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METABOLIC SYNDROME AND LIPOPROTEIN – RELATED PHOSPHOLIPASE A2: CORRELATIONAL EVIDENCES AND CLINICAL IMPLICATIONS

[1*]Halar Rahim, [1]Faraz Ahmad, [1]Ram Dass

[1]Department of Medicine, Jinnah Postgraduate Medical Center, Karachi, Sindh

***Corresponding Author:** Halar Rahim (dr.halarraim@gmail.com)

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ABSTRACT

Background: The significance of lipoprotein – associated phospholipase A2 (Lp-PLA2) for predicting cardiovascular and inflammatory disorders is garnering attention in the medical field. Moreover, a strong association has been observed between metabolic syndrome and persistent inflammation. This research focused on exploring possible link among metabolic syndrome and Lp-PLA2 levels.

Methodology: In this retrospective study, we analyzed the relationship among metabolic disorder and the Lp-PLA2 levels, aiming to identify a threshold value for Lp-PLA2. A total of 549 patients contributed in study, aged between 18-50 years. Additionally, an evaluation of the variation in Lp-PLA2 across different genders and age groups were analyzed.

Results: The study revealed that the participants had an average age of 43.6 years and an average Lp-PLA2 levels of 592.41 IU/L, with metabolic syndrome being prevalent in 21% of them. Furthermore, variances in Lp-PLA2 levels were detected between male and female participants. A notable association between levels of Lp-PLA2 and various health markers including body mass index (BMI), cholesterol levels, and triglycerides. The Lp-PLA2 was identified as a promising indicator for metabolic syndrome, particularly in female subjects, despite the fact that other markers like TG/HDL-C ratio and waist-hip ratio (WHR) had slightly more vigorous results in some assessments.

Conclusion: The findings indicated that Lp-PLA2 might serve as an effective biomarker for detecting a heightened risk of metabolic syndrome, especially among women. It warrants further exploration to elucidate the diagnostic potential as well as therapeutic effect of Lp-PLA2 in relation to metabolic syndrome.

Keywords: Metabolic syndrome. Lp-PLA2, risk factors, lipid profile, lipoproteins, Lp-PLA2.

Introduction

The initial interest in lipoprotein – related phospholipase A2 (Lp-PLA2) emerged during the 1980s, focusing on its role in the oxidative deterioration of low-density lipoprotein (LDL) and the subsequent influence on cardiovascular health[1]. Studies, including those by Brilakis et al., have shown a linkage between average Lp-+LA2 levels and various lipid profiles such as LDL, HDL as well as total cholesterol, creatinine, and fibrinogen[2]. Additionally, Lp-PLA2 was identified as an independent indicator for coronary artery disease (CAD), complementing markers like C-reactive protein (CRP)[3].

The dual function of Lp-PLA2 in the body encompasses both antioxidative and inflammatory functions. Produced by various cells including macrophages, mast cells, and T cells within the blood vessel walls, Lp-PLA2 works alongside LDL in the bloodstream. It plays a major part in neutralizing oxidative elements of partially oxidized LDL[4]. On the other hand, in response to oxidative stress, these cells ramp up Lp-PLA2 production, leading to increased infiltration of macrophages into the inner layers of blood vessels and the absorption of oxidized LDL[5]. This process results in the formation of foam cells, contributing to plaque buildup and elevating cardiovascular risk, hence linking Lp-PLA2 directly to inflammation.

The relationship between metabolic syndrome and inflammation is well – established. Modern lifestyle factors, particularly sedentary behavior and poor diet, have escalated the prevalence of metabolic syndrome, a condition not only associated with cardiovascular diseases and diabetes but also with chronic ailments like polycystic ovarian syndrome and non-alcoholic fatty liver disease (NAFLD). The metabolic syndrome usually triggers metabolic overwork, causing a surge in reactive oxygen species (ROS) and cytokines, and causing oxidative stress. This exacerbates inflammation and insulin resistance by promoting adipocyte enlargement and macrophage aggregation[6,7].

Therefore, our research seeks to assess the effectiveness of Lp-PLA2 as a marker for metabolic syndrome. We aim to analyze its correlation with various risk factors of metabolic syndrome in patients undergoing medical investigations. Moreover, we plan to establish the threshold level of Lp-PLA2 in individuals at elevated risk for the metabolic syndrome, aiming to enhance health managing strategies as well as mitigate severity and progression of metabolic syndrome in these patients.

