dialysis, and the result was statistically significant (P = 0.0001). **Conclusion:** The present study has encouraging results, with values of hs-cTnI raised in post-dialysis samples; however, the levels did not correlate with HD vintage. Further studies with larger sample sizes and longer follow-ups would provide more detailed information on hs-cTnI's role as a marker for HD-induced cardiac damage.

Key words: High-sensitivity cardiac Troponin I; Hemodialysis; Cardiac disease

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i10.68119

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Renal replacement therapy (RRT) is a treatment modality for end-stage renal disease (ESRD), and its requirement is escalating annually in India.[1] RRT includes maintenance hemodialysis (MHD)/peritoneal dialysis (PD)/renal transplant. As per published literature, 130,000 patients were undergoing dialysis in our country in the year 2018.[2] Over 80% of patients receiving hemodialysis (HD) have at least one cardiac diagnosis, at baseline, such as ischemic heart disease, congestive heart failure, arrhythmias, or other heart disorders.[3] ESRD patients have a higher risk of mortality from cardiovascular disease as compared to non-ESRD patients. The Indian Chronic Kidney Disease study aimed to identify factors associated with chronic kidney disease (CKD) progression. They recorded that in 4056 patients, 22% had cardiovascular disease (CVD).[4]

During HD, cardiac damage is due to acute hemodynamic instability, resulting in disordered cardiovascular physiology. In 20–30% of patients undergoing HD, intradialytic hypotension can be present, leading to the formation of

Address for Correspondence:
Dr. Gaurav Shekhar Sharma, Associate Professor, Department of Nephrology, SGRRIM & HS and SMI Hospital, Dehradun, Uttarakhand, India. **Mobile:** +91-9460384265. **E-mail:** shekhargaurav2012@gmail.com

coronary plaques.[5] The plaque formation further leads to myocardial ischemia and inadequate cardiac remodeling, leading to left ventricular dysfunction. It is assumed to be the primary mechanism of increased cardiovascular mortality due to HD. Cardiovascular risk stratification can detect the early stage of cardiac injury using biomarkers, and thus, the treatment can be optimized. One such biomarker is human cardiac troponin I. The current and recent troponin I estimation, called high-sensitivity cardiac troponin I (hs-cTnI), provides elevated sensitivity and specificity in diagnosis.[6] This marker has shown to be raised in a significant proportion of those receiving HD, where elevation in post-dialysis hs-cTnI was present by at least 23.1% in a study conducted by Jalalonmuhali et al.[7]

The increased levels point toward possible silent myocardial injury during high-flux HD. Others also concluded that in patients undergoing low-flux HD, the values of cTrop I were higher after receiving HD.[8]

These recent studies point out lacunae in the present knowledge regarding information related to hs-cTnI levels and HD-induced myocardial damage. Thus, to address this lacuna, the present study aimed to study hs-cTnI serum level as a marker of cardiovascular injury in patients receiving MHD. We have analyzed their pre- and post-HD samples and correlated these levels with HD vintage.

Aims and objectives

This study aimed to study high-sensitivity cardiac Troponin I (hs-cTnI) serum level as a marker of cardiovascular injury in patients receiving MHD. It was an attempt to envisage a correlation between serum hs-cTnI and Hemodialysis (HD) vintage (duration since initiation of dialysis till date).

MATERIALS AND METHODS

The approval for the study was obtained from the Institute Ethical Committee under the letter number (IEC, 249/IEM/MSc/2021). It was a cross-sectional pilot study conducted from October 2021 to March 2023 in the Department of Biochemistry in collaboration with the Department of Nephrology at a tertiary care teaching hospital in North India. The patients were divided into two groups: Group 1: Those who had received MHD for ≤24 months and Group 2: Those who had received MHD for more than 24 months. This being a pilot study, a sample size of 40 was taken. A sequential enrolment of the study participants was done till the achievement of sample size.

Inclusion criteria

Inclusion criteria were as follows: The patients, 18 years or older, who were enrolled in the institute's MHD program and provided consent were recruited in the study.

Exclusion criteria

Exclusion criteria were as follows: Patients younger than 18 years of age or having any documentary evidence of acute myocardial infarction or heart failure during the past 6 months were excluded from the study.

