ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Correlation of lipid profile with diastolic dysfunction in normotensive young patients under 40 years of age

Naman Jain[1], Kuwer Devi Singh[2], Himanshu Gupta[3], Umesh Pratap Singh[4], Sanjeev Sharma[5]

[1]Postgraduate Students, [2]Associate Professor, [4]Assistant Professor, Department of Medicine, [3]Assistant Professor, Department of Cardiology, [5]Professor, Department of Radiology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India

Submission: 18-01-2023 Revision: 03-03-2023 Publication: 01-04-2023

ABSTRACT

Background: Diastolic dysfunction in young adults is associated with increased morbidity and mortality. The identification of risk markers associated with diastolic dysfunction could allow for targeted primary prevention efforts. **Aims and Objectives:** The aim of the study was to study whether dyslipidemia is associated with diastolic dysfunction independent of systemic hypertension in young patients under 40 years of age. **Materials and Methods:** This was a cross-sectional analytical study done from April 2021 to March 2022 in SSMC and SGMH Rewa (M.P.), 214 normotensive cases under 40 years of age were taken as cases by simple random sampling. Sample size calculated by standard formula with confidence level of 95% and margin of error was <5%. Lipid profiles (S. Triglyceride [TG], S. Cholesterol, and S. low-density lipoprotein [LDL]) of all the patients were checked. 2D echocardiogram of patients was done to check for diastolic dysfunction. All data were compiled and compared with the previous studies. **Results:** We found that the prevalence of diastolic abnormalities in adults under 40 years of age was 21.9%. It was found that there was significant correlation between dyslipidemia and presence of diastolic dysfunction in patients. Patients with higher than normal levels of S. TG, S. Cholesterols, and S. LDL were found to have more prevalence of diastolic dysfunction then patients with normal levels of S. TG, S. Cholesterols, and S. LDL. Higher grades of diastolic dysfunction were found in patients with dyslipidemia as compared to patients without dyslipidemia. High levels of TG and LDL and even Borderline high levels of LDL can be good predictors of diastolic dysfunction. **Conclusion**: Dyslipidemia is associated with diastolic dysfunction in young patients even without systemic hypertension.

Key words: Dyslipidemia; Diastolic dysfunction; HFpEF; Lipid profiles

Access this article online

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

DOI: 10.3126/ajms.v14i4.51555

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Diastolic dysfunction in young adults is associated with increased morbidity and mortality.[1-3] The identification of prospective risk markers associated with diastolic dysfunction could allow for targeted primary prevention efforts. Diastolic dysfunction is also an independent predictor of the development of heart failure.[4]

It is an important component in the pathophysiology of heart failure with preserved ejection fraction.[5] The prevalence of diastolic dysfunction in the community has ranged from 11% to 35%, depending on the methodology and cohort.[1,2,6] Younger individuals 25–35 years of age the prevalence of diastolic dysfunction were 2.8%.[5] Traditional cardiovascular risk factors, including blood pressure, lipid profile, and elevated fasting glucose levels, were associated with abnormal relaxation.[6]

Lipids and their metabolism are as important in the pathogenesis of diastolic dysfunction as they are in other cardiovascular disorders. Lipid metabolism is a well-known

Address for Correspondence:
Dr. Naman Jain, Postgraduate Students, Department of Medicine, Shyam Shah Medical College, Rewa - 486 001, Madhya Pradesh, India.
Mobile: +91-9770904442. **E-mail:** njgmc14@gmail.com

contributor to cardiac conditions, including ventricular dysfunction.[7,8] Higher-than-normal triglycerides (TG) and cholesterol levels correlate with higher ventricular dysfunction in patients with type 2 diabetes.[9,10] Moreover, even remnants of lipid particles increase the risk of cardiovascular events.[11] Recent research has shown that lower high density lipoprotein cholesterol (HDL-C) levels and higher TG/HDL-C are significantly associated with deterioration of cardiac diastolic function.[12]

Only a few studies have been conducted to establish this correlation in young normotensive patients, specially in India. Following study aims to correlate dyslipidemia with diastolic dysfunction in normotensive young patients under 40 years of age.

