Correlation of progression EGFR with change in ankle brachial pressure index in non-dialyzed chronic kidney disease patients

By Nithesh Babu R

WORD COUNT 3467
TIME SUBMITTED 01-JUL-2024 03:49PM
PAPER ID 109972416

Original Article

Correlation of progression EGFR with change in ankle brachial pressure index in non-dialyzed chronic kidney disease patients

Nithesh Babu R, Abinaya Srinivasa Rangan, Shreenidhi R, Prasanna Karthik S

Department of General Medicine, Saveetha Medical College, Chennai, Tamil Nadu, India

CORRESPONDING AUTHOR:

Nithesh Babu Ramesh

nrt5596@gmail.com

ABSTRACT

Background. Chronic kidney disease (CKD) poses a significant public health issue worldwide, with prevalence rates varying between 11.9% and 16.2%. Chronic kidney disease (CKD) has a significant association with cardiovascular events and mortality, such as accelerated atherosclerosis, stroke, heart failure, coronary artery disease (CAD), and peripheral arterial disease (PAD). A high ankle-brachial index (ABI) is indicative of elevated cardiovascular disease (CVD) risk, whereas a low ABI is linked to angiographically confirmed atherosclerosis and mortality. Recent studies have revealed a U-shaped correlation between ABI and mortality,

underscoring the importance of early detection and intervention to mitigate potential complications.

Aim: To correlate ABI changes with eGFR changes in CKD patients to screen for peripheral vascular disease development.

Materials and Methods. The study was conducted at the Saveetha Medical College, Chennai, Tamil Nadu in India as a prospective cross-sectional study, and a total of 120 patients diagnosed with acute ischemic stroke were enrolled for this study from July 2023 to January 2024. **Results:** The study showed that at the end of the 3rd month, a positive correlation was observed between ABI and eGFR (r = 0.259), while when the 6th month ended, this correlation continued to persist (r = 0.245).

Conclusion. The present study concludes that there exists a direct relationship between decreasing eGFR and ABI, increasing susceptibility to peripheral artery disease and cardiovascular disease. Thus, a low ABI is linked to accelerated eGFR decline, indicating that systemic atherosclerosis predicts kidney function deterioration.

Keywords: Chronic Kidney Disease (CKD), Ankle Brachial Index, eGFR

INTRODUCTION

Chronic kidney disease (CKD) is a matter of great importance in global public health, with a prevalence that varies between 11.9% and 16.2% [1,2]. Chronic kidney disease (CKD) has a significant association with cardiovascular events and mortality, such as accelerated atherosclerosis, stroke, heart failure, coronary artery disease (CAD), and peripheral arterial disease (PAD) [3]. PAD symptoms, including cold extremities, peripheral numbness, and muscle cramps, are frequently observed in patients with CKD, suggesting a significant prevalence of PAD. The ankle brachial index (ABI), whether high or low, serves as a reliable predictor of cardiovascular disease (CVD) risk. Notably, a low ABI is particularly associated with a rapid

decline in estimated glomerular filtration rate (eGFR), indicating that systemic atherosclerosis plays a crucial role in predicting the deterioration of kidney function [4,5]. Recent research indicates a U-shaped relationship between ABI and mortality, emphasizing its importance in risk assessment [6]. Screening for peripheral vascular disease is crucial in preventing complications. This study aims to identify ABI changes and correlate them with eGFR changes in CKD patients to screen for peripheral vascular disease development.

MATERIALS AND METHODS

Study Design and Setting: This prospective cross-sectional study was carried out at the Outpatient Department of Saveetha Medical College situated in Chennai, Tamil Nadu, spanning six months from July 2023 to January 2024. Saveetha Medical College is a large multi-specialty hospital with 1600 beds, situated in Kuthambakkam, southwest of Chennai.

Study Population: The study included patients admitted with Chronic Kidney Disease to the Department of General Medicine

Sample Size Calculation: The sample size calculation, using the prevalence formula to calculate the sample size, using p of 53.5, a confidence interval of 95% and a margin of error of 10% came out to be 100. Therefore, 100 cases admitted to the medical wards of Saveetha Medical College, who provided consent and met the inclusion criteria, were incorporated into the study.

