



Prevalence of Anti-Cardiolipin Antibodies IgG and IgM in Young Myocardial Infarction Patients

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ABSTRACT

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¹Conception & Study Design, Data Collection & Processing, Critical Review.

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⁴Critical Review.

⁵Data Analysis and/or Interpretation.

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Objective: To assess the frequency of anti-cardiolipin antibodies IgG and IgM among young patients with myocardial infection (MI), determining the APLS earlier prevents the formation of thrombosis and risk of MI in future.

Methodology: This cross-sectional study was done on 486 patients at the department of cardiology LUMHS. diagnosed patients of MI aged 25-50 years and both genders were enrolled for the study. A 6.8cc blood was drawn after an aseptic method and anti-cardiolipin antibodies were determined by Roche 501 modular analyzer. All data were collected via study proforma and analyzed in Microsoft Excel 2021 & SPSS 21.0.

Results: A total of 486 patients of MI were studied, their mean age was 40.2±5.17 years and an average APTT was 37.67±7.81. According to the frequency of positive anti-cardiolipin antibodies, 8.4% were Anti-cardiolipin IgM positive with average antibodies as 3.04±3.97 MPLU/ml. Average of anticardiolipin IgG antibodies was 3.41±2.21 GPLU/ml and only 6.37% of cases were positive and rest of 93.63% were negative. Frequency of anticardiolipin IgM & IgG were statistically significant according to age different age groups ($p < 0.05$).

Conclusion: Frequency of anti-cardiolipin antibodies IgG and IgM were observed to be the 6.37% and 8.4% respectively. Among young patients with myocardial infection. Early screening and treatment of these antibodies may prevent vascular thrombosis and MI in the future of the young population.

Keywords: Myocardial infarction, antiphospholipid syndrome (APS).

INTRODUCTION

Myocardial infarction is the most common CVD chronic disease in Pakistan¹, in which blood flow to the heart is suddenly cut off due to a blockage in one of the coronary arteries caused by plaque or rupture of unstable plaque causing blood clots that also occlude the blood vessel and eventually cause heart necrosis. ² According to the WHO, CVD leads to 18 million deaths around the world, which makes up about 31% of total global deaths. ^{3,4} Unhealthy diet and lifestyle, obesity, smoking, and increases in apolipoprotein A1/B, HTN, and DM in families⁵ are some of the risk factors that have resulted in a frightening

increase in MI occurrence in younger populations over the last two decades.⁶ Anti-phospholipid antibodies are formed like in antiphospholipid syndrome (APS) where the body mistakenly produces antibodies directed against protein-bound phospholipids and forms blood clots anywhere in the body. The predisposition of blood clots leads to stroke, MI, DVT & other serious complications. APLAs comprise lupus anticoagulant (LA), anticardiolipin antibodies (ACLA), and anti- β 2 glycoprotein I (Anti- β 2GPI).^{7,8}

Coronary vessels vasoconstriction & innermost layer thickening caused by peroxidation of phospholipids &

esters of cholesterol is the early & cardinal event that occurs by APLs.⁹ The role of APLs in young patients with MI has been reported by some South Asian Studies which were found to be significantly positive and in coronary thrombosis, mild elevation of ACL antibodies may be considered significant.¹⁰⁻¹² A survey of 120 studies concluded that: APLA was found in 11% of patients with MI with no previous history of APS.^{13,14} International research (APS ACTION) has reported that young patients with stroke,(17%) & MI (14%) have evidence of APLs in their bodies. Furthermore, APLs raise the risk of thrombotic events while improving outcomes due to lower titers. ¹⁶ So proper screening & diagnosis for APLs in young patients already in the shadow of MI risk factors can prevent severe outcomes.¹⁷

This study has been done to evaluate the frequency of anti-cardiolipin antibodies IgG and IgM among young patients with myocardial infection (MI), determining the APLs earlier prevents the formation of thrombosis and risk of MI in the future.

