**Original Article** 

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# Prevalence of Asymptomatic Rise in Troponin I in Hemodialysis Patients at SIUT Hospital Karachi

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## **Abstract:**

## Objective:

To determine frequency of asymptomatic rise in troponin-I among hemodialysis patients.

To compare the mean of asymptomatic rise in troponin I between twice and thrice weekly hemodialysis patients.

#### Methods:

It is a Cross Sectional Study held in Sindh Institute of Urology and Transplantation outpatient dialysis department from June 25, 2020 to December 26, 2020 All patients of either gender age greater than 18-80 years undergoing hemodialysis via permanent angio-access without any history of shortness of breath and chest pain in preceding two weeks were consecutively enrolled. Information related to age, gender, causes of ESRD, duration of hemodialysis, date of last dialysis and date of sample collection was noted. Those whose tropon in I was in cardiac range was admitted.

#### Results:

Of 127 patients, mean age was  $38.17 \pm 14.75$  years. There were 64 (50.4%) females and 63 (49.6%) males. Twice weekly hemodialysis was observed in 64 (50.4%) and thrice weekly in 63 (49.6%) patients. Mean troponin I level was  $33.99 \pm 63.38$  ng/ml. Raised troponin I level was found in 26 (20.50%) patients. The mean troponin I level among with twice weekly hemodialysis was  $38.46 \pm 78.42$  while among thrice weekly hemodialysis session was  $29.45 \pm 43.27$  (p-value 0.425).

#### Conclusion:

The frequency of asymptomatic rise in troponin-I was found to be 20.5% among hemodialysis patients. However, the mean difference of troponin I level with number of sessions showed insignificant difference.

**Keywords:** Troponin-I level, Hemodialysis, acute coronary syndrome, arrythmia, prognosis

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#### Introduction

Ischemic heart disease and cardiac events are commonest cause of morbidity and mortality in end stage renal disease patients and its prevalence is 10 to 20 times higher than that in general population with 50% mortality due to cardiovascular disease. Sudden cardiac death is leading cause of death in patients with ESRD. After myocardial infarction the rate of survival in hemodialysis patients is much lower as compare to healthy individuals.

Several biochemical markers are used to detect myocardial injury and cardiac troponin is more specific among all indicating myocardial damage.<sup>4</sup> In end stage renal disease patients baseline troponin levels are often elevated therefore making diagnosis of acute myocardial damage more difficult. Guidelines recommend for diagnosis of

myocardial infarction value above 99th percentile is considered diagnostic.<sup>5</sup> Stably elevated level are frequently observed in asymptomatic patients with chronic kidney disease or on hemodialysis.<sup>6</sup> Therefore, in dialysis patients cardiac troponins has shifted from diagnostic use in suspected acute coronary syndrome towards the use of risk stratification.<sup>7</sup>

The increase in troponin level may be due to under excretion or abnormal catabolism induced by renal failure, uremia induced cardiomyopathy, subclinical myocardial damage and hemodialysis itself.<sup>2</sup> In end stage renal disease patients troponin I is generally been preferred as it has lower incidence of elevation (5 to 18%) using old generation assay and in (15 to 51%) of patients using new high sensitivity assays, whereas troponin T is elevated in about 29 to 99% of patients.<sup>8</sup> Elevated baseline troponin level has been associated with adverse long term outcome.<sup>8-10</sup> Everywhere standard dialyses of thrice per week sessions are done. But in our setup due to limited resources and excessive patient overload majority of patients are dialyzed twice per week and very few thrice per week.

End stage kidney disease patients are frequently hospitalized for intercurrent medical problems. In those with hemodynamic instability and/or pulmonary edema ECG and troponins are requested to rule out a cardiac cause. These patients usually have nonspecific ST segment and T wave changes in ECG, and elevated troponin levels leads to diagnostic dilemma and uncertainty in management. In a study performed among maintenance dialysis patients troponin levels pre dialysis were elevated in 30 percent of patients but degree of elevation was below the cutoff level noted for diagnosis of myocardial infarction. In addition, not all studies have shown elevation of troponin I in dialysis patients. To date there is no such information available among dialysis population of our country. This study helps in planning further treatment and workup and would avoid unnecessary treatment in hospitalized patients who do not have myocardial injury. The aim of study is to observe the difference in troponin I level of thrice weekly dialysis patients with twice weekly dialysis.