Inclusion and Exclusion Criteria: The inclusion criteria comprised of patients diagnosed with chronic kidney disease presenting with decreased eGFR (<60 ml/min/1.73m^2) and one or more markers for kidney damage, including albuminuria (urine albumin creatinine ratio >30mg/g or >3mg/mmol), structurally reduced kidney size (<8cm in ultrasound with an increase in cortical echoes and Cmd dissociation), urinary sediment abnormalities (microhematuria, renal tubular epithelial cells), or biopsy-proven kidney disease. The exclusion criteria comprised of patients with an established diagnosis of peripheral vascular disease, end-stage renal disease (stage V CKD, eGFR <15 ml/hour undergoing dialysis), amputated upper and lower limbs, hemodynamically unstable patients, and those who provide negative consent will be excluded from the study.

Method of Data Collection: After obtaining informed consent, eGFR was assessed using the standard MDRD equation and Ankle Brachial Index (ABI) was measured. This assessment occurred at baseline, 3-month, and 6-month visits, indicating peripheral vascular disease if <0.9. Changes in ABI were correlated with eGFR across these visits to screen for peripheral vascular disease development in non-dialyzed CKD patients at Saveetha Medical College.

Ethical Considerations: Before commencing the study, the Committee on Human Research Publication and Ethics of Saveetha Medical College, Chennai granted ethical clearance

(SAV/AP/22/92). Each participant provided written informed consent prior to the administration of the standard structured questionnaire and collection of blood samples. To ensure participant confidentiality and anonymize all collected data, eligible participants were required to sign or thumbprint a consent form before enrollment.

All participants in the study were provided with standard treatment in accordance with our established protocol, without incurring any costs for either the participants or the hospital involved in the study. Furthermore, the study participants did not receive any personal or professional benefits, whether directly or indirectly, from any commercial organization.

Data Collection: All participants underwent interviews utilizing a pre-tested structured questionnaire to collect demographic information and relevant data. Anthropometric measurements including weight and height were conducted using standard equipment, and Body Mass Index (BMI) was subsequently calculated. eGFR and Ankle Brachial Index were also calculated using standard methods.

Statistical Analysis: Statistical analysis was performed using SPSS Version 27. Continuous variables were displayed as mean (standard deviation), while discrete variables were shown as number (percentages). Descriptive statistics, such as frequency, percentages, and graphs, were employed to address the initial objective. The relationship between variables and healthcare seeking behavior was investigated using the Chi-square test for proportions, with Fisher's exact test utilized when appropriate. A significance level of $p < 0.05$ was selected to determine the strength and significance of associations. A p-value less than 0.05 indicates statistical significance, representing the likelihood of obtaining the result if the null hypothesis were true, indicating a Type I error.

RESULTS

Table 1: Frequency distribution of Age in the study

Age-wise distribution	Frequency	Percentage
20 - 40	20	20
41 – 60	48	48
61 – 80	28	28
>80	04	04

Table 1 illustrates the frequency distribution of age of our subjects in this study. Majority that is 48% of our subjects were between 41-60 years. 28% of them were between 61-80 years of age, 20% of the subjects were 20-40 years and only 4% of them were >80 years.

Table 2: Gender distribution among patients in the study

Gender	Percentage
Male	69
Female	31

Table 2 demonstrates the frequency distribution of gender. 69% of the study population were males and 31% of the study population was female.

Table 3: Comparison of Estimated GFR at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease patients by One way ANOVA

Parameter	EGFR at 0th Month Mean ± SD (n = 100)	EGFR at 3rd Month Mean ± SD (n = 100)	EGFR at 6th Month Mean ± SD (n = 100)	F- value	p -value
Estimated GFR	35.60 ± 11.64	34.70± 12.00	34.19 ± 12.20	0.355	0.701 (ns)

Table 3 describes the comparison of Estimated GFR at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease patients. eGFR progressively decreased from 0th to 6th month. eGRF was 35.60 ± 11.64 at 0th month, 34.70± 12.00 at 3rd month and 34.19 ± 12.20 at 6th month.

