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Association of Serum Albumin and Cardiovascular Risks in a Hiv Cohort on Art at a Tertiary Care Hospital

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Abstract

Background

The introduction of antiretroviral therapy led to drastic change in mortality and morbidity related to HIV and AIDS. Particularly now cardiovascular disease has emerged as most important cause of death in HIV individuals [2]. In additional to traditional risk factors of cardiovascular events, chronic inflammation, immune activation and endothelial dysfunction further attribute to cardiovascular risk in HIV population. It is vital to assess the cardiovascular risk in all PLHIV so as to mitigate and initiate risk reduction techniques [4].

Low serum albumin levels have been linked to an increased risk of cardiovascular death. In this study, we compared the cardiovascular risk score which is calculated by HIV specific CVD risk assessment tool (D:A:D score) with serum albumin.

Aim

To evaluate the relationship between serum albumin and calculated cardiovascular risk using D:A:D calculator in PLHIV on stable ART.

Patients and Methods

A hospital based cross- sectional analytical study was conducted among 159 patients attending ART clinic in a tertiary care center, who was on stable ART for minimum 2 years between age group of 18-60 was included.

Results

Among 159 patients, 37(23.3%) patients had low Albumin. D:A:D CVD risk at 5 years distribution among participants was calculated, around 28.9% (n=46) had very high risk of D:A:D CVD at 5 years and 20.8% (n=33) showed high risk.

Among patients with low risk of CVD at 5 years, the mean (SD) serum albumin was highest, 4.19 (0.25) mg/dl as compared to other risk categories and this difference was found to be statistically significant (p=0.04)

Among patients with low serum albumin, 40.5% (n=15) showed moderate and very high risk of CVD at 5 years whereas only 2.7% (n=1) showed low risk of CVD at 5 years. This difference was not found to be statistically significant

Conclusion

We found out that low risk of CVD at 5 years was significantly associated with high mean serum albumin levels. Lower levels of serum albumin can be used a predictor for cardiovascular risk among PLHIV. Serum albumin measurements could potentially improve the prediction of short-term adverse outcomes in HIV-infected individuals.

Keywords: Hiv Cardiovascular Risk; Serum Albumin; Hiv; Serum; Infectious Diseases

Introduction

In 2021, around 6,50,000 people have died due to causes related to HIV and 1.5 million people were infected by HIV. Globally, 38.0 million people are living with HIV as of 2019, of those 68% people were receiving lifelong antiretroviral therapy [1].

The introduction of antiretroviral therapy led to drastic change in mortality and morbidity related to HIV and AIDS. With recent advances in the treatment mortality and wide spread availability of more effective ART, the deaths due to HIV related events decreased in comparison to non HIV related events, most deaths in HIV population are now attributable to non-communicable illnesses [2]. Particularly now cardiovascular disease has emerged as most important cause of death in HIV individuals. In a meta-analysis and systemic review in comparison to general population there is a 2.16-fold increase in cardiovascular disease in HIV population. They also found association of HIV infection with risk of cardiovascular disease was stronger in younger than older individuals [3].

It is vital to assess the cardiovascular risk in all PLHIV so as to mitigate and initiate risk reduction techniques. Traditional risk factors for non-communicable diseases such as smoking, dyslipidaemia, diabetes mellitus, and hypertension are prevalent in HIV affected population. In addition to this chronic inflammation and immune activation, endothelial dysfunction is related to cardiovascular risk in HIV (even in setting of successful viral suppression using ART). Specific HIV medication like Abacavir, Protease inhibitors also showed to increase cardiovascular risk in HIV individuals. The relationship between HIV infection and atherosclerotic disease has been linked to endothelial dysfunction and arterial inflammation, according to studies. Cardiovascular risk prediction equations and scores have been developed worldwide and are widely used to predict individuals who are at risk of CVD. Still it is not very clear which is the most accurate and optimal one to predict risk of CVD.