## **Patients and Methods:**

This is a Cross Sectional Study done in Setting Sindh Institute of Urology and Transplantation outpatient dialysis department for Six months duration from June 25, 2020 to December 26, 2020. Ethical approval was obtained from institutional review board #SIUT-ERC-2019/A-166

**Sample Size:** From previous study the estimated elevated troponin I level in hemodialysis patients is 30 percent. With margin of error 8% and 95% confidence interval a total of 127 patients was needed for this study by using Open – Epi calculator.

Sample Technique: Non-probability consecutive sampling technique.

# Inclusion Criteria:

- Either gender
- Adult patients greater than 18-80 years of age undergoing hemodialysis via permanent angio- access without any history of shortness of breath and chest pain in preceding two weeks.
- Giving informed consent.

# Exclusion Criteria:

- Previous myocardial infarction
- History of coronary artery bypass graft surgery
- Chronic angina

# Data Collection Procedure:

Data collection was started after approval of the proposal from the institute's Ethical Review Committee. Patients coming for routine hemodialysis meeting the inclusion criteria was recruited in study. Informed consent was taken, and purpose of study was explained and pre dialysis blood sample was collected. All the information was collected on predesigned proforma. Information related to age, gender, causes of ESRD, duration of hemodialysis, date of last dialysis and date of sample collection was noted. Troponin I was measured on Architect i 2000 SR using ELISA kit. Those whose troponin I was in cardiac range was admitted.

# Data Analysis Procedure:

All the data was entered and analyzed in SPSS version 20. Mean and standard deviation was computed for the continuous variables such as age, duration of hemodialysis and troponin I level. Categorical variables like gender, cause of end stage renal disease, number of sessions per week, ECG findings, and elevated troponin I level was presented as frequencies and percentages. Stratification was done by age, gender, caused of ESRD, and number of sessions per week on outcome variable troponin I ranges. Post stratification chi-square test was applied. Mean of troponin I of twice and thrice weekly hemodialysis patients was compared. Independent t-test was applied. p-value ≤0.05 was considered as significant.

## **Results:**

Total numbers of patients were 127. The mean age of the patients was 38.17 ±14.75 years. (Table 1) There were 83 (65.4%) patients with ≤40 years and 44 (34.6%) patients with >40 years of age. Gender distribution showed 64 (50.4%) females and 63 (49.6%) males. Cause of ESRD showed that 27 (21.3%) patients had diabetes mellitus, 36 (28.3%) had HTN, 15 (11.80%) had obstructive nephropathy, 13 (10.20%) had primary and secondary glomerulonephritis each, 2 (1.6%) had plasma cell dyscrasis, 5 (3.9%) had hereditary or cystic cause of ESRD whereas 16 (12.6%) had unknown cause of ESRD. (Table 2) Mean duration of hemodialysis was 3.77 ±4.08 years. (Table 2) There were 86 (67.7%) patients with  $\leq 4$  years and 41 (32.3%) patients with > 4 years of duration of hemodialysis. Twice weekly hemodialysis was observed in 64 (50.4%) and thrice weekly hemodialysis was reported in 63 (49.6%) patients. Normal ECG findings were found in all 127 (100%) patients. (Table 2) Mean troponin I level was found to be 33.99 ±63.38 ng/ml. (Table 2) Raised troponin I level was found in 26 (20.50%) patients. There were 102 (80.3%) patients with 200 troponin I level. Comparison of raised troponin I level with general characteristics showed significant association with duration of hemodialysis (p-value 0.003), primary Glomerulonephritis as cause of ESRD (p-value 0.034), secondary glomerulonephritis/vasculitis as cause of ESRD (p-value 0.044), and neoplasm/ plasma cell dyscrasias as cause of ESRD (pvalue 0.010). (Table 2) The mean difference of troponin I level with number of sessions showed insignificant difference. The mean troponin I level among with twice weekly hemodialysis was 38.46 ±78.42 while mean troponin I level among patients with thrice weekly hemodialysis session was found to be 29.45 ±43.27 (p-value 0.425). (Table 2)

# **Discussion:**

The findings of the current study have reported raised troponin I level that was found in 26 (20.50%) patients. In ESRD patients, troponin I is generally been preferred as it has lower incidence of elevation (5 to 18%) using old generation assay and in (15 to 51%) of patients using new high sensitivity assays, whereas troponin T is elevated in about 29 to 99% of patients. Elevated baseline troponin level has been associated with adverse longterm outcome. It is widely recognized that chronically elevated levels of cardiac troponin I level are frequently observed in ESRD

	Mean ± SD	Minimum	Maximum
Age of the patients (years)	38.17 ± 14.75	21	76
Duration of hemodialysis (years)	3.77 ± 4.08	5 months	21 years
Troponin I level of the patients (ng/ml)	33.99 ± 63.38	0.20	536

Table 1: Patient characteristics and Troponin I levels among 127 maintenance hemodialysis patients.