Aims and objectives

The aim of the study was to study whether dyslipidemia is associated with diastolic dysfunction independent of systemic hypertension in young patients under 40 years of age.

MATERIALS AND METHODS

This was a cross-sectional analytical study done in admitted patients of Sanjay Gandhi memorial hospital associated with Shyam Shah Medical college, Rewa, between April 2021 and March 2022. 214 normotensive cases under 40 years of age were taken as cases by simple random sampling. Sample size calculated by standard formula with confidence level of 95% and margin of error was <5%. Informed consent was obtained from patients. The study was pre-approved by the Institutional Ethics Committee.

Medical history, family history, and addiction history of patients were noted. Clinical examination included resting pulse, blood pressure was recorded. Complete blood count, liver function test, renal function test, and Lipid profiles (S. TG, S. Cholesterol, and S. low-density lipoprotein [LDL]) of all the patients were checked. 2D Echocardiogram of patients was done to check the degree of diastolic dysfunction. All data were compiled and compared with the previous studies.

Inclusion criteria

- All patients more than 18 years of age presented in SGMH, Rewa, were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

- BP >140/90 mmHg in sitting position on two separate occasions
- Patient who were known to have hypertension with or without antihypertensive medications
- Prior history of CAD, valvular heart disease, or congenital heart disease
- Evidence of renal dysfunction
- Patients with age more than 40 years.

Statistical analysis

Data were collected and managed on an Excel worksheet and the mean values were calculated and denoted as mean±standard deviation. Appropriate statistical tests were used to determine significance of values. $P<0.05$ was considered statistically significant.

RESULTS

Out of 214 cases 105 (49%) were male and 109 were female (51%). Mean age of the patients was 27.84±8.27 years. Out of 214 patients normal diastolic dysfunction found in 167 (78.04%) cases followed by the 26 (12.15%) cases had Grade 1, 15 (7.0%) cases had Grade 2, and 06 (2.81%) patients had Grade 3 diastolic dysfunction.

Correlation between diastolic dysfunction and TG

Out of 64 (29.90%) patients with normal range of TG (<150 mg/dL), 60 (93.76%) were found to have no diastolic dysfunction while 2 (3.12%) cases had Grade 1, 2 (3.12%) cases had Grade 2, and none of patients were Grade 3.

Cases with borderline TG (150–199 mg/dL) levels were found in 127 (59.3%) patients out of which 91 (71.6%) had normal diastolic function while 21 (16.5%) cases had Grade 1, 11 (8.6%) cases had Grade 2, and 04 (3.1%) cases had Grade 3 diastolic dysfunction.

Cases with high TG (>200 mg/dL) levels were found in 23 (10.7%) patients out of which 16 (13.0%) had normal diastolic function while 3 (13%) cases had Grade 1, 2 (8.6%) cases had Grade 2, and 02 (8.6%) cases had Grade 3 diastolic dysfunction (Table 1).

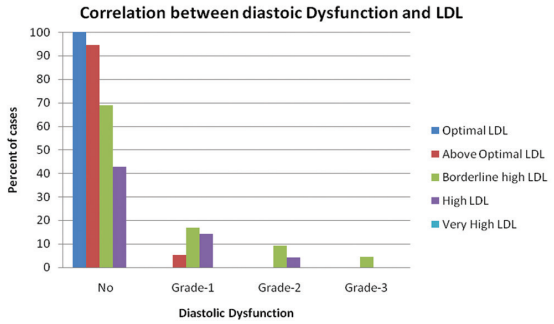
Correlation between diastolic dysfunction and LDL

Normal range of LDL (<100 mg/dL) levels was found in 22 (10.2%) and none of the patients with normal range LDL had any grade of diastolic dysfunction.

Above optimal levels of LDL (100–129 mg/dL) were found in 56 (26.1%) of cases out of which 53 (94.6%) of cases had normal diastolic function while 3 (5.3%) cases had grade 1 diastolic dysfunction.