D:A:D score developed in a study on Data Collection on Adverse Effects of Anti-HIV Drugs Cohortby Friis--Moller et al was based on incorporation of some HIV related factors such as IND,LPV/r,ABC exposure in cardiovascular risk assessment tool and it has improved the predictability [6].

In HIV infected individuals the serum albumin has been recognized as an independent prognostic factor in cardiovascular risk assessment. The two mechanism which are directly related to pathogenesis of cardiovascular disease is chronic inflammation and hypertriglyceridemia. Low serum albumin levels have been linked to an increased risk of cardiovascular death. In patients with HIV, lower serum albumin concentration has been associated with an increased risk of mortality. In people living with HIV, low

serum albumin concentration may be associated with the development of serious non-AIDS events (SNAEs).

There is paucity of data regarding association of serum albumin and cardiovascular risk in HIV population. In this study, we compared the cardiovascular risk score which is calculated by HIV specific CVD risk assessment tool (D:A:D score) with serum albumin. If an association between serum albumin which is easily available and low of cost is found, it can be used as an additional tool in cardiovascular risk stratification in patient living with HIV.

Material and Methods

A hospital based cross-sectional analytical study was conducted among patients attending ART clinic in a tertiary care center. The study was conducted over a period of 2 years.

Total sample size calculated was 159. Sample size was calculated based on the assumption that 11.7% of PLHIV will have hypoalbuminemia based on previous studies, with following assumptions Z= 1.96, 5% level of significance, 80% power, 95% confidence interval.

Inclusion criteria

Patients with the following criteria were included in the study. On stable ART at least for 2 years and age group between 18- 60 years.

Exclusion criteria

Factors affecting albumin levels (CLD, Nephrotic syndrome, malnutrition syndrome, trauma, surgery), on statins, Patient not adherent to ART (<95%), Terminal illness (malignancy), Pregnancy.

Results

The mean age of the population was 43.7 years. 54.1%(n=86) were male and 45.9%(n=73) were females. 45.9%(n=73) from urban and 54.1%(n=86) from rural, The body mass index distribution among participants. 35.9% (n=57) were normal weight, whereas 33.9% (n=54) were found to be in obese BMI category. 14.5% (n=23) had positive family history of CVD and 85.5% (n=136) had no family history of CVD. 4.4% (n=7) were found to be diabetic and 95.6% (n=152) were non-diabetic. Only 9.4% (n=15) were found to be hypertensive and 90.6% (n=144) were non-hypertensive. ART duration distribution among participants. 24.5% (n=39) had less than 5 years of ART duration, 70.4% (n=112) had 6-10 years of ART duration and only 5.1% (n=8) had more than 10 years of ART duration.

Only 23.3% (n=37) had low serum albumin and 76.7% (n=122) had normal level of serum albumin. D:A:D CVD risk at 5 years distribution among participants is described in Table 22. Around 28.9% (n=46) had very high risk of D:A:D CVD at 5 years and 20.8% (n=33) showed high risk.

Among patients with low serum albumin, 40.5% (n=15) showed moderate and very high risk of CVD at 5 years whereas only 2.7% (n=1) showed low risk of CVD at 5 years. This difference was not found to be statistically significant (p=0.30).

Correlation between Serum albumin and D:A:D CVD risk at 5 years with Pearson correlation coefficient is -0.005 (weak correlation) and it is not statistically significant (p=0.95).

Among patients with low risk of CVD at 5 years, the mean (SD) serum albumin was highest, 4.19 (0.25) mg/dl as compared to other risk categories and this difference was found to be statistically significant (p=0.04).

Discussion

In this study, we aimed to evaluate the relationship between serum albumin/albumin globulin ratio and cardiovascular risk using D:A:D calculator in PLHIV on stable ART. According to our study results around 50% of the population are coming under high and very high risk category of cardiovascular risk. A significant association between mean serum albumin level and CVD risk at 5 years was also found among the study patients.