Males   13   50   63   0.086	Etiology	Subgroup	Raised Troponin I Level (Yes)	Raised Troponin I Level (No)	Total	p-value
SAD years   12   32   44	Age	≤40 years	18	65	83	0.481
Females		>40 years	12	32	44	
Females	Gender	Males	13	50	63	0.086
Number of Sessions   Females   Fem		Females	17	47	64	
DM as cause of ESRD	Duration of Hemodialysis	≤4 years	27	59	86	0.003
HTN as cause of ESRD		>4 years	3	38	44	
Obstructive uropathy		DM as cause of ESRD	8	19	27	0.408
Primary glomerulonephritis   0		HTN as cause of ESRD	9	27	36	0.818
Causes of ESRD         Secondary glomerulonephritis/vasculitis         6         7         13         0.044           Neoplasm/plasma cell dyscrasia         2         0         2         0.010           Hereditary/cystic         2         3         5         0.379           Unknown         1         15         16         0.080           Number of Sessions per Week         Twice         17         47         64         0.432           Etiology         Subgroup         Raised Troponin I Level (Yes)         Raised Troponin I Level (No)         P-value           Age         ≤40 years         18         65         83         0.481           Sender         Males         13         50         63         0.086           Females         17         47         64         0.086           Females         17         47         64         0.086           Hemodialysis         >4 years         3         38         44           Causes of ESRD         B         19         27         0.408           HTN as cause of ESRD         9         27         36         0.818           Obstructive uropathy         2         13         15         0.318		Obstructive uropathy	2	13	15	0.318
Secondary   glomerulonephritis/vasculitis   6		Primary glomerulonephritis	0	13	13	0.034
Hereditary/cystic   2   3   5   0.379     Unknown   1   15   16   0.080     Number of Sessions per Week   Thrice   13   50   63     Etiology   Subgroup   Raised Troponin   Level (Yes)   (No)     Age	Causes of ESRD		6	7	13	0.044
Number of Sessions per Week   Trice   17   47   64   0.432		Neoplasm/plasma cell dyscrasia	2	0	2	0.010
Number of Sessions per Week         Twice         17         47         64         0.432 per Week           Etiology         Subgroup         Raised Troponin I Level (Yes)         Raised Troponin I Level (No)         Total (No)         p-value (Per)           Age         ≤40 years         18         65         83         0.481           Gender         Males         13         50         63         0.086           Females         17         47         64         0.003           Hemodialysis         ≥4 years         27         59         86         0.003           Causes of ESRD         B         19         27         0.408           HTN as cause of ESRD         9         27         36         0.818           Obstructive uropathy         2         13         15         0.318           Primary glomerulonephritis         0         13         13         0.044           Secondary glomerulonephritis/vasulitis         2         0         2         0.010           Neoplasm/plasma cell dyscrasia         2         3         5         0.379           Unknown         1         15         16         0.080		Hereditary/cystic	2	3	5	0.379
Per Week   Thrice   13   50   63		Unknown	1	15	16	0.080
Etiology         Subgroup         Raised Troponin I Level (Yes)         Raised Troponin I Level (No)         Total p-value           Age         ≤40 years         18         65         83         0.481           >40 years         12         32         44         47           Gender         Males         13         50         63         0.086           Females         17         47         64         4           Duration of Hemodialysis         ≤4 years         27         59         86         0.003           54 years         3         38         44         44           Causes of ESRD         DM as cause of ESRD         8         19         27         0.408           HTN as cause of ESRD         9         27         36         0.818           Obstructive uropathy         2         13         15         0.318           Primary glomerulonephritis         0         13         13         0.044           Secondary glomerulonephritis/vasculitis         7         13         0.044           Neoplasm/plasma cell dyscrasia         2         0         2         0.010           Hereditary/cystic         2         3         5         0.379	Number of Sessions	Twice	17	47	64	0.432
(Yes)       (No)       Resided       ≤40 years       18       65       83       0.481         Age       ≤40 years       12       32       44         Gender       Males       13       50       63       0.086         Females       17       47       64       44         Duration of Hemodialysis       ≤4 years       27       59       86       0.003         Hemodialysis       >4 years       3       38       44       44         Causes of ESRD       8       19       27       0.408         HTN as cause of ESRD       9       27       36       0.818         Obstructive uropathy       2       13       15       0.318         Primary glomerulonephritis       0       13       13       0.044         Secondary glomerulonephritis/vasculitis       6       7       13       0.044         Neoplasm/plasma cell dyscrasia       2       0       2       0.010         Hereditary/cystic       2       3       5       0.379         Unknown       1       15       16       0.080         Number of       Twice       17       47       64       0.432	per Week	Thrice	13	50	63	
Secondary glomerulonephritis   Neoplasm/plasma cell dyscrasia   Number of	Etiology	Subgroup	-	I -	Total	p-value