Materials and Methods

In this retrospective study, we analyzed medical history of participants aged between 18 to 55 years who received health screening at tertiary care hospital during 2021-2022. Exclusion criteria included pregnancy, less than 12 hours of fasting, treatment for hypertension or hyperlipidemia, chronic thyroid, liver disorders, and incomplete record data. A total of 549 patients were selected consisting of 182 males and 368 females. The selected participants underwent a series of anthropometric and biochemical tests, measuring factors like height, blood pressure, weight, waist

circumference, fasting glucose, total cholesterol, triglycerides, HDL, and LDL.

A range of clinical biochemistry analyses were performed, such as fasting serum glucose levels determined by Hexokinase enzyme assay (Cobas Mira). We also measured cholesterol profiles and triglycerides using an automatic analyzer. Lp-PLA2 was assessed through a turbidimetric immunology assay. Anthropometric measurements, such as height and weight, were taken by standardized instruments, and BMI (weight (kg) divided by height (m^2). Circumference of waist was assessed midway among lowest rib and the iliac crest. Blood pressure was recorded after 15 minutes of rest using an automated device, and mean arterial pressure was calculated. Diabetes was recognized as a level of fasting serum glucose of 7 mmol/L or increased. Metabolic syndrome was identified in subjects meeting three of more criteria, including specific threshold for waist circumference, HDL, triglycerides, fasting glucose, and blood pressure.

By identifying normal distribution, we chose to use the mean and standard deviation for central tendency analyses. Comparative analyses between subjects involving by independent t-tests for continuous variables and chi-square tests for categorical variables. Furthermore, we explored relationship between levels of Lp-PLA2 and various health conditions, such as diabetes, hypertension, metabolic syndrome, and lipid profiles, with sex – based stratification. Pairwise comparisons were made with Bonferroni correction in cases of significant overall tests. Logistic regression was used to analyze Lp-PLA2 levels, adjusting for age and BMI. All tests were two – tailed, with a significant levels of $p<0.05$. Data analyses was performed using SPSS 24.

Results

The study includes 549 participants, with an average age among them was 43.6 years. The mean Lp-PLA2 levels across participants was 592.41 IU/L. Basic participant characteristics and cardiometabolic risk factors are summarized in Table 1. Average levels of Lp-PLA2 were distinctly different between genders, being 615.87 ± 155.70IU/L in men and 541.81 ± 149.91 IU/L in women. This significant gender – based difference in Lp-PLA2, along with other factors, is summarized in in Table 1.

Table 2 displays association between Lp-PLA2 levels and various metabolic and clinical features, segregated by genders. In both genders, variables such as BMI, waist-to-height ration, waist circumference, total cholesterol, HDL cholesterol, triglycerides, LDL cholesterol, and TG/HDL-C showed a significant association with levels of Lp-PLA2 ($p<0.05$). Moreover, among males, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were significantly correlated to Lp-PLA2 ($p<0.05$), whereas among females, fasting levels of glucose were significantly correlated ($p<0.05$).

To explore association between specific characteristics and levels of Lp-PLA2, participants were divided into tertiles for Pearson's correlation analysis (Table 3). This analysis revealed a significant statistical linear trend through all features in Lp-PLA2 level –

based subgroups ($p<0.05$). Notable, incidence of metabolic syndrome in females increased with increasing levels of Lp-PLA2, showing various prevalence rates through different tertiles ($p<0.05$).

Regression analyses, adjusting for age and BMI, further supported these findings, as shown in Table 4. In female group, levels of Lp-PLA2 remained significantly associated ($p<0.05$) even after adjustment, suggesting its utility as an indicator of MetS in women.

Predictive powers for 3 biomarkers stratified by gender are presented in Table 5. In males, C value for TG/HDL-C, WHtR, and Lp-PLA2 were 0.86, 0.84, and 0.53 respectively, whereas, in females, these values were 0.93, 0.87, and 0.59. While TG/HDL-C and WHtR showed better predictive accuracy, Lp-PLA2 still emerged as a potential MetS indicator, especially in females.

Discussion

This study included 182 men and 367 women to assess the connection among Lp-PLA2 and metabolic syndrome. The findings revealed an important relationship between levels of Lp-PLA2 and indicators of metabolic syndrome, especially among females. Even after BMI and age adjustment, a strong link between levels of Lp-PLA2 and metabolic syndrome in females was observed, having a critical threshold. These findings indicate potential of Lp-PLA2 being marker of detecting and preventing MetS in females, offering essential insights for healthcare experts and decision – makers in creating target - specific prevention and management plans for metabolic syndrome.

