RESEARCH PAPER

Association of Mean Corpuscular Volume as A Haematological Marker of Alcohol Consumption with Left Ventricular Dysfunction

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ABSTRACT

Alcohol use disorder is also considered to be among key public health problems that cause heart-related complications and deaths. The long-term use of alcohol is associated with such conditions as macrocytosis, myocardial damage, which in its turn may lead to left ventricular dysfunction. Mean corpuscular volume can be considered an easy-to-acquire hematology parameter, reflecting the chronic alcohol abuse in many patients. At the same time, no attention was paid to the correlation between mean corpuscular volume and left ventricular dysfunction in previous studies. This case-control study was conducted during 18 months at CMC Multispeciality Hospital in Hisar, Haryana. To be more specific, 114 individuals suffering from alcohol use disorder were enrolled using AUDIT scale results and were divided into groups as case subjects (MCV>100 fL; n=57) or control subjects (MCV≤100 fL ; n=57). All patients participated in physical examination, complete blood count, liver function tests and transthoracic echocardiography, as well as estimation of global longitudinal strain. As for the case group, the results reflected high levels of alcohol use disorder, high AUDIT score, elevated liver enzyme activity, as well as high mean corpuscular volume in comparison with control ($p<0.001$).

In evaluating the results of the echocardiography studies, a significant decrease in LVEF was noted, along with an increase in LVMI, a decrease in GLS, and a high prevalence of diastolic dysfunction in our sample group ($p<0.05$). In addition, we observed some statistically important correlations – MCV inversely correlated with LVEF and GLS, and positively correlated with LVMI and the AUDIT score.

Further, in multiple regression analysis, a level of MCV higher than 100 fL was found to be an independent risk factor for LV dysfunction. Thus, in general, increased MCV levels corresponded with increased alcohol consumption and LV dysfunction. It could be considered as a diagnostic marker of alcohol- induced heart disorders.

Keywords: AUDIT score, echocardiography, myocardial damage, LV dysfunction, mean corpuscular volume

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INTRODUCTION

Abuse of alcohol is a health issue of global significance, and it keeps being one of the major causes behind morbidity and mortality in different regions of the world. Based on WHO data, alcohol abuse contributed to roughly 3 million deaths (these are about 5.1% of all deaths worldwide) and around 133 million disability-adjusted life years in 2016 (WHO, 2019). When someone abuses alcohol, it can lead to many harmful outcomes, which in turn may affect a persons wellbeing, like really not in a good way. This type of problem also has the potential to damage several body structures, including the liver, nervous system, blood-forming tissues, and even the heart. Given the large health burden created by alcohol abuse, it is hard to deny how important it is to spot those patients who might run into these complications.

However, actually pinpointing alcohol intake still feels difficult. It is often because many studies and clinical settings rely on self-report, and that can be off, due to memory issues or because stigma sometimes makes people understate what they drank. Because of that, clinicians and researchers commonly use different biological indicators to identify long term consumption. The "Mean Corpuscular Volume (MCV) and Gamma-Glutamyl Transferase (GGT)" are among the most common biological markers linked to chronic alcohol use in patients (Bornhorst and Mbughuni, 2019). Mean

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Corpuscular Volume is one of the measures found within the complete blood count, and it reflects the average cell volume in erythrocytes, even if the wording sounds simple it is pretty specific.

Multiple studies show some sort of link between how long someone has been drinking alcohol and higher MCV measurements, like in Wakabayashi, 2019; Varghese et al., 2007; Wu et al., 2019. In general, long-term alcohol intake seems tied to macrocytosis where, the MCV stays elevated, and that happens because of a range of mechanisms such as toxicity affecting the bone marrow, changes in the erythrocyte membrane makeup, disruption in the erythropoiesis process, plus deficiencies in vitamin intake, particularly vitamins B12 and folates. In fact, people who drink heavily, more than 60 g per day, have been observed with raised MCV, and the value can stay high for a couple of months even after stopping alcohol use, sometimes it hangs around, even then.

That said, relying on MCV for judging chronic alcoholism is not entirely straightforward, there are certain practical points to keep in mind. Factors like age, sex, smoking pattern, nutrient shortfalls, body mass index, liver conditions, and other diseases can all shift the MCV result even if the patient s drinking habits are not the main driver. Still, despite all these influences, MCV as a marker for chronic alcoholism is often considered quite a lot, mainly because the test is easy to access and fairly inexpensive. So, even with its limits, laboratories continue to use MCV testing for chronic alcoholism evaluation.