Gender         Males         13         50         63         0.086           Females         17         47         64           Duration of Hemodialysis         \$\frac{4}{2}\$ years         27         59         86         0.003           Causes of ESRD         9         38         44         44           Causes of ESRD         9         27         36         0.818           HTN as cause of ESRD         9         27         36         0.818           Obstructive uropathy         2         13         15         0.318           Primary glomerulonephritis         0         13         13         0.034           Secondary glomerulonephritis/vasculitis         6         7         13         0.044           Neoplasm/plasma cell dyscrasia         2         0         2         0.010           Hereditary/cystic         2         3         5         0.379           Number of         Twice         17         47         64         0.432	Age			(/		
Females   17	Age	≤40 years		• •	83	0.481
Duration of Hemodialysis         ≤4 years         27         59         86         0.003           Causes of ESRD         >4 years         3         38         44           Causes of ESRD         DM as cause of ESRD         8         19         27         0.408           HTN as cause of ESRD         9         27         36         0.818           Obstructive uropathy         2         13         15         0.318           Primary glomerulonephritis         0         13         13         0.034           Secondary glomerulonephritis/vasculitis         6         7         13         0.044           Neoplasm/plasma cell dyscrasia         2         0         2         0.010           Hereditary/cystic         2         3         5         0.379           Unknown         1         15         16         0.080           Number of         Twice         17         47         64         0.432	Age	•	18	65		0.481
Number of   Numb	Age Gender	>40 years	18 12	65 32	44	
Causes of ESRD DM as cause of ESRD 8 19 27 0.408 HTN as cause of ESRD 9 27 36 0.818 Obstructive uropathy 2 13 15 0.318 Primary glomerulonephritis 0 13 13 0.034 Secondary glomerulonephritis/vasculitis Neoplasm/plasma cell dyscrasia Hereditary/cystic 2 3 5 0.379 Unknown 1 15 16 0.080  Number of Twice 17 47 64 0.432		>40 years Males	18 12 13	65 32 50	44 63	
HTN as cause of ESRD   9   27   36   0.818     Obstructive uropathy   2   13   15   0.318     Primary glomerulonephritis   0   13   13   0.034     Secondary   6   7   13   0.044     glomerulonephritis/vasculitis   0   2   0   2   0.010     dyscrasia   Hereditary/cystic   2   3   5   0.379     Unknown   1   15   16   0.080     Number of   Twice   17   47   64   0.432	Gender  Duration of	>40 years Males Females	18 12 13 17	65 32 50 47	44 63 64	0.086
Obstructive uropathy   2   13   15   0.318	Gender  Duration of	>40 years  Males  Females  ≤4 years	18 12 13 17 27	65 32 50 47 59	44 63 64 86	0.086
Primary glomerulonephritis   0	Gender  Duration of  Hemodialysis	>40 years  Males  Females  ≤4 years  >4 years	18 12 13 17 27 3	65 32 50 47 59 38	44 63 64 86 44	0.086
Secondary   6   7   13   0.044	Gender  Duration of  Hemodialysis	>40 years  Males Females  ≤4 years  >4 years  DM as cause of ESRD	18 12 13 17 27 3 8	65 32 50 47 59 38 19	44 63 64 86 44 27	0.086
September   Sept	Gender  Duration of  Hemodialysis	>40 years  Males  Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD	18 12 13 17 27 3 8 9	65 32 50 47 59 38 19 27	44 63 64 86 44 27 36	0.086 0.003 0.408 0.818
dyscrasia           Hereditary/cystic         2         3         5         0.379           Unknown         1         15         16         0.080           Number of         Twice         17         47         64         0.432	Gender  Duration of  Hemodialysis	>40 years  Males  Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD  Obstructive uropathy	18 12 13 17 27 3 8 9	65 32 50 47 59 38 19 27 13	44 63 64 86 44 27 36 15	0.086 0.003 0.408 0.818 0.318
Unknown         1         15         16         0.080           Number of         Twice         17         47         64         0.432	Gender  Duration of  Hemodialysis	>40 years  Males Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD  Obstructive uropathy  Primary glomerulonephritis  Secondary	18 12 13 17 27 3 8 9 2 0	65 32 50 47 59 38 19 27 13 13	44 63 64 86 44 27 36 15	0.086 0.003 0.408 0.818 0.318
Number of         Twice         17         47         64         0.432	Gender  Duration of  Hemodialysis	>40 years  Males  Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD  Obstructive uropathy  Primary glomerulonephritis  Secondary glomerulonephritis/vasculitis  Neoplasm/plasma cell	18 12 13 17 27 3 8 9 2 0 6	65 32 50 47 59 38 19 27 13 13	44 63 64 86 44 27 36 15 13	0.086 0.003 0.408 0.818 0.318 0.034 0.044
Casting and World	Gender  Duration of  Hemodialysis	>40 years  Males  Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD  Obstructive uropathy  Primary glomerulonephritis  Secondary glomerulonephritis/vasculitis  Neoplasm/plasma cell dyscrasia	18 12 13 17 27 3 8 9 2 0 6	65 32 50 47 59 38 19 27 13 13 7	44 63 64 86 44 27 36 15 13	0.086 0.003 0.408 0.818 0.318 0.034 0.044
Sessions per Week Thrice 13 50 63	Gender  Duration of  Hemodialysis	>40 years  Males  Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD  Obstructive uropathy  Primary glomerulonephritis  Secondary glomerulonephritis/vasculitis  Neoplasm/plasma cell dyscrasia Hereditary/cystic	18 12 13 17 27 3 8 9 2 0 6	65 32 50 47 59 38 19 27 13 13 7	44 63 64 86 44 27 36 15 13	0.086 0.003 0.408 0.818 0.318 0.034 0.044 0.010
	Gender  Duration of Hemodialysis  Causes of ESRD	>40 years  Males  Females  ≤4 years  >4 years  DM as cause of ESRD  HTN as cause of ESRD  Obstructive uropathy  Primary glomerulonephritis  Secondary glomerulonephritis/vasculitis  Neoplasm/plasma cell dyscrasia Hereditary/cystic  Unknown	18 12 13 17 27 3 8 9 2 0 6 2 1	65 32 50 47 59 38 19 27 13 13 7 0 3 15	44 63 64 86 44 27 36 15 13 2 5	0.086 0.003 0.408 0.818 0.318 0.034 0.044 0.010 0.379 0.080