Table 4: Inter group comparison of Estimated GFR at different time in non – dialyzed chronic kidney disease patients by Repeated measure ANOVA (RANOVA)

Factor	Mauchly's W	Sig	Greenhouse Geisser				
			Type III Sum of Squares	df	Mean Square	F	Sig.
Within groups	0.722	0.000	101.557	1.565	64.904	23.039	**0.000**** *

Table 4 shows the inter group comparison of Estimated GFR at different time in non – dialyzed chronic kidney disease patients. There was significant difference within groups and it was statistically significant (p=0.000).

Table 5: Comparison of Ankle Brachial Index at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease patients by One way ANOVA

Parameter	Ankle Brachial Index at 0th Month Mean ± SD (n = 100)	Ankle Brachial Index at 3rd Month Mean ± SD (n = 100)	Ankle Brachial Index at 6th Month Mean ± SD (n = 100)	F- value	p -value
Ankle Brachial Index	0.883 ± .032	0.861± .057	0.848 ± .055	12.431	**0.000****

Table 5 demonstrates the comparison of ankle brachial index at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease. ABI index decreased at 6th month compared to 3rd and 6th month and it was found to be statistically significant. It was 0.883 ± .032 at 0th month, 0.861± .057 at 3rd month and 0.848 ± .055 at 6th month and it was found to be highly statistically significant (p=0.000).

Table 6: Inter group comparison of Ankle Brachial Index at different time in non – dialyzed chronic kidney disease patients by Repeated measure ANOVA (RANOVA)

Factor	Mauchly's W	Sig	Greenhouse Geisser				
			Type III Sum of Squares	df	Mean Square	F	Sig.
Within groups	0.338	0.000	0.061	1.203	0.051	37.576	**0.000*** **

Table 6 shows that Inter group comparison of Ankle Brachial Index at different time in non – dialyzed chronic kidney disease patients shown in table 8 showed statistically significant results (p=0.000).

Table 7: Comparison of EGFR and ABI at 0th month and ABI at 0th month in non – dialyzed chronic kidney disease patients by Pearson Correlation

		EGFR 0th Month	EGFR 3rd Month	EGFR 6th Month	ABI 0th Month	ABI 3rd Month	ABI 6th Month
EGFR 0th Month	**Pearson Correlation**	1	.993**	.979**	.243*	.486**	.494**
	Sig. (2-tailed)		**.000**	**.000**	**.015**	**.000**	**.000**
EGFR 3rd Month	**Pearson Correlation**	.993**	1	.984**	.271**	.509**	.514**
	Sig. (2-tailed)	**.000**		**.000**	**.006**	**.000**	**.000**

EGFR 6th Month	**Pearson Correlation**	.979**	.984**	1	.251*	.495**	.495**
	Sig. (2-tailed)	**.000**	**.000**		**.012**	**.000**	**.000**
ABI 0th Month	**Pearson Correlation**	.243*	.271**	.251*	1	.533**	.525**
	Sig. (2-tailed)	**.015**	**.006**	**.012**		**.000**	**.000**
ABI 3rd Month	**Pearson Correlation**	.486**	.509**	.495**	.533**	1	.953**
	Sig. (2-tailed)	**.000**	**.000**	**.000**	**.000**		**.000**
ABI 6thmonth	**Pearson Correlation**	.494**	.514**	.495**	.525**	.953**	1
	Sig. (2-tailed)	**.000**	**.000**	**.000**	**.000**	**.000**	

Table 7 presents the Pearson correlation coefficients between estimated glomerular filtration rate (EGFR) and ankle-brachial index (ABI) at 0th, 3rd, and 6th months in non-dialyzed chronic kidney disease patients. The correlations reveal strong positive associations between EGFR and ABI measurements across the three time points, indicating a significant relationship between kidney function and peripheral arterial health over time.