Among the various ailments associated with alcohol consumption, one of the more severe problems that could arise as a result is that of heart problems. Continued abuse of alcohol will eventually result in the development of a condition known as ACM, which stands for alcoholic cardiomyopathy. The condition is actually a type of non-ischemic dilated cardiomyopathy, whereby ventricular dilatation takes place along with poor myocardial contractility – only if there is no other underlying reason except coronary artery disease. It has been found that a fairly large number of non-ischemic dilated cardiomyopathy cases stem from ACM, and that around 10% of cardiomyopathy cases are ACM. However, there is no clear-cut amount of alcohol consumption beyond which cardiomyopathy will develop. Nevertheless, individuals that have been consuming at least 80 grams of alcohol on a daily basis for over five years face an increased risk...

Alcohol-induced heart muscle injury appears to operate in a manner somewhat complex. Both the alcohol and its metabolites appear to work directly on the myocardium by generating “oxidative stress, mitochondrial dysfunction, disruption of calcium homeostasis, protein synthesis inhibition, as well as induction of apoptosis, ultimately leading to cell death”. However, whereas initial impairment of myocardial function due to the effects of alcohol is probably reversible, prolonged exposure through abuse leads to structural changes that will finally result in myocardial dysfunction. At that point, there may often be progression towards left ventricular dysfunction, or LVD.

The clinical significance of LVD is enormous, as it comes as no surprise that increased morbidity and mortality from cardiovascular disease are strongly associated with LVD. Structural and functional modifications associated with the left ventricle occur prior to development of obvious heart failure and can persist longer than heart failure itself. According to the results obtained during The Coronary Artery Risk Development in Young Adults (CARDIA) study, chronic alcohol consumption was associated with increased left ventricular mass and left ventricular end-diastolic volume; thus, there were some hints that chronic alcohol consumption may have a negative impact not only on cardiac structure but also remodeling. Besides, LVD increases the probability of development of heart failure, arrhythmia, stroke, and cardiovascular death. Thus, the identification of patients who are susceptible to the development of LVD is quite important.

The increased MCV being linked to chronic abuse of alcohol coupled with prolonged alcohol consumption being one of the causes for myocardial problems and dysfunction of the left ventricle implies that there could be a possible correlation between MCV and alcoholic cardiomyopathy. However, even though MCV has traditionally been used as a hematologic indicator of chronic alcoholism for quite a long time, the correlation between MCV and LVD has scarcely ever been investigated before. Investigation of the possible correlation between MCV and LVD could prove to be very helpful in understanding the part played by MCV as an inexpensive marker for cardiac complications from chronic alcohol abuse.

MATERIAL AND METHOD

The hospital based case control study was conducted at the Department of General Medicine, CMC Multispeciality Hospital, Hisar, Haryana for a period of 18 months after receiving approval from the Institutional Ethics Committee. Participants in the study were mostly in the adult age bracket, and they were considered to have alcohol use disorder either by the time they reached the OPD, or later once they were admitted to the medicine wards of the hospital. For assessing their alcohol use disorders AUDIT (Alcohol Use Disorders Identification Test) was used, more like to figure out the pattern among the participants.

Even so, the employment of MCV for assessing long term alcoholism really needs a few considerations. There are many factors such as age, gender, smoking habits, nutrient shortage, body mass index, liver diseases, and other coexisting illnesses. All these can sway the MCV readings even if the person’s drinking habits are unchanged. Still, despite these issues that can affect MCV, MCV remains quite useful, and it is greatly taken into account as a biomarker for chronic alcoholism, mainly because the approach is easy to access and inexpensive. Because of

this, the test continues to be used in laboratories for examining chronic alcoholism.**Sample Size**

A sample size was calculated by following Hulley et al., (2013).

$N = [(Z\alpha + Z\beta)/C]^2 + 3$

Thus, if we have the significance level α equal to 0.05 and β significance level of 80% (which means 0.20) and select the value of the correlation coefficient r equal to 0.26, the sample size is estimated to be approximately equal to 114 persons (in either case). In reality, 114 people were involved, half of which being cases and the other half control groups.

Inclusion Criteria

1. Age ≥18 years.
2. Patients diagnosed with alcohol use disorder based on AUDIT score.
3. Sinus rhythm at the time of examination.
4. Willingness to participate in the study and provide written informed consent.
5. No previous history of coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease, bronchial asthma, uncontrolled hypertension, cardiomyopathy, or significant valvular heart disease.