The research examined significance of Lp-PLA2 in indicating MetS across different age groups. Participants were divided by age to assess MetS risk. Results confirmed an important relationship among total cholesterol, LDL, and levels of Lp-PLA2, regardless of age, indicating a simultaneous presence of LDL and Lp-PLA2 in blood and strong link between LDL and total cholesterol levels. These findings are steady with findings of Huang et al., which also identified a significant connection between LDL and Lp-PLA2 in patients of acute coronary syndrome or those with post – recovery LDL levels, suggesting that LDL might be a crucial factor in determining serum Lp-PLA2 levels[8].

Beyond total cholesterol and LDL, additional parameters of lipid including TG and HDL-C showed noteworthy relationship between levels of Lp-PLA2. These components are thought to originate from fat tissue. Evidence for this link was found in studies demonstrating that atorvastatin reduced mass of Lp-PLA2 in patients of coronary heart disease[9–11]. Moreover, our research revealed an important relationship among ration of TG/HDL and Lp-PLA2 levels. Elevated TG/HDL ratios have been linked with coronary disease, insulin resistance, and atherosclerosis in other studies[12,13].

Additionally, our research noted a significant linear correlation between waist circumference, a critical MetS diagnostic criterion, and Lp-PLA2 levels. This is favored by Silva et al. that also found a positive association among levels of Lp-PLA2 and waist circumference in teenagers[14]. A

similar link in adults suggests its relevance across different age groups. Our study further identified a significant relationship between the Lp-PLA2 and WHtR by gender, with WHtR known as the predictor marker for coronary diseases and an obesity – related marker for metabolic syndrome

Table 4: General Characteristics of Participants (n=549)

Variables	Male	Female	Total	p-value
Age (years)	42.78 ± 6.88	43.87 ± 7.01	43.98 ± 6.98	<0.001
BMI (kg/m^2)	24.19 ± 3.98	23.85 ± 3.81	24.15 ± 3.53	<0.001
Waist circumference (cm)	88.42 ± 8.35	79.23 ± 8.11	82.44 ± 8.59	<0.001
Waist-to-height ratio	0.51 ± 0.04	0.49 ± 0.04	0.50 ± 0.04	<0.001
SBP (mmHg)	125.32 ± 16.19	115.32 ± 17.45	121.39 ± 18.21	<0.001
DBP (mmHg)	79.22 ± 12.01	69.31 ± 11.93	75.87 ± 12.09	<0.001
MAP (mmHg)	94.89 ± 12.34	84.41 ± 12.98	88.78 ± 13.24	<0.001
Fasting glucose (mmol/L)	5.40 ± 1.41	4.99 ± 1.01	5.19 ± 1.29	<0.001
TC (mmol/L)	5.22 ± 1.01	4.97 ± 0.97	5.15 ± 0.99	<0.001
TG (mmol/L)	1.91 ± 1.58	1.21 ± 1.01	1.66 ± 1.51	<0.001
LDL-C (mmol/L)	3.61 ± 0.92	3.29 ± 0.98	3.39 ± 1.01	<0.001
HCL-C (mmol/L)	1.28 ± 0.22	1.51 ± 0.29	1.43 ± 1.59	<0.001
TG/HDL-C	1.79 ± 2.19	0.91 ± 1.23	1.39 ± 1.79	<0.001
Lp-PLA2 (IU/L)	615.87 ± 155.70	541.81 ± 149.91	592.41 ± 152.84	<0.001
Diabetes (in %)	79	30	48	<0.001
Metabolic syndrome (in %)	65	58	21	<0.001

BMI, body mass index; SBP, systolic blood pressure; DPB, diastolic blood pressure; MAP, mean arterial pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; Lp-PLA2, lipoprotein-related phospholipase A2; TC, total cholesterol

Table 5: Pearson Correlation between Lp-LPA2 and Risk Factors of Metabolic Syndrome (n=549)

Variables	Male		Female	
	r	*p-value*	*r*	*p-value*
Age (years)	0.03	0.24	0.06	0.003
BMI (kg/m^2)	0.06	<0.001	0.05	0.02
Waist circumference (cm)	0.13	<0.001	0.07	0.002
Waist-to-height ratio	0.11	<0.001	0.08	0.001
SBP (mmHg)	0.04	0.02	0.03	0.23
DBP (mmHg)	0.05	0.01	0.04	0.25
MAP (mmHg)	0.07	0.02	0.04	0.24
Fasting glucose (mmol/L)	0.04	0.16	0.08	0.01
TC (mmol/L)	0.40	<0.001	0.33	<0.001
TG (mmol/L)	0.06	0.02	0.08	0.002
LDL-C (mmol/L)	0.46	<0.001	0.38	<0.001
HCL-C (in mmol/L)	-0.09	<0.001	-0.05	0.04
TG/HDL-C	0.05	0.04	0.05	0.01