Figure 1: Comparison of Estimated GFR at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease patients

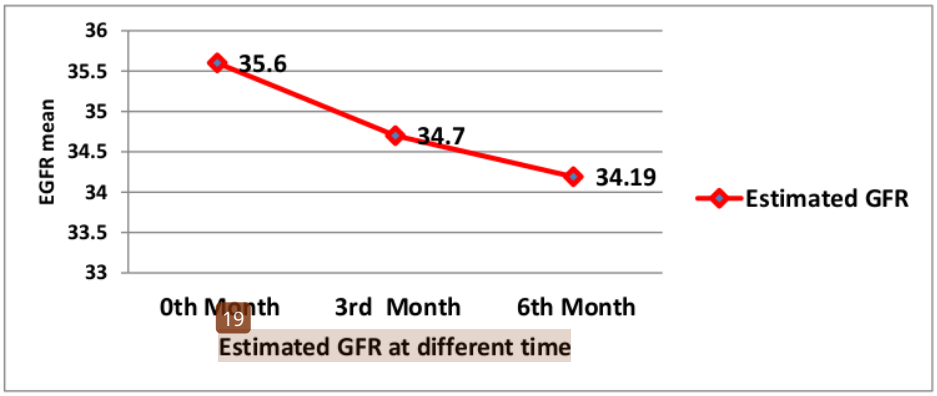

Figure 1 shows the comparison of Estimated GFR at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease patients. eGFR progressively decreased from 0th to 6th

month. eGRF was 35.60 ± 11.64 at 0th month, 34.70± 12.00 at 3rd month and 34.19 ± 12.20 at 6th month.

Figure 2: Comparison of Ankle Brachial Index at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease patients

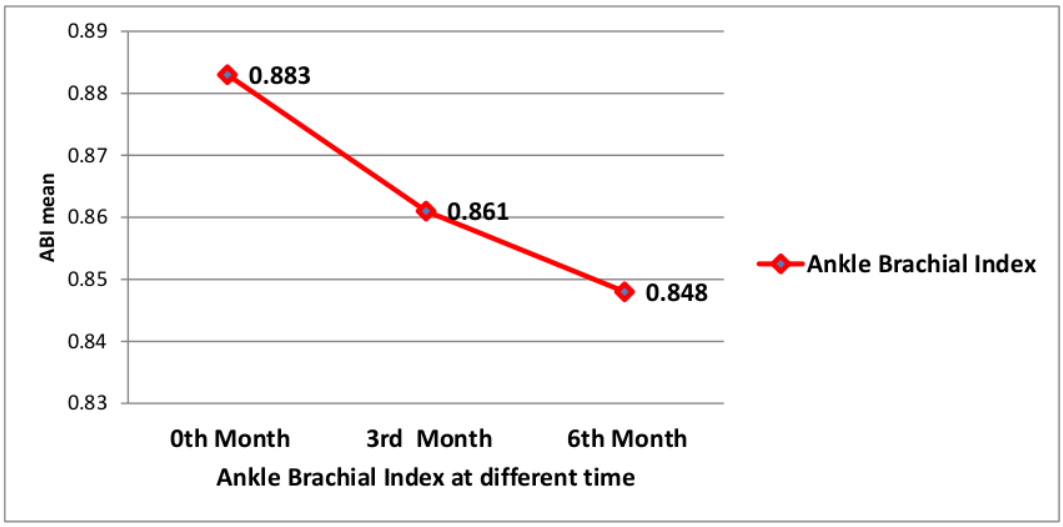

Figure 2 shows the comparison of ankle brachial index at different time (0th, 3rd, and 6th month) in non – dialyzed chronic kidney disease. ABI index decreased at 6th month compared to 3rd and 6th month and it was found to be statistically significant. It was 0.883 ± .032 at 0th month, 0.861± .057 at 3rd month and 0.848 ± .055 at 6th month and it was found to be highly statistically significant (p=0.000).