Exclusion Criteria

1. Patients unwilling to participate in the study.
2. Known coronary artery disease, previous myocardial infarction, or history of coronary revascularization.
3. Clinical suspicion or documented evidence of myocardial ischemia.
4. Persistent or permanent atrial fibrillation.
5. Known cardiomyopathies other than alcohol-related cardiac disease.
6. Significant valvular heart disease.
7. Pregnancy.
8. Anaemia.
9. Thyroid disorders.
10. Vitamin B12 deficiency.
11. Chronic obstructive pulmonary disease or bronchial asthma.
12. Patients receiving antiepileptic drugs, chemotherapeutic agents, or antiretroviral therapy.
13. Any condition known to independently influence mean corpuscular volume.

Ethical Considerations

The study protocol was approved by the institutional ethics committee of CMC multispeciality hospital, Hisar. Written informed consent was taken from all the participants prior to their inclusion in the study. Confidentiality of all the participants was maintained throughout the study.

Study Procedure

Informed consent was taken and inclusion criteria were fulfilled in this manner. A medical history along with a demographic history and drinking history were recorded by predesigned proforma. AUDIT score was used for determining the alcohol use disorder in patient.

Venous blood sample was collected aseptically followed by analysis of complete blood counts on automated hematological analyzer. Mean corpuscular volume (MCV) was recorded as an index among others of red blood cells and this was considered to be abnormal when more than 100 fL..

Then, a transthoracic echocardiography examination was conducted for each participant utilizing the Siemens ACUSON X-300 with the P4/2 probe. This test was performed by a cardiologist specialist, who analyzed the LV systolic function and measured the indices indicating LV dysfunction. The measurement of the GLS was done by the use of two-dimensional speckle tracking echocardiography because this method allows us to identify the LV dysfunction in cases where symptoms may not be present. Finally, the relationship between MCV and LV dysfunction was established through the echocardiography test results.

Statistical Analysis

The data entry process as well as the statistical analysis was conducted via Microsoft Excel and Statistical Package for the Social Sciences (SPSS), specifically version 26.0 (IBM Corp., Armonk, NY, USA). Continuous data were expressed as mean ± SD, whereas categorical data were presented by numbers, and percentages. For comparison of the cases versus the controls, an unpaired t test was used in case of normal distribution for continuous variables. In other cases, the Mann-Whitney U test was utilized. Concerning categorical variables, Chi-square test or Fisher's exact test was conducted in order to compare these data. Correlations between mean corpuscular volume (MCV) and echocardiographic parameters associated with left ventricular function were performed by utilizing Pearson's or Spearman's correlation coefficients. Finally, we conducted ROC curve analysis just to find out predictive ability of the MCV.

RESULT AND DISCUSSION

Demographic and Baseline Characteristics

In the current study, there was a total of 114 subjects, sort of evenly split with 57 in the cases, and 57 in the controls. On average the case group age was 46.82±8.74 years, and for the controls it was 45.21±9.12 years, and overall, this contrast didn't look statistically meaningful (p=0.3379). Also, the way age was spread out, sex pattern, BMI, and smoking status seemed pretty comparable across the two groups, p>0.05.

For sex specifically, it was observed that 89.47% of the patients in the case group were males, and 87.72% of the controls were also males, so this condition is mostly being noticed in men, especially since alcohol use disorder is usually more frequent in the male population.

Still, the case patients were drinking significantly more each day than the control group, 9.22±3.14 vs 6.72±2.45 units/day, with p<0.001. However, the length of consumption did not really differ between groups, even if the case group was a little higher: 12.42±4.76 vs 9.63±3.86 years, p>0.05.

Table 1. Demographic and Baseline Characteristics of Study Participants.

Parameter	Cases (n=57)	Controls (n=57)	p value
Age (years)	46.82 ± 8.74	45.21 ± 9.12	0.3379
BMI (kg/m²)	23.87 ± 3.13	24.22 ± 2.85	0.5337
Duration of alcohol use (years)	12.42 ± 4.76	9.63 ± 3.86	0.6242
Daily alcohol units	9.22 ± 3.14	6.72 ± 2.45	<0.001*
Smokers, n (%)	33 (57.9)	28 (49.1)	0.3478
Male sex, n (%)	51 (89.5)	50 (87.7)	0.2947

The possibility of confounding factors was reduced in the analysis by taking into account comparable cases and controls in terms of age, sex and BMI. Studies conducted by Glantz et al., (2020), found a similar trend of increased prevalence of alcohol use disorder amongst men. Similarly, middle aged men were found to be the main consumers of alcohol in India according to Balasubramani et al, (2021). Increase in the size of MCV is indicative of increased consumption of alcohol, evident from the higher alcohol consumption by cases.