MATERIALS AND METHODS

This cross-sectional study was conducted at the cardiology department in conjunction with the physiology department at LUMHS Jamshoro and the Diagnostic Laboratory at Civil Hyderabad after receiving permission from the LUMHS Research and Ethical Committee. All the diagnosed patients of MI aged 25-50 years and both genders were enrolled for the study. Patients having any autoimmune diseases or on any blood coagulation drugs or cases present with age above > 50yrs were excluded. After taking informed consent from each patient, a 6.8 cc of blood sample was drawn from the cubital vein following an

aseptic method, in which 5cc was transferred in the red cap bottle to determine anti-cardiolipin antibodies by the Alegria test kit, which contains strips that run on an automated analyzer called Alegria. An antibody-antigen complex formed, which was measured photometrical at 650nm by Roche 501 modular analyzer. The remaining 1.8cc blood was drawn for APTT which is measured by the clotting method. All data were collected via study proforma and analyzed in Microsoft Excel 2021 & SPSS 21.0.

For quantitative variables like age & APTT, mean & standard deviation were used. IgG & IgM Antibodies were determined by applying a chi-square test and p-values < 0.05 was taken as statistically significant.

RESULTS

The result of this study was carried out to highlight the significance of early screening of anticardiolipin antibodies in subjects that were already at risk for MI. The mean age of the patients was 40.0±5.17 years, with a minimum of 27 years and a maximum of 50 years, alongwith an average APTT was 37.67±7.81. (Table I)

Out of all study subjects, according to the frequency of positive anti-cardiolipin antibodies, 8.4% were anti-cardiolipin IgM positive, with average antibodies as 3.04±3.97 MPLU/ml. Average of anticardiolipin IgG antibodies was 3.41±2.21 GPLU/ml and only 6.37% of cases were positive and rest of 93.63% were negative. (Table II)

Frequency of anticardiolipin IgM & IgG were statistically significant according to age different age groups (p=<0.05). (Table III)

Table I: Descriptive Statistics of Demographic Variables (n=486)

Characteristics	Mean ± SD
Age	40.0 ± 5.17 years
APTT	37.6±7.81
Anti-cardiolipin IgM	3.04±3.97
Anti-cardiolipin IgG	3.44±2.21

Table II: Mean Anticardiolipin Antibodies in Accordance with Different Age Groups (n=486)

Age groups	Immunoglobulin G			Immunoglobulin M		
	N	Mean±SD	P value	N	Mean± SD	P value
25-35 years	200	9.11±2.12	0.014	200	13.76±3.15	0.043
36-45 years	179	7.89±1.134		179	11.54±2.96	
>45 years	106	6.14±0.213		106	8.53±4.63	

Table III: Frequency of Anti-cardiolipin IgM & IgG Antibodies (n=486)

IgM	Anticardiolipin antibodies IgM		IgG	Anticardiolipin antibodies IgG	
	N	%		N	%
Positive	41	8.4	Positive	31	6.37
Negative	445	91.6	Negative	455	93.63
Total	486	100	Total	486	100

Table IV: Frequency of Anti-cardiolipin IgM & IgG Antibodies According to Age (n=486)

Anticardiolipin antibodies	Age groups			p-value
	25-35 years	36-45 years	>45 years	
IgM	Positive	22	13	0.0001
	Negative	44	112	
	Total	66	125	
IgG	Positive	18	9	0.0001
	Negative	48	116	
	Total	66	125	

DISCUSSION

Myocardial infarction, non-communicable disease of the heart makes an exceedingly large number of deaths & morbidity globally, requiring a lot of research & modern approach to make lifestyles better for all age groups, especially youth. Our research is also one way to provide information regarding the prevalence of antiphospholipid in young, diagnosed MI patients. It is reported in Channamma G et al¹⁸ studies, out of his 40 patients, mostly belonged to the 50-59 years of age group while in our study, the mean age group was 40.19±5.86 years. In Nazir S, et al¹⁹ surveys, however, it shows a mean age group of 41.10±13.61 years with a male having 55% of supremacy over 45% of females in the occurrence of MI & in our study, the incidence of MI was 92.5% in the male gender & only 7.5% in the female population with average APTT was 37.67±7.81 sec.