Figure 3: Comparison of EGFR at 0th month and ABI at 0th month in non – dialyzed chronic kidney disease patients by Pearson Correlation

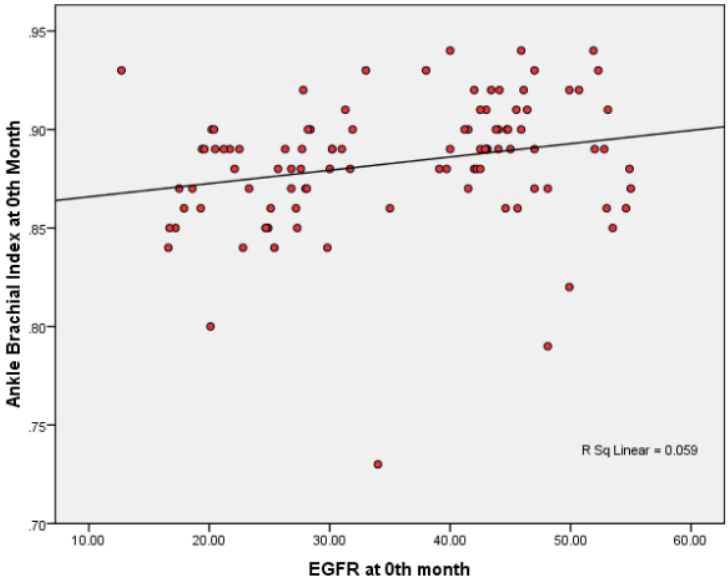

Figure 3 represents the comparison of EGFR at 0th month and ABI at 0th month in non – dialyzed chronic kidney disease patients by Pearson Correlation. The correlation between ABI and eGFR shows mild positive correlation and the r value is 0.059.

Figure 4: Comparison of EGFR at 3rd month and ABI at 3rd month in non – dialyzed chronic kidney disease patients by Pearson Correlation