The increased risk of CVD among PLWH has been clearly demonstrated in earlier studies [11,12]. Hence in this population, the development of interventions for cardiovascular health promotion and CVD prevention is war-

ranted. However, most of the CVD risk assessment tools have been derived from the general population and not from PLHIV. So, their ability to predict CVD in PLHIV is inconsistent and inaccurate. Therefore, to accurately predict CVD risk in PLHIV, a new CVD risk assessment tool derived from PLHIV accounting for variables specific to HIV infection such as CD4 count, treatment and duration of ART along with various traditional risk factors. This tool could determine which patients would most benefit from primary prevention strategies [13,14].

In our study we found males had high risk of CVD at 5 years than females. In a cross-sectional study conducted among people with HIV undergoing ART treatment in South Africa, males showed higher prevalence of metabolic CVD risk factors than females [16]. Our study showed high risk of CVD scores among age group between 40-60 years of age. These findings were consistent with other study where people above 50 years of age showed risk factors of CVD as compared to younger age groups [16].

Around 50% of the participants in our study had higher BMI and were overweight and obese. Overweight people have been demonstrated to have higher rates of cardiovascular disease mortality and morbidity, especially when there is central adipose tissue accumulation [17].

We found a high proportion of patients with HTN, DM, and dyslipidemia. The findings are similar to other Indian studies that have shown high prevalence of these diseases in the Indian population. In India, non-communicable diseases account for over 63% of all fatalities, with cardiovascular disease accounting for 27% of these deaths and affecting 45% of adults between the ages of 40 and 69 [18]. Overall prevalence for hypertension in India was 29.8% (95% con) [19]. Prevalence of DM and impaired fasting blood glucose (IFG) in India was 9.3% and 24.5% respectively. In India, 25-30% urban population and 15-20% rural population have dyslipidemia [21].

The results of our study are in line with those of previous studies. A previous study indicated that a low serum albumin level is a predictor for both short- and long-term significant non-AIDS events, including cardiovascular events. This finding was independent of other prognostic factors, including both traditional cardiovascular disease risk factors (age, lipid profile, hemoglobin level, and blood pressure), HIV-specific risk factors (HIV-1 RNA load and $CD4^+$ T-cell count). The authors highlighted that a low serum albumin level may be a useful marker of risk of non--communicable diseases, particularly in resource-limited settings [10]. An association between serum albumin levels and subsequent clinical events, including cardiovascular events, has been demonstrated previously in PLHIV [23,24]. Like in our study, several observational studies have also demonstrated the association between serum albumin and mortality in HIV-infected persons. The researchers of these studies have shown a uniform and strong inverse association between serum albumin level and incident health-related outcomes, including overall mortality and AIDS-related cardiovascular morbidities [24,25].

In our study, we could not find a correlation between serum albumin level and D:A:DCVD risk at 5 years and between serum albumin level and CD4 count at the time of the initiation of ART. Likewise, an earlier study also found no association between serum albumin and AIDS [8]. However, contradictory results were also obtained. In an earlier study, in HIV/AIDS patient's serum albumin level was found to correlate with CD4 counts and was used as a marker of immune suppression. The discrepancy in the results might be due to the small sample size of our study [26].

The findings of this study are relevant in the context of low- and middle-income countries like India. Serum albumin is also more easily obtained than other expensive biomarkers that have previously been associated with non-AIDS disease and related morbidity and mortality (e.g., chronic inflammatory markers, microbial translocation, hypercoagulation, and immune activation markers) [28,29]. None of these biomarkers have been found to be reliable to be used in routine clinical practice. Thus, based on our data, and previous reports, serum albumin may be considered to be included in future HIV prognostic indices for non-AIDS morbidity, especially cardiovascular morbidity. Thus, identification of serum albumin level as a clinically available prognostic marker may help inform non-communicable disease pathogenesis (e.g. cardiovascular diseases) in PLHIV as well as provide added value for a personalized approach to these conditions to stratify the risk.