One of the systematic reviews shows a positive relationship between high IgG APL titers and possibility of recurrent major adverse cardiac events in already diagnosed MI patients.²⁰ but APL prevalence in the general population is hard to find for it showing no symptoms in carrier patients or not remain positive over time in asymptomatic APL carriers. In this study, 11.8% of the cases were anti-cardiolipin antibodies IgM positive while 3.8% of subjects were showing IgG positive outcomes. Similarly, Dhason TM et al²¹ study showed that among the 100 patients, ACLa IgM was seen positive in 5 patients and 16 patients were IgG positive. In another study, Vaarala O et al.²² discovered that 20% of patients with antiphospholipid syndrome experienced MI. In 1,000 diagnosed patients of APS, 2.8% of

subjects have reported an episode of MI in one of the longitudinal studies.²³

APTT was found significantly raised according to Anti-cardiolipin anti-bodies IgG and IgM (p<0.05). Ginsburg KS et al and Levine JS et al had done several studies that showed abnormal vascular events & poor pregnancy outcomes in those APS diagnosed patients with a high titer of APL antibodies^{24,25} In another European cohort study conducted in 2002 by Cervera R et al in 1000 diagnosed APS patients, 25% had MI and other abnormal vascular events as an early symptom.²⁶ A meta-analysis by Galli et al²⁷ reported high Lupus anticoagulant in blood shows the same incidence of abnormal vascular events as the high titer of ACA has shown in many studies. Studies have proposed that IgM isotypes are more predominant in arterial events, whereas IgG isotypes in venous disease.^{28,29}

CONCLUSION

The frequency of anti-cardiolipin antibodies IgG and IgM were observed to be 6.37% and 8.4%, respectively, among young patients with myocardial infarction. Presence of APS i.e. anti-cardiolipins IgG & IgM in patients of MI as a prognostic marker. Early screening and treatment of these antibodies may prevent vascular thrombosis and MI in the future among the young population.

Recommendation: DM & MI in family history are considered major risk factors for MI in the young population globally, so evaluation is recommended to avoid future cardiac issues. Secondly, such studies should be done in large populations to highlight APS as a prognostic biomarker in MI patients.