Table 2: Comparison of end stage kidney disease etiology with Trop I levels among 127 maintenance hemodialysis patients.

patients independently of the presence of acute signs of cardiac disease. <sup>9,10</sup> Since cardiac troponin I level are considered the reference biomarkers for the diagnosis of acute myocardial infarction, these persistently elevated levels represent a potentially serious diagnostic challenge in ESRD patients. <sup>11-13</sup> According to this observation, some authors suggest that troponin's trends and not just absolute single cardiac troponin I level value be observed in this population. <sup>14</sup>

According to the current study findings, Comparison of raised troponin I level with general characteristics showed significant association with duration of hemodialysis (p-value 0.003), primary Glomerulonephritis as cause of ESRD (p-value 0.034), secondary glomerulonephritis/vasculitis as cause of ESRD (p-value 0.044), and neoplasm/ plasma cell dyscrasias as cause of ESRD (p-value 0.010). Previous studies showed a significant association of elevated baseline cardiac troponin I level with age, male gender, diabetes, history of coronary artery disease, left ventricular ejection fraction, phosphate levels, and dialysis vintage. 15-18

Besides altered renal function, other mechanisms are involved in chronic cardiac troponin I elevation in ESRD patients. Chronic cardiac dysfunction and myocardial injury related to the presence of diabetes, hypertensive left ventricular hypertrophy, and subclinical or silent coronary artery disease may play a role. Moreover, there are several evidences that the hemodialysis procedure itself may determine subclinical cardiac injury by exerting negative effects on myocardial perfusion and function. <sup>19-21</sup>In the current study, the mean difference of troponin I level with number of sessions showed insignificant difference. Assa et al.(138) and Ingec et al.(142), using sensitive assays, observed a significant increase in cardiac troponin I levels during hemodialysis, providing support to potential negative effects of HD on myocardial perfusion with repetitive subtle cardiac injury and cardiac troponin I elevation. In accordance to this, Assa et al.(138) showed a significant correlation between cardiac troponin I rise and dialysis vintage and a significant association with the incidence of adverse cardiovascular events.

## Conclusion:

The frequency of asymptomatic rise in troponin-I was found to be 20.5% among hemodialysis patients. However, the mean difference of troponin I level with number of sessions showed insignificant difference.

## **Conflict of interest:** I have no conflict of interest.

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