Conclusion

In our study, we calculated cardiovascular risk score at 5 years for people with HIV which is calculated by HIV specific CVD risk assessment tool (D:A:D score) and compared with serum albumin as a prognostic factor. We also studied demographic and clinical profile of PLHIV undergoing stable ART. A significant association between mean serum albumin level and CVD risk at 5 years was also found among the study patients. We found out that low risk of CVD at 5 years was significantly associated with high mean serum albumin levels. Lower levels of serum albumin can be used a predictor for cardiovascular risk among PLHIV. Serum albumin measurements could potentially improve the prediction of short-term adverse outcomes in HIV-infected individuals.

Table 1: Age distribution of participants (N=159)

Age (in years)	Frequency	Percentage (%)
19-30	18	11.3
31-40	35	22.0
41-50	69	43.4
51-60	37	23.3
Total	**159**	**100**

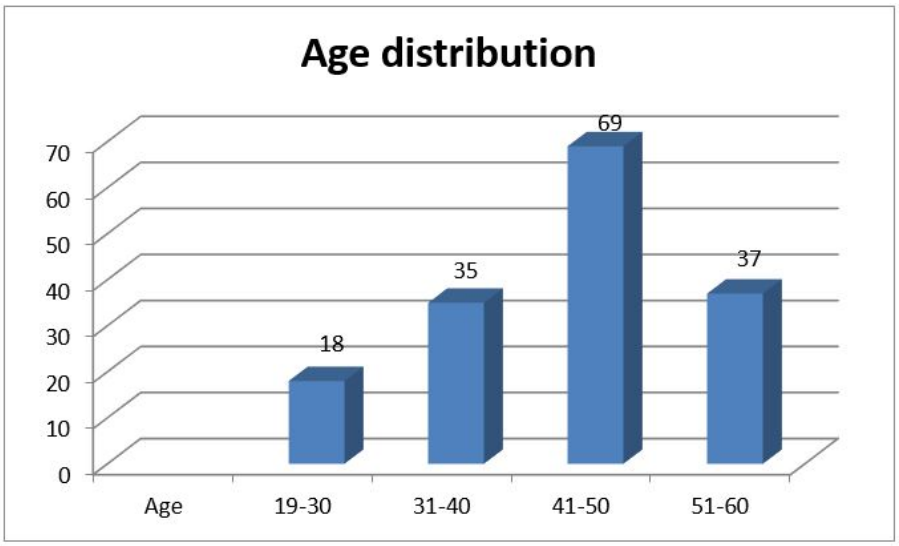

Figure 1: Age distribution of participants (N=159)

Table 2: Gender distribution of participants (N=159)

Gender	Frequency	Percentage (%)
Male	86	54.1
Female	73	45.9
Total	**159**	**100**

Table 3: Residence distribution of participants (N=159)

Residence	Frequency	Percentage (%)
Urban	73	45.9
Rural	86	54.1
Total	**159**	**100**

Table 4: Body Mass Index distribution of participants (N=159)

Body Mass Index	Frequency	Percentage (%)
Underweight	20	12.6
Normal	57	35.9
Overweight	28	17.6
Obese	54	33.9
Total	**159**	**100**

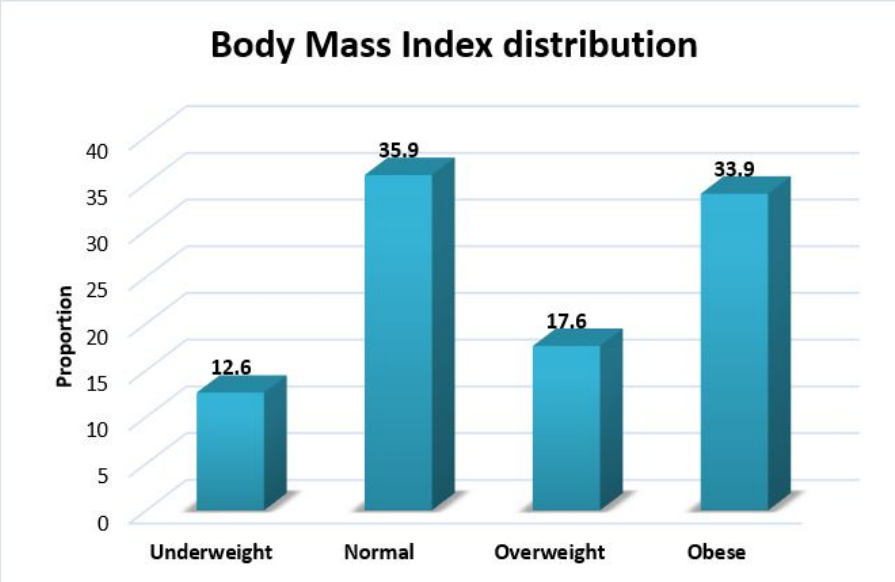

Figure 2: Body Mass Index distribution of participants (N=159)