REFERENCES

- 1- Li H, Sureda A, Devkota HP, Pittalà V, Barreca D, Silva AS, Tewari D, Xu S, et al, the golden spice in treating cardiovascular diseases. *Biotechnology advances*. 2020;1;38:107343.
<https://doi.org/10.1016/j.biotechadv.2019.01.010>
- 2- Osula S, Bell GM, Hornung RS. Acute myocardial infarction in young adults causes and management. *Postgrad. Med. J.* 2002;78(915):27-30.
<https://doi.org/10.1136/pmj.78.915.27>
- 3- Xu S, Ilyas I, Little, PJ, Li H, Kamato D, Zheng X, Luo S, et al. Endothelial dysfunction in atherosclerotic cardiovascular diseases and beyond: from mechanism to pharmacotherapies. *Pharmacol. Rev.* 2021;73(3):924-67.
<https://doi.org/10.1124/pharmrev.120.000096>
- 4- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD, et al. Fourth universal definition of myocardial infarction. *Eur. Heart J.*2018;40(3):237-69.
- 5- Iwańczyk S, Skorupski W, Grygier M, Sikora T, Araszkievicz A, Lesiak M. Myocardial infarction with nonobstructive coronary arteries in a young woman: the key role of optical coherence tomography. *Kardiologia Polska. Polish Heart Journal.*2019;77(7-8):728-9.
<https://doi.org/10.33963/KP.14881>
- 6- Weber B, Biery DW, Singh A, Divakaran S, Berman AN, Wu WY, Brown JM, et al. Association of inflammatory disease and long-term outcomes among young adults with myocardial infarction: the Mass General Brigham YOUNG-MI Registry. *Eur. J. Prev. Cardiol.*2022;(2):352-9.
<https://doi.org/10.1093/eurjpc/zwaa154>
- 7- Radin M, Schreiber K, Costanzo P, Cecchi I, Roccatello D, Bazzan M, Cuadrado MJ, et al. The adjusted Global Antiphospholipid Syndrome Score (aGAPSS) for risk stratification in young APS patients with acute myocardial infarction. *Int. J. Cardiol.*2017;240:72-7.
<https://doi.org/10.1016/j.ijcard.2017.02.155>
- 8- Mancy T, Tsai BW, Chamley. Antiphospholipid antibodies and vesicles in pregnancy. *Am. J. Reprod. Immunol.* 2021;85(2):e13312.
<https://doi.org/10.1111/aji.13312>
- 9- Malbora B, Eris Bilaloglu E. Lupus anticoagulant positivity in pediatric patients with prolonged activated partial thromboplastin time: A single-center experience and review of the literature. *Pediatr. Hematol. Oncol. J.* 2015;3;32(7):495-505.
<https://doi.org/10.3109/08880018.2015.1065302>
- 10- Mancy T, Tsai BW, Chamley LW. Antiphospholipid antibodies and extracellular vesicles in pregnancy. *Am. J. Reprod. Immunol.* 2021;85(2):e13312.
<https://doi.org/10.1111/aji.13312>
- 11- Wang G, Zhong C, Peng H, Bu X, Wang A, Xu T, Peng Y, Li Q, Geng D. Renal Function Affects Prognostic Role of Ant phosphatidylserine Antibodies for Acute Ischemic Stroke Patients. *Cerebrovasc. Dis.* 2019;48(1-2):1-8.
<https://doi.org/10.1159/000501957>
- 12- Stepien K, Nowak K, Wypasek E, Zalewski J, Undas A. High prevalence of inherited thrombophilia and antiphospholipid syndrome in myocardial infarction with non-obstructive coronary arteries: Comparison with cryptogenic stroke. *Int. J. Cardiol.*2019;290:1-6.
<https://doi.org/10.1016/j.ijcard.2019.05.037>
- 13- Gacoń J, Przewłocki T, Podolec J, Badacz R, Pieniążek P, Ryniewicz W, Kabłak-Ziembicka A. Prospective study on the prognostic value of repeated carotid intima-media thickness assessment in patients with coronary steno-occlusive arterial disease. *Pol Arch Intern Med.* 2019;129(1):12-21.
<https://doi.org/10.20452/pamw.4407>
- 14- Bagoly Z. Uncovering the genetic background of natural anticoagulant deficiencies: time to look behind the scenes. *Pol. Arch. Intern. Med.*2017;127(7-8):165-7.
<https://doi.org/10.20452/pamw.4069>
- 15- Tomasello R, Giordano G, Romano F, Vaccarino F, Siragusa S, Lucchesi A, Napolitano M. Immune thrombocytopenia in antiphospholipid syndrome: Is it primary or secondary. *Biomedicines.*2021;9(9):1170.
<https://doi.org/10.3390/biomedicines9091170>
- 16- Mishra MN, Kalra R, Gupta MK. Antiphospholipid antibodies in young myocardial infarction patients. *IJBB.*2007; Vol.44(6) 481-484
- 17- Maor E, Fefer P, Varon D, Rosenberg N, Levi N, Hod H, Matetzky S. Thrombophilic state in young patients with acute myocardial infarction. *Journal of Thrombosis and Thrombolysis.*2015;39(4):474-80.
<https://doi.org/10.1007/s11239-014-1166-2>
- 18- Kampolis C, Tektonidou M, Moysakis I, Tzelepis GE, Moutsopoulos H, Vlachoyiannopoulos PG. Evolution of cardiac dysfunction in patients with antiphospholipid antibodies and/or antiphospholipid syndrome: a 10-year follow-up study. In *Seminars in arthritis and rheumatism* 2014; 43(4):558-565. WB Saunders.
<https://doi.org/10.1016/j.semarthrit.2013.07.016>
- 19- Tektonidou MG, Ioannidis JP, Moysakis I, Boki KA, Vassiliou V, Vlachoyiannopoulos PG, Kyriakidis MK, et al. Right ventricular diastolic dysfunction in patients with anticardiolipin antibodies and antiphospholipid syndrome. *Annals of rheumatic diseases.* 2001;60(1):43-8.
<https://doi.org/10.1136/ard.60.1.43>
- 20- Denas G, Jose SP, Bracco A, Zoppellaro G, Pengo V. Antiphospholipid syndrome, and the heart: a case series and literature review. *Autoimmunity reviews.* 2015;14(3):214-22.
<https://doi.org/10.1016/j.autrev.2014.11.003>
- 21- Boekholdt SM, Kramer MH. Arterial thrombosis and the role of thrombophilia. In *Seminars in thrombosis and hemostasis* 2007; 33(6): 588-596. Copyright© 2007 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
<https://doi.org/10.1055/s-2007-985755>
- 22- Adler Y, Finkelstein Y, Zandeman-Goddard G, Blank M, Lorber M, Lorber A, Faden D, et al. The presence of antiphospholipid antibodies in acute myocardial infarction. *Lupus.* 1995;4(4):309-13.
<https://doi.org/10.1177/096120339500400413>
- 23- Meroni PL, Peyvandi F, Foco L, Bernardinelli L, Fetiveau R, Tincani A, Atherosclerosis, Thrombosis And Vascular Biology Italian Study Group. Anti-beta 2 glycoprotein I antibodies and the risk of myocardial infarction in young premenopausal women. *J Thromb Haemost.* 2007;5(14):2421-9.
<https://doi.org/10.1111/j.1538-7836.2007.02763.x>