Table 6: Metabolic and Clinical Characteristics of Patients according to Lp-PLA2 (n=549)

Variables	Lp-PLA2 (in IU/L)			p-value
Male	**Tertile 1**	**Tertile 2**	**Tertile 3**	
Age (years)	44.32 ± 6.98	44.81 ± 7.01	44.51 ± 6.92	0.08
BMI (kg/m^2)	25.42 ± 3.87	25.85 ± 3.48	27.64 ± 3.19	<0.002
Waist-to-height ratio	0.53 ± 0.04	0.52 ± 0.04	0.55 ± 0.05	<0.001
MAP (mmHg)	94.22 ± 12.59	94.87 ± 12.88	95.52 ± 12.88	0.15
Fasting glucose (mmol/L)	5.89 ± 1.87	5.72 ± 1.81	5.48 ± 1.58	0.07
TC (mmol/L)	5.04 ± 0.91	5.57 ± 1.01	6.45 ± 1.02	<0.001
TG (mmol/L)	1.92 ± 1.51	1.88 ± 1.61	2.11 ± 1.84	0.02
LDL-C (mmol/L)	3.87 ± 0.97	4.09 ± 0.87	4.87 ± 1.02	<0.001
HCL-C (mmol/L)	1.38 ± 0.41	1.31 ± 0.33	1.22 ± 0.29	<0.001
TG/HDL-C	1.78 ± 1.98	1.71 ± 1.91	2.01 ± 2.31	0.02
Females				
Age (years)	44.12 ± 6.95	45.31 ± 6.81	37.13 ± 6.88	<0.001
BMI (kg/m^2)	23.21 ± 2.81	23.81 ± 3.11	24.21 ± 3.42	0.02
Waist-to-height ratio	0.51 ± 0.04	0.51 ± 0.04	0.53 ± 0.05	<0.001
MAP (mmHg)	84.21 ± 12.91	85.42 ± 13.19	85.71 ± 13.28	0.07
Fasting glucose (mmol/L)	5.01 ± 0.78	5.18 ± 1.01	5.32 ± 1.18	0.002
TC (mmol/L)	4.81 ± 0.94	5.12 ± 0.77	6.81 ± 1.02	<0.001
TG (mmol/L)	1.12 ± 0.89	1.25 ± 0.91	1.49 ± 1.12	<0.001
LDL-C (mmol/L)	2.92 ± 0.82	3.29 ± 0.66	3.91 ± 0.91	<0.001
HCL-C (mmol/L)	1.62 ± 0.51	1.68 ± 0.55	1.47 ± 0.39	0.04
TG/HDL-C	0.98 ± 0.95	1.02 ± 0.98	1.14 ± 1.28	0.003

Table 7: Analysis of Logistic Regression of Lp-PLA2 and Metabolic Syndrome (n=549)

Variables	Crude OR (CI 95%)	p-value	Adjusted OR (CI 95%)	p-value
Male	1.00 (1.000-1.001)	0.03	1.00 (1.000-1.001)	0.03
Female	1.00 (1.000-1.002)	0.001	1.00 (1.000-1.002)	0.01

Table 8: Threshold Value and Predictive Capability for Parameters of Metabolic Syndrome (n=549)

Variables	AUC	CI (95%)	Cut-off Point (according to Youden's Index)	Sensitivity (%)	Specificity (%)
Male					
TG/HDL-C	0.85	(0.83-0.89)	1.36	0.87	0.72
WHR	0.82	(0.83-0.87)	0.54	0.85	0.71
Lp-PLA2	0.55	(0.51-0.57)	691.81	0.39	0.70
Female					
TG/HDL-C	0.94	(0.90-0.95)	1.02	0.88	0.89
WHR	0.86	(0.82-0.87)	0.47	0.90	0.69
Lp-PLA2	0.61	(0.56-0.67)	631.48	0.36	0.81

and hypertension and, ultimately supporting relationship among metabolic syndrome and Lp-PLA2.