Table 5: Family history of CVD distribution among participants (N=159)

Family history of CVD	Frequency	Percentage (%)
Yes	23	14.5
No	136	85.5
Total	**159**	**100**

Table 6: Diabetes distribution among participants (N=159)

Diabetes	Frequency	Percentage (%)
Yes	7	4.4
No	152	95.6
Total	**159**	**100**

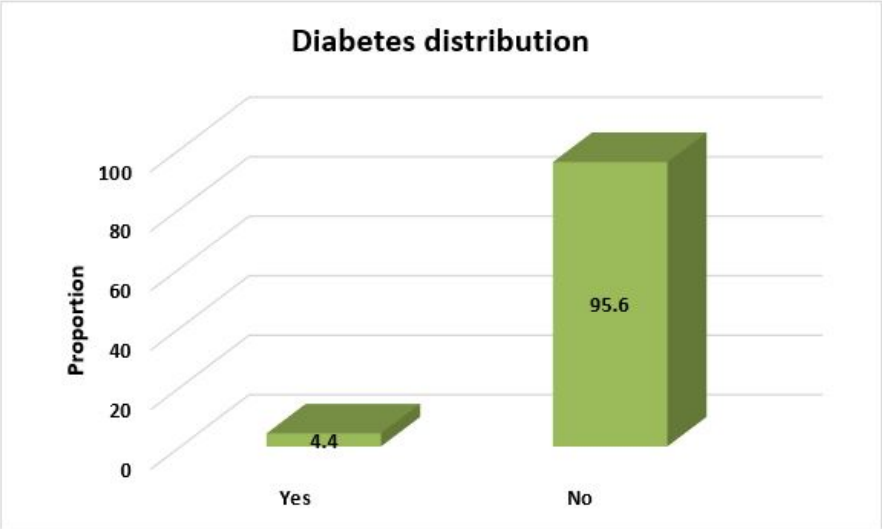

Figure 3: Diabetes distribution among participants (N=159)

Table 7: Hypertension distribution among participants (N=159)

Hypertension	Frequency	Percentage (%)
Yes	15	9.4
No	144	90.6
Total	**159**	**100**

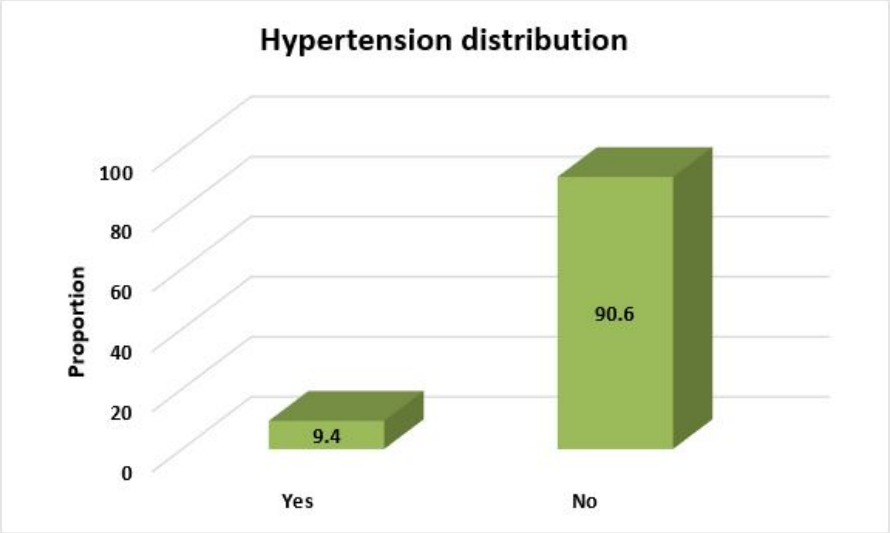

Figure 4: Hypertension distribution among participants (N=159)