A thorough medical history and examination were conducted for all study participants. Relevant demographic and clinical parameters were noted. In a plain vial, 2 mL of blood was collected before and after the MHD session after obtaining informed consent. The concentration was measured using direct chemiluminometric technology by 3-site sandwich Immunoassay. The serum hs-cTnI level was estimated using Advia Centaur High Sensitivity Troponin I assay (TNIH) using Advia Centaur XP immunoassay systems. The data were entered into an Excel spreadsheet and checked for errors. It was analyzed using the IBM Statistical Package for the Social Sciences (SPSS) statistics version 23, SPSS South Asia Private Limited, Bangalore, India. All the parameters were subjected to appropriate normality tests. Parameters following the Gaussian distribution were expressed as mean±SD; the comparison was made by t-test and correlation among parameters was made by Pearson's correlation analysis. $P<0.05$ was considered statistically significant for all statistical analyses.

RESULTS

A total of forty subjects (thirty-two males and eight females; mean age 46.25±17.34 years) receiving maintenance hemodialysis were enrolled. The clinical characteristics and demographic features of the two groups depending on the dialysis vintage (those who have received MHD for ≤24 months and for more than 24 months) are presented in Table 1. Most patients (n=34, 85%) received MHD for an average of 4 h per session. Only 6 (15 %) patients received MHD for an average of 6 h per session.

The mean pre- and post-HD serum hs-cTnI levels in the patients were 71.85±324.08 ng/mL and 95.78±329.52 ng/mL. The correlation of pre-HD and post-HD serum hs-cTnI levels with the duration of HD was not statistically significant (using the Mann–Whitney Test and Wilcoxon W test), as illustrated in Table 2. The serum hs-cTnI levels were raised in 34 out of 40 patients post-HD, and the result was statistically significant ($P=0.0001$) (based on positive ranks and using the Wilcoxon signed-rank test) (Table 3).

Table 1: Demographic and clinical characteristics data of chronic kidney disease patients receiving MHD

Characteristics of participants	Group 1 (MHD duration ≤24 months) Mean±SD, n=27	Group 2 (MHD duration >24 months) Mean±SD, n=13	P-value
Age (years) Mean±SD 46.25±17.34 years (including both male and female)	46.41±18.72	45.92±14.74	0.935
Diabetes (n [%]) Total in both groups: 14	9 (33.3%)	5 (38.5%)	1.000
Hypertension (n [%]) Total in both groups: 22	15 (55.6%)	7 (53.8%)	0.919
Pre-HD systolic BP (mmHg)	147.52±15.32	152.85±8.88	0.254
Pre-HD diastolic BP (mmHg)	85.33±11.16	83.38±9.11	0.588
Post-HD systolic BP (mmHg)	145.11±17.60	145.08±10.61	0.995
Post-HD diastolic BP (mmHg)	82.85±9.56	82.38±7.65	0.879
Duration of HD session (min)	241.11±56.73	240.0±0.0	1.000
Blood flow rate (mL/min)	214.14±35.668	242.31±18.78	0.013
Dialysate flow rate (mL/min)	466.67±62.018	500.0±0.00	0.047

MHD: Maintenance hemodialysis, HD: Hemodialysis, BP: Blood pressure

Table 2: Pre- and post-HD serum hs-cTnI levels correlation with dialysis

Characteristics	Group 1 (MHD duration ≤24 months) Mean±SD, n=27	Group 2 (MHD duration >24 months) Mean±SD, n=13	P-value
Pre-HD hs-TnI (ng/mL)	97.378±393.2847	18.840±41.2474	0.204
Post-HD hs-TnI (ng/mL)	116.919±390.9870	51.883±136.3165	0.285

HD: Hemodialysis, hs-cTnI: High-sensitivity cardiac troponin I

Table 3: Pre- and post-HD serum hs-cTnI levels

Pre-HD and Post-HD serum hs-TnI levels	Number of patients	P-value
Serum Pre-HD hs-TnI level <serum post-HD hs-TnI level	34	0.0001
Serum Pre-HD hs-TnI level >serum post-HD hs-TnI level	06	

HD: Hemodialysis, hs-cTnI: High-sensitivity cardiac Troponin I

DISCUSSION

In the present study, 32 patients were males (80%) and eight females (20%) with a male: female ratio of 4:1. In the present study, the male gender has a preponderance proportion-wise in those suffering from CKD and requiring maintenance hemodialysis. Harris and Zhang point out that the ESRD incidence is 50% higher in men as compared to women even though prevalence is much higher in women.[9] Our study has a higher male proportion and mirrors a recent study by Mohanty et al., in a tertiary care referral center in Eastern India.[10]

The mean age of the enrolled patients in the present study was 46.25±17.34 years (including both males and females), which is slightly lower than the consistent mean age in the CKD registry of India reported as 50 years.[11] Upon the contrary, international data from the United States confirm that CKD is more common in people aged 65 years or older (38%) than in people aged 45–64 years (12%) or 18–44 years (6%).[12]