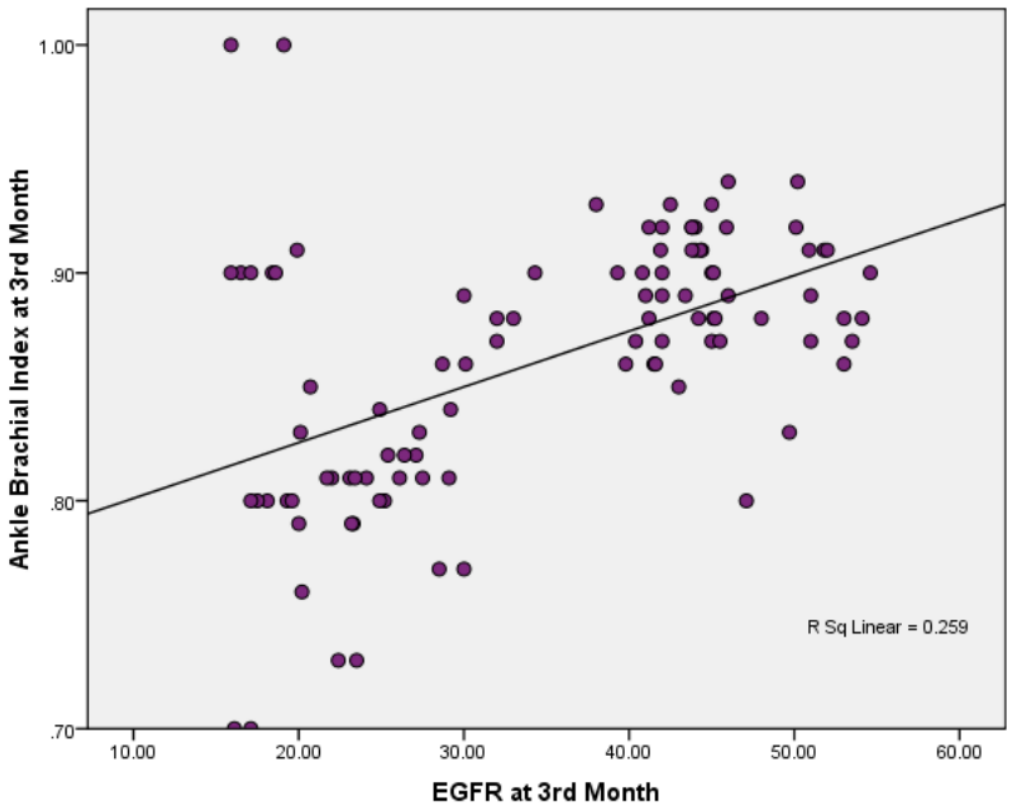

Figure 4 represents the comparison of EGFR at 3rd month and ABI at 3rd month in non – dialyzed chronic kidney disease patients by Pearson Correlation. The correlation between ABI and eGFR shows positive correlation and the r value is 0.259.

Figure 5: Comparison of EGFR at 6th month and ABI at 3th month in non – dialyzed chronic kidney disease patients by Pearson Correlation

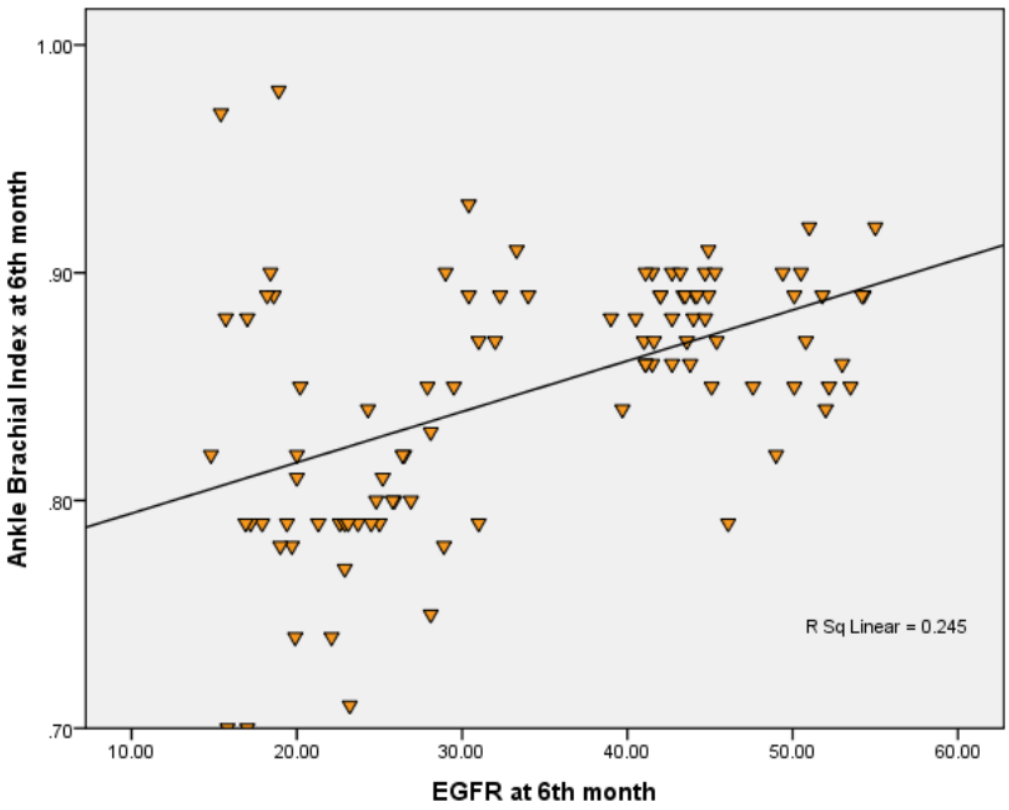

Figure 5 represents the comparison of EGFR at 6th month and ABI at 6th month in non – dialyzed chronic kidney disease patients by Pearson Correlation. The correlation between ABI and eGFR shows positive correlation and the r value is 0.245.