Table 8: ART duration distribution

ART duration (in years)	Frequency	Percentage (%)
<5	39	24.5
5-10	112	70.4
>10	8	5.1
Total	**159**	**100**

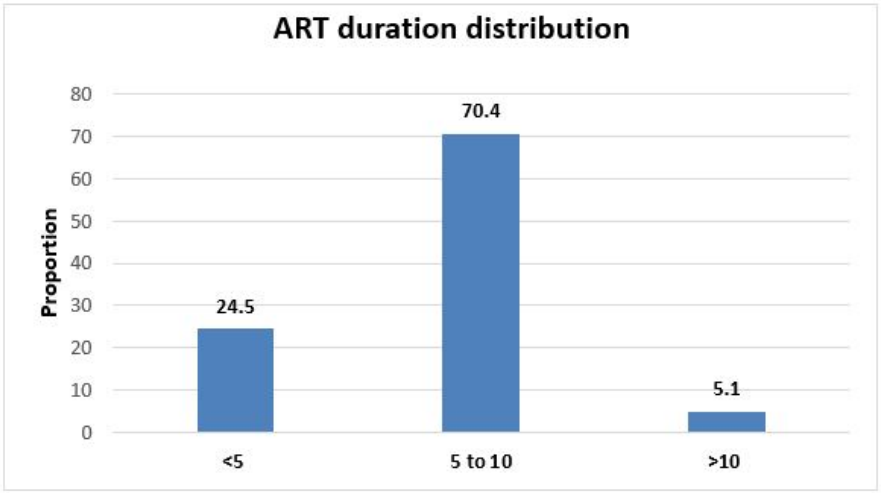

Figure 5: ART duration distribution

Table 9: Descriptive statistics of participants (N=159)

Variables	Mean	Median	Percentiles		
			25	50	75
Age (in years)	43.7±9.9	45	38	45	50
BMI (kg/m^2)	23.5 ± 4.6	23.2	20.0	23.2	25.9
Systolic Blood Pressure (mmHg)	118.2 ±12.4	120	110	120	130
CD4 at start of ART (cells/mm^3)	379.1±239.5	367	189	367	473
CD4 at 6 months (cells/mm^3)	451.4±254.5	410	245	410	605
CD4 at 12 months (cells/mm^3)	510.3±263.2	458	327	458	660
CD4 at latest (cells/mm^3)	570.2±219.6	556	420	556	701
Serum albumin (mg/dl)	4.2±0.6	4.2	4	4.2	4.5
HDL (mg/dl)	43.9±13.6	42	37.3	42	48
Total cholesterol (mg/dl)	177.4±40.9	172	150	172	197
RBS	118.3±40.9	108	96	108	132
Serum creatinine (mg/dl)	0.9±0.2	0.98	0.84	0.98	1.1
Haemoglobin (gm%)	12.3±1.9	12.4	11	12.4	13.5
AST (IU/L)	29.0±15.3	24	20	24	34
ALT (IU/L)	31.9±19.3	26	21	26	36

Table 10: Serum albumin distribution among participants (N=159)