In the present study, 14/40 patients (35%) were found to be suffering from diabetes mellitus, and 22/40 patients (55%) were hypertensive. In our study, we also found that 12/40 (30%) of patients had both diabetes and hypertension. There are many studies done that observed hypertension as a risk factor for CKD. It is known that hypertension affects 80%–85% of people with CKD, being an important prominent cause of ESRD worldwide.[13] Bingi et al.'s recent original research study in Telangana, India, observed that 96% of CKD patients had diabetic nephropathy and 85.7% of CKD patients had hypertensive nephropathy, making them the two most common causes of CKD.[14] Noppakun et al., studied pre-dialysis values of hs-cTnT and I in 198 patients receiving MHD and concluded that 180 (90.9%) patients were hypertensive, 89 (44.9%) patients had diabetes, and 105 (53%) patients were having dyslipidemia.[15]

The pre-dialysis and post-dialysis blood pressure was also observed in all patients in the present study, and a decline in post-dialysis blood pressure was seen. Similar findings were analyzed in a recent study (2020) by Rudhani et al., which observed that mean systolic and diastolic blood pressures before hemodialysis were higher than values after hemodialysis.[16]

The serum hs-cTnI level is a recommended biomarker for diagnosing acute myocardial infarction, but its cut-off level is derived from epidemiological data in the general population without taking into account CKD. The other common conditions leading to elevation of the serum troponin level are physical exertion, toxic damage to the heart, pulmonary embolism, and sepsis. In a study by Mohamed et al., who analyzed the influence of MHD on the hs-TnI serum level in children with ESRD, it was found that these children had statically significantly higher pre-dialysis serum hsTnI values as compared to post-dialysis levels.[17] However, in the present study, comparing pre-dialysis and post-dialysis hs-TnI levels of the ongoing dialysis patients showed elevation in post-HD samples in 34 patients out of 40 (85.7%).

The present study did not provide any correlation between serum hs-cTnI and HD vintage (duration since initiation of dialysis till date). Similarly, many studies reported no or variable change in troponin I levels post-dialysis. Snaedal et al., found that variability assessment using reference change values gave results of high variability values of +68/−41%, which on analysis was found to be related to age, male sex, wasting, and heart failure. It was not related to ischemic heart disease or type of dialysis (increased in both hemodialysis and PD).[18]

Wongcharoen et al., found a higher prevalence of elevated hs-cTnT in patients with regular HD compared to hs-cTnI. Their results indicated that hs-cTnT is more sensitive than hs-cTnI to detect minor degrees of myocardial injury in patients receiving HD. However, they also mention that hs-cTnI is preferred as a diagnostic marker in patients with suspected acute myocardial infarction as compared to hs-cTnT.[19]

Lim et al., used 1144 CKD patient data to determine cut-off of both biomarkers. Out of 82 patients with MI (75 on hemodialysis and 7 on PD), they found that the optimal cut-off value of hsTnI was 75 ng/L for hemodialysis patients as compared to a higher cut-off of 144 ng/L for those on PD. This study highlighted the need to consider the type of dialysis while making a diagnosis of myocardial infarction using hsTnI in ESRD patients.[20]

Limitations of the study

The present study is limited by a smaller sample size, as it's a pilot study.

CONCLUSION

To conclude, the present study has encouraging results, with serum values of hs-TnI raised in post-HD samples collected from ESRD patients on MHD. The levels did not correlate with HD vintage. However, further studies with larger sample sizes and longer follow-ups would provide more detailed information on hs-cTnI's role as a marker for HD-induced cardiac damage.

ACKNOWLEDGMENTS

The authors express their gratitude to the staff of the Department of Biochemistry and Department of Nephrology, All India Institute of Medical Sciences, Rishikesh, India, for their help and support.

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Authors' Contribution:
SM- Data collection, manuscript preparation, and submission of the article; **MN**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **AAM**- Design of study, statistical analysis, and interpretation; **SKM**- Statistical analysis, review manuscript; **SKM**- Manuscript preparation, review manuscript; **GSS**- Manuscript preparation, editing, manuscript revision and supervision of work.

Work attributed to:
All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.

Orcid ID:
Saloni Malik - https://orcid.org/0000-0001-7896-4553
Manisha Naithani - https://orcid.org/0000-0002-0984-4176
Anissa Atif Mirza - https://orcid.org/0000-0002-7531-3445
Sharon Kandari - https://orcid.org/0000-0002-5411-5837
Suman KM - https://orcid.org/0009-0007-9878-8084
Gaurav Shekhar Sharma - https://orcid.org/0000-0002-4529-9048

Source of Funding: This work was funded as an Intramural Fund by All India Institute of Medical Sciences, Rishikesh, **Conflicts of Interest:** None.