Borderline high levels of LDL (130–159 mg/dL) were found in 129 (60.2%) of cases out of which 89 (68.9%) of cases had normal diastolic function while 22 (17.0%) cases had Grade 1, 12 (9.3%) cases had Grade 2, and only 6 (4.6%) patients had Grade 3 diastolic dysfunction.

High levels of LDL (>160 mg/dL) were found in 7 (3.2%) of cases out of which 3 (42.8%) of cases had normal diastolic function while 1 (14.2%) cases had Grade 1, 3 (4.2%) cases had Grade 2 diastolic dysfunction (Table 2).



Correlation between diastolic dysfunction and cholesterol

Normal range of cholesterol level (<200 mg/dL) was found in 70 (32.72%) cases out of which 66 (94.28%) had no diastolic dysfunction; while the 2 (2.86%) cases had Grade 1 and 2, and none of patients had Grade 3 diastolic dysfunction.

The raised of cholesterol level (>200 mg/dL) found in 144 (67.28%) of cases, out of which 101 (70.13%) had normal diastolic dysfunction, while the 24 (16.66%) cases had Grade 1, 13 (9.02%) cases had Grade 2, and only 06 (4.16%) patients had Grade 3 diastolic dysfunction (Table 3).

Table 1: Correlation between diastolic dysfunction and TG

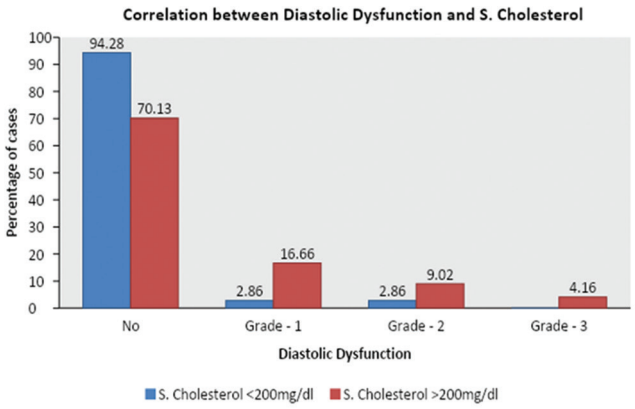
Diastolic dysfunction (DD)	No DD	Grade 1 DD	Grade 2 DD	Grade 3 DD	Total
TG (<150 mg/dL)					
Desirable					
No.	60	2	2	0	64
%	93.7	3.1	3.1	-	29.9
TG (150–199 mg/dL)					
Borderline					
No.	91	21	11	4	127
%	71.6	16.5	8.6	3.1	59.3
TG (200–499 mg/dL)					
High					
No.	16	3	2	2	23
%	69.5	13	8.6	8.6	10.7
Total					
No.	167	26	15	6	214
%	78.0	12.1	7.0	2.8	100

χ^2=19.62 P<0.0001 highly significant

Table 2: Correlation between diastolic dysfunction and LDL

Diastolic Dysfunction (DD)	No DD	Grade 1 DD	Grade 2 DD	Grade 3 DD	Total
LDL (<100 mg/dL)					
Optimal					
No.	22	0	0	0	22
%	100	-	-	-	10.2
LDL (100–129 mg/dL)					
Above optimal					
No.	53	3	0	0	56
%	94.6	5.3	-	-	26.1
LDL (130–159 mg/dL)					
borderline high					
No.	89	22	12	6	129
%	68.9	17.0	9.3	4.6	60.2
LDL (160–189 mg/dL)					
High					
No.	3	1	3	0	7
%	42.8	14.2	42	-	3.2
Total					
No.	167	26	15	6	214
%	78.0	12.1	7.0	2.8	100

χ^2=15.21 P<0.0001 highly significant



DISCUSSION

We found that the prevalence of diastolic abnormalities in adults under 40 years of age with fatty liver was 21.9%. In a study by Kuznetsova et al., the overall prevalence of LV diastolic dysfunction in a random sample of a general population, as estimated from echocardiographic measurements was as high as 27.3%; however, their mean age was 52.5 years as compared to 27.8 years in our study.[13]

While impaired LV diastolic relaxation is another common cardiac change observed in hypertensive patients, some significant metabolic factors, which are independent of BP and LV mass index, have been associated with this diastolic dysfunction.[14] In fact, abnormalities in glucose and insulin metabolism have been shown to accelerate the deterioration of arterial stiffness and LV diastolic function.[15,16] Dyslipidemia is one of metabolic abnormalities.