Haematological and Biochemical Parameters

Cases seemed to show noticeably higher MCV values than what we saw in the control individuals, it was 107.66 ± 4.82 fL compared with 91.85 ± 5.26 fL , with p<0.001. Likewise, MCH was also significantly higher, yet the red blood cells were significantly lower in cases relative to controls, again p<0.001. Still, when it came to hemoglobin level, there were no meaningful differences detected between the groups., MCHC and Vitamin B12 levels between cases and controls. Nonetheless, comparison between both groups clearly showed significant difference regarding higher levels of AST, ALT, and γ-GT which indicated some form of increased alcohol-related liver injury.

Table 2. Hematological and Biochemical Parameters.

Parameter	Cases (n=57)	Controls (n=57)	p value
Hemoglobin (g/dL)	13.42 ± 1.21	13.78 ± 1.16	0.1077
RBC count (×10⁶/μL)	4.21 ± 0.45	4.62 ± 0.52	<0.001*
MCV (fL)	107.66 ± 4.82	91.85 ± 5.26	<0.001*
MCH (pg)	33.16 ± 2.42	31.52 ± 1.84	<0.001*
MCHC (g/dL)	32.43 ± 1.34	32.17 ± 1.46	0.3240
Vitamin B12 (pg/mL)	367.64 ± 72.85	372.74 ± 80.88	0.7242
AST (U/L)	61.83 ± 15.45	42.36 ± 12.82	<0.001*
ALT (U/L)	58.20 ± 17.60	41.26 ± 11.96	<0.001*
γ-GT (U/L)	87.63 ± 28.46	49.55 ± 22.14	<0.001*

*Statistically significant

Higher values of MCV in the cases confirmed the presence of macrocytosis caused by the effects of long-term alcohol consumption. With no considerable variance in terms of vitamin B12 level, it may be concluded that the observed macrocytosis due to alcohol in this study occurred due to the toxic effect of alcohol on the process of erythropoiesis. The findings of this research coincide with results of the investigations carried out by Varghese et al., (2019). Thus, cases of chronic alcoholism had significantly increased MCV values but decreased numbers of RBCs. In turn, according to Elanchezhian et al., (2017), hemogram deteriorated in line with the severity of alcohol dependence.

AUDIT Score and Patterns of Alcohol Consumption

It seems like cases had much higher scores for AUDIT than controls, (21.38 ± 5.23 vs. 15.82 ± 4.75; p<0.001). Moreover, the proportion of severe drinkers who had a score of AUDIT ≥20 was also higher in cases than controls, (52.6% vs. 22.8%; p=0.001). Further, alcohol consumption for more than 10 years and daily consumption was also higher in cases (Table 3).

Table 3. Alcohol Consumption Profile.

Parameter	Cases (n=57)	Controls (n=57)	p value
AUDIT score	21.38 ± 5.23	15.82 ± 4.75	<0.001*
AUDIT ≥20, n (%)	30 (52.6)	13 (22.8)	0.001*
Duration >10 years, n (%)	35 (61.4)	19 (33.3)	0.0027*
Daily drinkers, n (%)	28 (49.1)	16 (28.1)	0.021*

*Statistically significant

This means that high MCV levels tend to correlate with high and sustained alcohol intake. According to Kilo et al., (2016), there exists a significant correlation between MCV and alcohol intake using biological analysis. This observation is evidenced by the significantly high AUDIT scores of the cases within the study.

Echocardiographic Parameters

When comparing the two groups of participants, we could observe a relatively obvious impairment in left ventricular systolic function in the patients. The mean value of LVEF was found to be notably lower in the patient population (49.28±7.43%) when compared to the control population (56.83±5.27%, p<0.001). In addition to this, we could observe the left ventricular mass index to be considerably higher in the former case (118.64±22.87g/m²) compared to that of the latter (102.43±17.98g/m², p<0.001). Regarding global longitudinal strain (GLS), its values appeared lower among the patients (17.17±2.38%) than that of the controls (20.27±2.14%, p<0.001). The endocardial GLS and epicardial GLS were also significantly lower (cases: p<0.001). Diastolic dysfunction was present in 36.8% of the patients but only in 14.0% of the control group. This finding was found to be statistically significant (p=0.0052; Table 4).

Table 4. Echocardiographic Parameters.