DISCUSSION

The study included 100 patients with Chronic kidney disease, between the ages of 18 and 60, who presented at the Outpatient department in the Department of General Medicine at Saveetha Medical College, Chennai. Among the patients assessed, a notable distribution across different age groups was observed. The mean age of our subject was 54.26 years. The minimum age was found to be 21 years and maximum was found to be 97 years. Majority of the study population, that is, 48% of our subjects, were between 41-60 years. 28% of them were between 61-80 years

of age, 20% of the subjects were 20-40 years and only 4% of them were >80 years. In our study about 69% of them were males.

We have observed that estimated GFR in our subjects was progressively decreased from 0^{th}, 3^{rd}, and 6^{th} months. The eGFR was 35.60 ± 11.64 at 0^{th} month, 34.70± 12.00 in 3^{rd} month and 34.19 ± 12.20 in 6^{th} month. Thus, eGFR progressively decreased from 0^{th} month to 6^{th} month and it was found to be statistically significant (p=0.000).

Obideyi T O et al, found that a decreased eGFR was linked to PAD. A reduced eGFR serves as a standalone predictor of both PAD and CVD morbidity and mortality [7]. This discovery aligns with Baber et al's research, which revealed that the occurrence of PAD is 14.8% and 25.4% in individuals with solely decreased eGFR and in those with both decreased eGFR and microalbuminuria, respectively [8].

Chen J and colleagues found that an ABI of less than 1.0 was markedly and significantly linked to a higher risk of clinical PAD, MI, composite CVD, and all-cause mortality in individuals with CKD [9]. In our study the mean ABI at 0^{th} month was 0.883 ± .032 and it started declining at 3^{rd} month which was 0.861± .057 and at the end of 6^{th} month it further declined to 0.848 ± .055. This was found to be highly statistically significant (p=0.000) [9].

Laghari S et al, demonstrated that 27.8% of patients with chronic kidney disease (CKD) exhibited an ankle-brachial index (ABI) indicative of peripheral artery disease (PAD) (10). The presence of a low ABI has proven to be both highly sensitive and specific in identifying more than 50% stenosis of the lower extremity vessels through angiography. Furthermore, it has been reported that CKD patients with a low ABI experience a heightened risk of cardiovascular events and mortality [10,11].

Chen FA et al, reported that there is 3.3-fold higher risk for developing cardiovascular events in patients with ABI < 0.9 than in patients with ABI ≥ 0.9 [12].

In our study, the estimated glomerular filtration rate (eGFR) showed a significant progressive decline from the 0th to the 6th month, with values of 35.60 ± 11.64, 34.70 ± 12.00, and 34.19 ±

12.20, respectively (p=0.000). Concurrently, the mean ankle-brachial index (ABI) also exhibited a substantial decrease over time, dropping from 0.883 ± .032 at the 0th month to 0.848 ± .055 at the 6th month (p=0.000), indicating deteriorating peripheral arterial health. Correlation analysis revealed a mild positive correlation between ABI and eGFR at the 0th month (r=0.059), which strengthened by the 3rd and 6th months (r=0.259 and r=0.245, respectively). These findings suggest that as eGFR declines, ABI decreases as well, heightening the risk of peripheral artery disease and cardiovascular complications. Therefore, a low ABI signifies an increased likelihood of rapid eGFR decline, underscoring the predictive relationship between systemic atherosclerosis and kidney function deterioration.

CONCLUSION

Our study highlights a significant association between ankle-brachial index (ABI) and future clinical peripheral arterial disease (PAD) among chronic kidney disease (CKD) patients. Specifically, a decreased ABI (<0.9) is notably linked with heightened risks of myocardial infarction (MI), cardiovascular disease (CVD), and all the other causes of mortality in this population. Moreover, we observed a positive correlation between reduced ABI and estimated glomerular filtration rate (eGFR) in CKD patients, indicating that lower ABI levels are associated with a more rapid decline in kidney function. These findings underscore the predictive value of systemic atherosclerosis in anticipating declines in kidney health among CKD patients.