Study by Horio et al., and Miao et al., suggest that low HDL-C may pose an independent adverse effect on LV diastolic function in hypertensive patients independently of age, sex, BMI, smoking status, BP, total cholesterol, LDL cholesterol, TG, glucose, LV mass index, heart rate, and arterial stiffness.[17,18]

In our study, we found a significant correlation between raising levels of TG and diastolic dysfunction with P<0.0001%. There was a significant increase in the number of patients with diastolic dysfunction in borderline raised and high TG levels as compared to normal TG levels. In study by Horio et al., TG were weakly correlated with LV mass and A/E.[17] This difference can be because of different demographic composition of two studies.

In our study, we found a significant correlation between raising levels of LDL and diastolic dysfunction with P<0.0001%. There was a significant increase in the number of patients with diastolic dysfunction in patients with borderline high and high LDL levels as compared to normal and above optimal LDL levels. Not only incidence but severity of diastolic dysfunction also increases with rising levels of LDL. In patients with normal and above optimal levels of LDL, no patient had Grade 3 diastolic dysfunction while in patients with borderline high LDL 4.6% of patients had Grade 3 diastolic dysfunction. With these results, we can say that there was increased incidence and also increase in severity of diastolic dysfunction with raising levels of LDL.

In our study, we found a significant correlation between rising levels of S. Cholesterol and diastolic dysfunction <0.0001%. There was a significant increase in the number of patients with diastolic dysfunction in patients with high S. Cholesterol levels as compared to normal levels. Not only incidence but severity of diastolic dysfunction also increases with rising levels of S.Cholesterol. In patients with normal S. Cholesterol, no patient had Grade 3 diastolic dysfunction, while in patients with high S. Cholesterol, 4.1% of patients had Grade 3 diastolic dysfunction. With these results, we can say that there was an increased incidence and also an increase in severity of diastolic dysfunction with rising levels of S. Cholesterol. In a study by Ayman et al., patients with LVDD had significant dyslipidemia in comparison to those without LVDD.[19] Our study is in support of their results.

Table 3: Correlation between diastolic dysfunction and S. cholesterol

Diastolic dysfunction	No DD	Grade 1 DD	Grade 2 DD	Grade 3 DD	Total
S. Cholesterol (<200 mg/dL)					
No.	66	2	2	0	70
%	94.2	2.8	2.8	-	32.7
LDL (>200 mg/dL)					
No.	101	24	13	6	144
%	70.1	16.6	9.0	4.1	67.2
Total					
No.	167	26	15	6	214
%	78.0	12.1	7.0	2.81	100

χ^2=21.31 P<0.0001 highly significant

Mizuguchi and associates reported that statin therapy could promote LV diastolic function accompanied with the improvement of blood lipid level.[20]

Alterations of lipid metabolism in cardiac muscle and cardiac lipid content induce alterations in myocardial lipid metabolism, increase myocardial fat content and epicardial fat thickness, and increase inflammation and oxidative stress which ultimately lead to cardiac lipotoxicity and diastolic dysfunction.[21] Lipid profile and metabolism are as important in the pathogenesis of diastolic dysfunction as they are in other cardiovascular disorders. A more careful look at cardiac lipid metabolism in molecular, histological, and gross levels results in a more precise understanding of its role in myocardial function and leads to development of potential treatments for diastolic dysfunction.

Limitations of the study

1. The study had a small sample size
2. This was a cross-sectional study and no long-term follow-up of patients was done.

CONCLUSION

We found that the prevalence of diastolic abnormalities in adults under 40 years of age 21.9%. It was found that there was significant correlation between dyslipidemia and presence of diastolic dysfunction in patients. Therefore, the presence of dyslipidemia in patients should not be ignored and clinicians who manage patients should not focus only on dyslipidemia but should also consider the increased risk of cardiovascular disease and undertake early and aggressive risk factor modification.