The study also explored the role of Lp-PLA2 being a MetS biomarker among genders. Recent research involving diabetic participants underscored the effect of obesity, blood pressure, and, lipid profiles on levels of Lp-PLA2, revealing gender–specific differences[15,16]. This corroborates our findings, suggesting the utility of Lp-PLA2 being a predictor marker of MetS in Asian demographic. Further studies indicate that Lp-PLA2 may contribute to resistance of insulin and the onset of diabetes type 2, likely due to the inflammatory response from breakdown of Lp-PLA2 for oxidized phospholipids, potentially leading to resistance of insulin and dysfunction of pancreatic β-cell[17,18].

The impact of estrogen, particularly 17β-estradiol (E2) on Lp-PLA2 activity is noteworthy. E2 enhances endothelial cell repair and reduces inflammation. Its role in modulating lipid profile of liver and prevention of non-alcoholic fatty liver disease (NAFLD)/Steatohepatiis is essential. Lower levels of estrogen in men and postmenopausal women might elevate the risk of NAFLD/steatohepatitis because of compromised assembly of lipid and its secretion in liver.[19] Understanding these gender differences is key to comprehending lipid profile and MetS progression.

Our analyses underscore the importance of gender in considering Lp-PLA2 being a biomarker for metabolic syndrome. The research revealed a more robust relationship among MetS and levels of Lp-PLA2 in women. This highlights the need to factor in gender in diagnosing and managing MetS.

While our study benefits from significant results, it has limitations. Its cross – sectional nature precludes establishing causality, and sample derived from routine health checks may not accurately represent the broader population. Furthermore, personal data gathered through questionnaires could miss certain medical histories, and socio-economic factors were not accounted for. The study assessed mass of Lp-PLA2 rather than its functionality, warranting further investigation to fully understand relationship between levels of Lp-PLA2 and metabolic syndrome.

Conclusion

The findings of this investigation indicates an essential link among Lp-PLA2 and numerous indicators of metabolic development risk, highlighting its importance as independent predictor of metabolic syndrome, particularly in female population. Our results argument to probability of Lp-PLA2 as an effective tool for recognizing individual at risk for development of metabolic syndrome, by specific emphasis on its impact among women. It is essential to conduct further studies to comprehensively understand diagnostic and treatment possibilities for Lp-PLA2 in the context of metabolic syndrome.