- 24- Veres K, Lakos G, Kerenyi A, Szekanecz Z, Szegedi G, Shoenfeld Y, Soltesz P. Antiphospholipid antibodies in acute coronary syndrome. *Lupus*. 2004;13(6):423-7. <https://doi.org/10.1191/0961203304lu1011oa>
- 25- Urbanus RT, Siegerink B, Roest M, Rosendaal FR, Antiphospholipid antibodies and risk of myocardial infarction and ischemic stroke in young women in the RATIO study: *The Lancet Neurology*. 2009;8(11):998-1005. [https://doi.org/10.1016/S1474-4422\(09\)70239-X](https://doi.org/10.1016/S1474-4422(09)70239-X)
- 26- Kolitz T, Shiber S, Sharabi I, Winder A, Zandman-Goddard G. Cardiac manifestations of antiphospholipid syndrome with focus on its primary form. *Front. Immunol.* 2019; 10;10:941. <https://doi.org/10.3389/fimmu.2019.00941>
- 27- Yoo S, Jang S, Kim JA, Troponin-positive non-obstructive coronary arteries, and myocardial infarction non-obstructive coronary arteries: definition, etiologies, and role of CT and MR imaging. *Korean J Radiol.* 2020;21(12):1305. <https://doi.org/10.3348/kjr.2020.0064>
- 28- Niccoli G, Camici PG. Myocardial infarction with non-obstructive coronary arteries: *European Heart Journal Supplements*. 2020;22(Supplement_E):E40-5. <https://doi.org/10.1093/eurheartj/suaa057>
- 29- Arachchillage DR, Laffan M. Pathogenesis and management of antiphospholipid syndrome. *Br. J. Haematol.* 2017 Jul;178(2):181-95. <https://doi.org/10.1111/bjh.14632>



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