ACKNOWLEDGMENT

We thank all the individuals included in the study and the institute, Shyam Shah Medical College and Sanjay Gandhi Medical Hospital Rewa for providing platform to conduct the study.

REFERENCES

1. Redfield MM, Jacobsen SJ, Burnett JC Jr., Mahoney DW, Bailey KR, Rodeheffer RJ, et al. Burden of systolic and diastolic ventricular dysfunction in the community: Appreciating the scope of the heart failure epidemic. JAMA. 2003;289(2):194-202.
   https://doi.org/10.1001/jama.289.2.194
2. Abhayaratna WP, Marwick TH, Smith WT and Becker NG. Characteristics of left ventricular diastolic dysfunction in the community: An echocardiographic survey, Heart. 2006;92(9):1259-1264.
   https://doi.org/10.1136/hrt.2005.080150
3. Achong N, Wahi S and Marwick TH. Evolution and outcome of diastolic dysfunction. Heart. 2009;95(10):813-818.
   https://doi.org/10.1136/hrt.2008.159020
4. Aurigemma GP, Gottdiener JS, Shemanski L and Kitzman D. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: The cardiovascular health study. J Am Coll Cardiol. 2001;37(4):1042-1048.
   https://doi.org/10.1016/s0735-1097(01)01110-x
5. Fischer M, Baessler A, Hense HW, Hengstenberg C, Muscholl M, Holmer S, et al. Prevalence of left ventricular diastolic dysfunction in the community. Results from a doppler echocardiographic-based survey of a population sample. Eur Heart J. 2003;24(4):320-328.
   https://doi.org/10.1016/s0195-668x(02)00428-1
6. Desai CS, Colangelo LA, Liu K, Jacobs DR Jr., Cook NL, Lloyd-Jones DM, et al. Ogunyankin, prevalence, prospective risk markers, and prognosis associated with the presence of left ventricular diastolic dysfunction in young adults: The coronary artery risk development in young adults study. Am J Epidemiol. 2013;177(1):20-32.
   https://doi.org/10.1093/aje/kws224
7. Arhlade F, Asadi A, Raboukhi S and Habbal R. 0097: Influence of dyslipidemia on clinical characteristics in heart failure patients. Series of 583 cases. Arch Cardiovasc Dis Suppl. 2015;7(2):178.
   https://doi.org/10.1016/S1878-6480(15)30130-0
8. Shin MS, Yu J, Hong KS, Kim MA, Shin GJ and Shim WJ. Dyslipidemia, diastolic dysfunction and exercise intolerance in women. Atherosclerosis. 2017;263:e192.
   https://doi.org/10.1016/j.atherosclerosis.2017.06.617
9. Adil A. Cholesterol and triglyceride indices are linked to the left ventricle diastolic dysfunction: An echocardiography and tissue Doppler study. Indian J Public Health Res Dev. 2019;10(4):1485-1490.
10. Diamant M, Lamb HJ, Groeneveld Y, Endert EL, Smit JW, Bax JJ, et al. Diastolic dysfunction is associated with altered myocardial metabolism in asymptomatic normotensive patients with well-controlled Type 2 diabetes mellitus. J Am Coll Cardiol. 2003;42(2):328-335.
    https://doi.org/10.1016/s0735-1097(03)00625-9
11. Jorgensen PG, Jensen MT, Biering-Sorensen T, Mogelvang R, Galatius S, Fritz-Hansen T, et al. Cholesterol remnants and triglycerides are associated with decreased myocardial function in patients with Type 2 diabetes. Cardiovasc Diabetol. 2016;15:137.
    https://doi.org/10.1186/s12933-016-0454-x
12. Khedr D, Hafez M, Lumpuy-Castillo J, Emam S, Abdel-Massih A, Elmougy F, et al. Lipid biomarkers as predictors of diastolic dysfunction in diabetes with poor glycemic control. Int J Mol Sci. 2020;21(14):5079.
    https://doi.org/10.3390/ijms21145079
13. Kuznetsova T, Herbots L, López B, Jin Y, Richart T, Thijs L, et al. Prevalence of left ventricular diastolic dysfunction in a general population. Circ Heart Fail. 2009;2(2):105-112.
    https://doi.org/10.1161/CIRCHEARTFAILURE.108.822627
14. Schillaci G, Pasqualini L, Verdecchia P, Vaudo G, MarchesiS, Porcellati C, et al. Prognostic significance of left ventricular diastolic dysfunction in essential hypertension. J Am Coll Cardiol. 2002;39(12):2005-2011.
    https://doi.org/10.1016/s0735-1097(02)01896-x
15. Miyazato J, Horio T, Takishita S and Kawano Y. Fasting plasma glucose is an independent determinant of left ventricular diastolic dysfunction in non-diabetic patients with treated essential hypertension. Hypertens Res. 2002;25(3):403-409.
    https://doi.org/10.1291/hypres.25.403