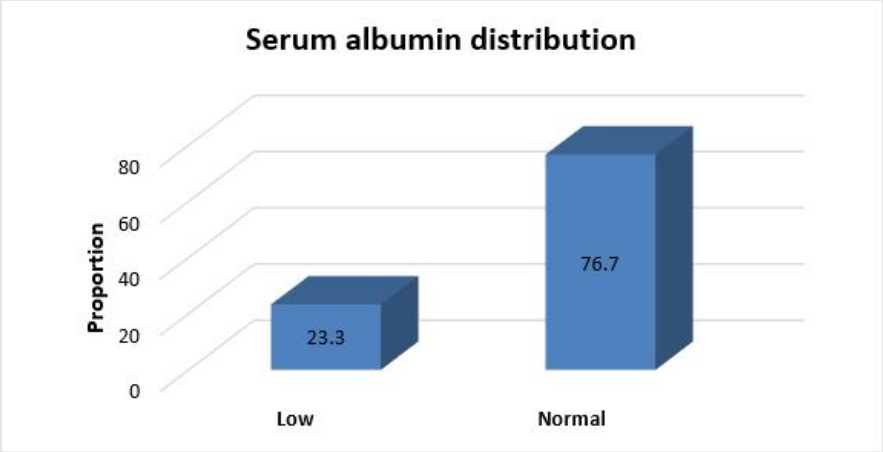

Figure 6: Serum albumin distribution among participants (N=159)

Table 11: D:A:D CVD risk at 5 years distribution among participants (N=159)

D:A:D CVD risk 5 years	Frequency	Percentage (%)
Low	9	5.7

Moderate	71	44.6
High	33	20.8
Very High	46	28.9
Total	**159**	**100**

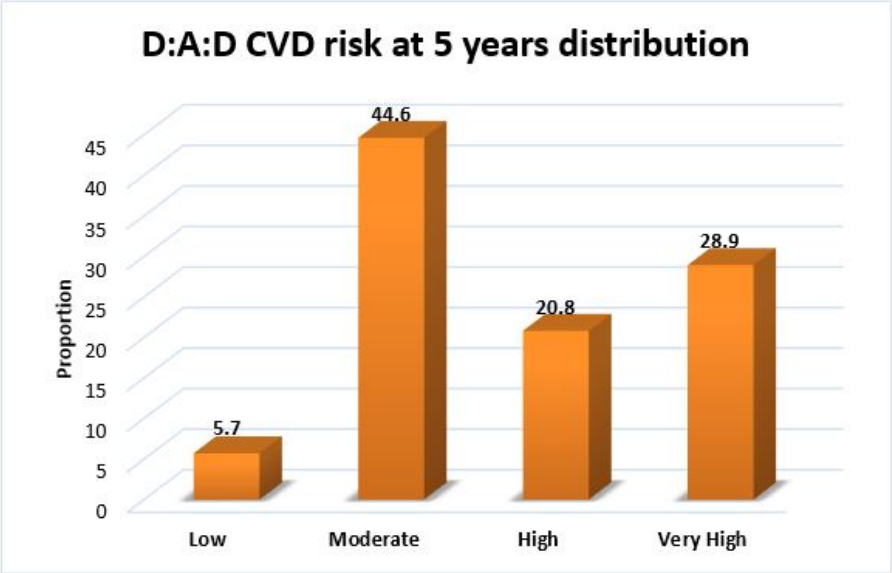

Figure 7: D:A:D CVD risk at 5 years distribution among participants (N=159)

Table 12: Association of Serum albumin and D:A:D CVD risk at 5 years among participants

D:A:D CVD risk at 5 years	Serum Albumin		P value*
	Lown (%)	Normal n (%)	
Low	1 (2.7)	8 (6.6)	0.30
Moderate	15 (40.5)	56 (45.9)	
High	6 (16.2)	27 (22.1)	
Very High	15 (40.5)	31 (25.4)	
Total	**37 (100.0)**	**122 (100.0)**	

*Chi-Squared test was used

Table 13: Correlation between Serum albumin and D:A:D CVD risk at 5 years

		D:A:D CVD risk 5 years
Serum albumin	Pearson Correlation	-0.005
	P value	0.95
	N	159
Correlation is non-significant (p value = 0.95)		

Table 14: Association of Mean Serum albumin and D:A:D CVD risk at 5 years among participants

D:A:D CVD risk at 5 years	Serum Albumin		P value*
	Mean	SD	
Low	4.19	0.25	0.04
Moderate	4.18	0.54	
High	4.17	0.64	
Very High	4.13	0.59	

*One-way ANOVA test was used

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