Parameter	Cases (n=57)	Controls (n=57)	p value
LVEF (%)	49.28 ± 7.43	56.83 ± 5.27	<0.001*
LV Mass Index (g/m²)	118.64 ± 22.87	102.43 ± 17.98	<0.001*
GLS (%)	17.17 ± 2.38	20.27 ± 2.14	<0.001*
GLS Endo (%)	21.53 ± 2.95	25.83 ± 2.76	<0.001*
GLS Epi (%)	16.85 ± 2.16	19.76 ± 1.87	<0.001*
Diastolic Dysfunction, n (%)	21 (36.8)	8 (14.0)	0.0052*

As can be seen from the above findings, remodeling and dysfunction of the heart muscle could be potential contributors to the increase in MCV levels. The same finding was observed in a study conducted by Hamala et al., (2021), where increased left ventricle mass, impaired systolic and diastolic functions, and reduced GLS measurements were found among long-term drinkers. As such, it is important to note that reduced GLS levels are critical in the case of early heart impairments observed through strain imaging.

Prevalence of Left Ventricular Dysfunction

LV function remained normal, indicating an EF of ≥55% in roughly 57.9% of the cases, while controls had a percentage of 86.0%. LV dysfunction mild was observed in 24.6% of the cases and 10.5% of the control group. Moderate LV dysfunction was seen in 14.0% of the cases and 3.5% in the other group. Finally, LV dysfunction severe was noted only in the case group, making up a total of 3.5%.

Table 5. Correlation of MCV with Alcohol Use and Echocardiographic Parameters.

Variables	Correlation Coefficient (r)	p value
MCV vs LVEF	-0.46	<0.001*
MCV vs GLS	-0.51	<0.001*
MCV vs LV Mass Index	+0.41	0.002*
MCV vs AUDIT Score	+0.59	<0.001*
AUDIT Score vs LVEF	-0.48	<0.001*

LV dysfunction seems more common in patients with higher MCV, so there is kinda an association, between raised MCV and alcohol induced myocardial injury. Alcohol intake is thought to lead to myocardial fibrosis, LV remodeling, a fall in contractile performance, and then, finally the appearance of alcoholic cardiomyopathy.

Analysis of Multivariate Results

From what the multivariate logistic regression results suggest, a high MCV, meaning above 100 fL, came out as a meaningful predictor of LV dysfunction by itself (OR = 2.54; 95% CI = 1.20-5.38, p = 0.014). In a similar direction, heavy alcohol drinking, defined as AUDIT ≥ 20, also appeared as an independent predictor of LV dysfunction (OR = 2.39; 95% CI = 1.12-5.09, p = 0.023). Morever, if someone had been under the influence of alcohol for more than 10 years this also stayed as an independent predictor (OR = 2.06; 95% CI = 1.01-4.22; p = 0.047). By contrast, neither age, meaning older than 50 years, nor BMI, meaning above 25 kg/m2, showed up as independent predictors for LV dysfunction (Table 6).

Table 6. Multivariate Logistic Regression Analysis for Predictors of Left Ventricular Dysfunction.

Variable	Odds Ratio (OR)	95% CI	p value
MCV >100 fL	2.54	1.20–5.38	0.014*
AUDIT ≥20	2.39	1.12–5.09	0.023*
Duration >10 years	2.06	1.01–4.22	0.047*
Age >50 years	1.46	0.68–3.13	0.330
BMI >25 kg/m²	0.88	0.41–1.86	0.740

*Statistically significant

From what we got in the results, the things we measured about alcohol intake and the alcohol-related weirdities of blood markers seem to work better as predictors for left ventricular dysfunction than the usual demographic predictors people often use. There is also, in a separate way, this link between having a higher MCV level and left ventricular dysfunction, which you could use to detect alcohol abuse, via screening.

CONCLUSION

Mean Corpuscular Volume (MCV) can serve as a low-cost hemogram index in detecting individuals with chronic alcohol consumption, as well as those who are at risk of developing cardiovascular complications due to their unhealthy behavior. In addition to being a common hemogram parameter, MCV would provide additional information not only for conventional hemogram examination but also to facilitate early diagnosis of silent myocardial disease. As such, the application of MCV in the diagnosis and monitoring of alcohol dependence could contribute to necessary diagnostic procedures and initiate appropriate treatment at the earliest opportunity. Furthermore, being widely available and low-cost, MCV can serve as a convenient diagnostic technique in cases when more sophisticated methods such as echocardiography are out of question.

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