CONFLICT OF INTEREST

Nil

AUTHOR'S CONTRIBUTIONS

Conceptualization: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan, Dr Prasanna Karthik Suthakaran*

Methodology: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan*

Software: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan*

Validation: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan, Dr Prasanna Karthik Suthakaran*

Formal analysis: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan, Dr Prasanna Karthik Suthakaran*

Investigation: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan*

Resources: *Dr. Nithesh Babu Ramesh, Dr Shreenidhi Rangarajan*

Data curation: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan*

Writing—original draft preparation: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan*

Writing—review and editing: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan, Dr Prasanna Karthik Suthakaran*

Visualization: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan, Dr Shreenidhi Rangarajan, Dr Prasanna Karthik Suthakaran*

Supervision: *Dr. Nithesh Babu Ramesh, Dr Prasanna Karthik Suthakaran*

Project administration: *Dr Shreenidhi Rangarajan, Dr Prasanna Karthik Suthakaran*

Funding acquisition: *Dr. Nithesh Babu Ramesh, Dr Abinaya Srinivasa Rangan*

18
All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Wen CP, Cheng TYD, Tsai MK, Chang YC, Chan HT, Tsai SP, et al. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. Lancet. 2008 Jun 28;371(9631):2173–82.
2. Imai E, Horio M, Watanabe T, Iseki K, Yamagata K, Hara S, et al. Prevalence of chronic kidney disease in the Japanese general population. Clin Exp Nephrol. 2009 Dec;13(6):621–30.
3. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C-Y. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004 Sep 23;351(13):1296–305.
4. Vogt MT, McKenna M, Anderson SJ, Wolfson SK, Kuller LH. The relationship between ankle-arm index and mortality in older men and women. J Am Geriatr Soc. 1993 May;41(5):523–30.
5. Ankle Brachial Index Collaboration, Fowkes FGR, Murray GD, Butcher I, Heald CL, Lee RJ, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA. 2008 Jul 9;300(2):197–208.
6. Sutton-Tyrrell K, Venkitachalam L, Kanaya AM, Boudreau R, Harris T, Thompson T, et al. Relationship of ankle blood pressures to cardiovascular events in older adults. Stroke. 2008 Mar;39(3):863–9.
7. Obideyi TO, Raji YR, Ajayi SO, Salako BL, Arije A, Kadiri S. Correlation between Albuminuria and Ankle Brachial Index among Nigerians with Chronic Kidney Disease. African Journal of Health Sciences. 2021;34(6):728–41.

8. Baber U, Mann D, Shimbo D, Woodward M, Olin JW, Muntner P. Combined role of reduced estimated glomerular filtration rate and microalbuminuria on the prevalence of peripheral arterial disease. Am J Cardiol. 2009 Nov 15;104(10):1446–51.

9. Chen J, Mohler ER 3rd, Garimella PS, Hamm LL, Xie D, Kimmel S, et al. Ankle brachial index and subsequent cardiovascular disease risk in patients with chronic kidney disease. J Am Heart Assoc [Internet]. 2016 May 31;5(6). Available from: http://dx.doi.org/10.1161/JAHA.116.003339

10. Laghari S, Ullah K, Masroor I, Butt G, Kifayat F. Prevalence of peripheral arterial disease diagnosed by ankle brachial index among chronic kidney disease patients in a tertiary care unit. Saudi J Kidney Dis Transpl. 2015 Sep;26(5):924–30.

11. Ono K, Tsuchida A, Kawai H, Matsuo H, Wakamatsu R, Maezawa A, et al. Ankle-brachial blood pressure index predicts all-cause and cardiovascular mortality in hemodialysis patients. J Am Soc Nephrol. 2003 Jun;14(6):1591–8.

12. Chen F-A, Yang C-Y, Yang W-C, Chen J-Y, Ng Y-Y, Li S-Y, et al. Ankle-brachial index is a powerful predictor of renal outcome and cardiovascular events in patients with chronic kidney disease. ScientificWorldJournal. 2012 Jan 4;2012:238494.