References

1. Huang F, Wang K, Shen J. Lipoprotein-associated phospholipase A2: The story continues. Med Res Rev. 2020;40(1):79–134.
2. Brilakis ES, McConnell JP, Lennon RJ, Elesber AA, Meyer JG, Berger PB. Association of lipoprotein-associated phospholipase A2 levels with coronary artery disease risk factors, angiographic coronary artery disease, and major adverse events at follow-up. Eur Hear J [Internet]. 2005 Jan [cited 2024 Jan 20];26(2):137–44. Available from: https://pubmed.ncbi.nlm.nih.gov/15618069/
3. Sabatine MS, Morrow DA, O'Donoghue M, Jablonksi KA, Rice MM, Solomon S, et al. Prognostic utility of lipoprotein-associated phospholipase A2 for cardiovascular outcomes in patients with stable coronary artery disease. Arter Thromb Vasc Biol [Internet]. 2007 Nov [cited 2024 Jan 20];27(11):2463–9. Available from: https://pubmed.ncbi.nlm.nih.gov/17766330/
4. Silva IT, Mello APQ, Damasceno NRT. Antioxidant and inflammatory aspects of lipoprotein-associated phospholipase A_2 (Lp-PLA_2): a review. Lipids Heal Dis [Internet]. 2011 [cited 2024 Jan 20];10:170. Available from: https://pubmed.ncbi.nlm.nih.gov/21955667/
5. Dossena S, Marino A. Cellular Oxidative Stress. Antioxidants [Internet]. 2021 Mar 1 [cited 2024 Jan 20];10(3):399. Available from: /pmc/articles/PMC7998990/
6. Park JH, Moon JH, Kim HJ, Kong MH, Oh YH. Sedentary Lifestyle: Overview of Updated Evidence of Potential Health Risks. Korean J Fam Med [Internet]. 2020 Nov 1 [cited 2024 Jan 20];41(6):365–373. Available from: /pmc/articles/PMC7700832/
7. Fahed G, Aoun L, Zerdan MB, Allam S, Zerdan MB, Bouferraa Y, et al. Metabolic Syndrome: Updates on Pathophysiology and Management in 2021. Int J Mol Sci2. 2022;23(2):786.
8. Huang Y, Wu Y, Yang Y, Li W, Lu J, Hu Y. Lipoprotein-associated phospholipase A2 and oxidized low-density lipoprotein in young patients with acute coronary syndrome in China. Sci Rep [Internet]. 2017 Dec 1 [cited 2024 Jan 20];7(1):16092. Available from: https://pubmed.ncbi.nlm.nih.gov/29170433/
9. Li J, Wang H, Tian J, Chen B, Du F. Change in lipoprotein-associated phospholipase A2 and its association with cardiovascular outcomes in patients with acute coronary syndrome. Medicine (Baltimore) [Internet]. 2018 Jul 1 [cited 2024 Jan 20];97(28):e11517. Available from: /pmc/articles/PMC6076090/
10. Zheng D, Cai A, Xu R, Mai Z, Zhou Y, Zeng F, et al. Effects and potential mechanism of atorvastatin treatment on Lp-PLA2 in rats with dyslipidemia. Arch Med Sci [Internet]. 2018 [cited 2024 Jan 20];14(3):629–634. Available from: /pmc/articles/PMC5949919/
11. Thompson A, Gao P, Orfei L, Watson S, Di Angelantonio E, Kaptoge S, et al. Lipoprotein-associated phospholipase A2 and risk of coronary disease, stroke, and mortality: collaborative analysis of 32 prospective studies. Lancet [Internet]. 2010 May 5 [cited 2024 Jan 20];375(9725):1536–1544. Available from: /pmc/articles/PMC2864403/
12. Kosmas CE, Polanco SR, Bousvarou MD, Papakonstantinou EJ, Genao EP, Guzman E, et al. The Triglyceride/High-Density Lipoprotein Cholesterol (TG/HDL-C) Ratio as a Risk Marker for Metabolic Syndrome and Cardiovascular Disease. Diagnostics (Basel). 2023;13(5):929.
13. Caselli C, De Caterina R, Smit JM, Campolo J, El Mahdiui M, Ragusa R, et al. Triglycerides and low HDL cholesterol predict coronary heart disease risk in patients with stable angina. Sci Rep [Internet]. 2021 Oct 20 [cited 2024 Jan 20];11(1):1–12. Available from: https://www.nature.com/articles/s41598-021-00020-3
14. Da Silva IT, De Souza Timm A, Damasceno NRT. Influence of obesity and cardiometabolic makers on lipoprotein-associated phospholipase A2 (Lp-PLA2) activity in adolescents: the healthy young cross-sectional study. Lipid Heal Dis. 2013;12(1):1–10.
15. Li P, Chen K, Nie Y, Guo LL, Wang H Bin, Wang SS, et al. Association of obesity with

glucose, blood pressure, and lipid goals attainment in patients with concomitant diabetes and hypertension. Curr Med Res Opin [Internet]. 2015 [cited 2024 Jan 20];31(9):1623–31. Available from: https://pubmed.ncbi.nlm.nih.gov/26051230/

16. Kurniawan LB, Rampo H, Soraya GV, Adnan E, Esa T, Widaningsih Y, et al. Effect of obesity, glucose control, lipid profiles, and blood pressure on Lp-PLA2 levels in type 2 diabetes mellitus patients. Obes Med. 2021 Mar 1;22:100318.
17. Nelson TL, Biggs ML, Kizer JR, Cushman M, Hokanson JE, Furberg CD, et al. Lipoprotein-associated phospholipase A2 (Lp-PLA2) and future risk of type 2 diabetes: results from the Cardiovascular Health Study. J Clin Endocrinol Metab [Internet]. 2012 May [cited 2024 Jan 20];97(5):1695–701. Available from: https://pubmed.ncbi.nlm.nih.gov/22399516/
18. Wang GH, Jin J, Liu YQ, Yang FY, Shi D, Zhang Y, et al. The changes of Lp-PLA2 in patients with gestational diabetes and its clinical significance. Medicine (Baltimore) [Internet]. 2021 Jul 30 [cited 2024 Jan 20];100(30):E26786. Available from: https://journals.lww.com/md-journal/fulltext/2021/07300/the_changes_of_lp_pla2_in_patients_with.50.aspx
19. Cheng H, Huang H, Guo Z, Chang Y, Li Z. Role of prostaglandin E2 in tissue repair and regeneration. Theranostics [Internet]. 2021 [cited 2024 Jan 20];11(18):8836–8854. Available from: /pmc/articles/PMC8419039/