16. Vinereanu D, Nicolaides E, Tweddel AC, Mädler CF, Holst B, Boden LE, et al. Subclinical left ventricular dysfunction in asymptomatic patients with Type II diabetes mellitus, related to serum lipids and glycated haemoglobin. Clin Sci(Lond). 2003;105(5):591-599.
https://doi.org/10.1042/CS20030168
17. Horio T, Miyazato J, Kamide K, Takiuchi S and Kawano Y. Influence of low high-density lipoprotein cholesterol on left ventricular hypertrophy and diastolic function in essential hypertension. Am J Hypertens. 2003;16(11 Pt 1):938-944.
https://doi.org/10.1016/s0895-7061(03)01015-x
18. Miao DM, Ye P, Xiao WK, Gao P, Zhang JY and Wu HM. Influence of low high-density lipoprotein cholesterol on arterial stiffening and left ventricular diastolic dysfunction in essential hypertension. J Clin Hypertens (Greenwich). 2011;13(10):710-715.
https://doi.org/10.1111/j.1751-7176.2011.00501.x
19. Ayman KM, Mahmoud AA, Eman, AA, Marwa S, Mona MS and Yehia TK. Correlation between left ventricular diastolic dysfunction and dyslipidaemia in asymptomatic patients with new-onset Type 2 diabetes mellitus. Egypt J Intern Med. 2021;33(1):8.
https://doi.org/10.1186/s43162-021-00037-0
20. Mizuguchi Y, Oishi Y, Miyoshi H, Iuchi A, Nagase N, Oki T, et al. Impact of statin therapy on left ventricular function and carotid arterial stiffness in patients with hypercholesterolemia. Circ J. 2008;72(4):538-544.
https://doi.org/10.1253/circj.72.538
21. Bednarski TK, Duda MK and Dobrzyn P. Alterations of lipid metabolism in the heart in spontaneously hypertensive rats precedes left ventricular hypertrophy and cardiac dysfunction. Cells. 2022;11(19):3032.
https://doi.org/10.3390/cells11193032

Authors' Contributions:
NJ- Concept, review of literatures, data collection, preparation of first draft, and submission of article; **KDS-** Study design and protocol, interpretation of results, and preparation of final manuscript; **HG-** Definition of intelluectual content, 2D Echocardiogram of cases and its interpretation, and review manuscript; **UPS-** Statistical analysis and revision of manuscript**; and SS-** Review manuscript and preparation of final manuscript.

Work attributed to:
Shyam Shah Medical College, Rewa, Madhya Pradesh, India.

ORCID ID:
Naman Jain - https://orcid.org/0000-0001-8627-4552
Kuwer Devi Singh - https://orcid.org/0000-0001-6722-4103
Himanshu Gupta - https://orcid.org/0000-0002-9317-1380
Umesh Pratap Singh - https://orcid.org/0000-0002-8247-2700
Sanjeev Sharma - https://orcid.org/0000-0003-3789-0134

Source of Funding: Nil, **Conflicts of Interest:** None declared.