Open Access
Full Length Article

ORIGINAL ARTICLE

Comparison of Fasting Plasma Glucose, Lipid Profile and Small Dense Low Density Lipoprotein in Severe Persistent Asthmatic and Non-Asthmatic Adults

Haji Muhammad Rashid[1,*], Nadia Awan[1], Hiza Hassan[2], Anjum Rashid[3], Rabia Arshad[3], Saffora Shoukat[3]

[1]Department of Chemical Pathology, University of Health Sciences, Lahore, Pakistan.
[2]Department of Medical Lab Technology, University of Haripur, KPK, Pakistan.
[3]Shikh Zaid Hospital, Lahore, Pakistan.

ABSTRACT

Background: The most effective and commonly used control therapy for asthma is oral or parenteral corticosteroids, which are quite effective. But at the same time, they are considered notorious for their side effects like contributing to increasing rates of related metabolic disorders for eg: obesity and Type 2 diabetes. Studies of blood glucose and lipid profiles in relation to severe persistent asthma are still a few, and the results are ambiguous.

Objectives: The aim of current study was to evaluate the changes in Fasting Plasma Glucose (FPG), Lipid profile (LP) and Small Dense Lipoprotein Cholesterol (Sd-LDL-C) in Severe Persistent Asthmatic (SPA) patients in comparison with non-asthmatic adults, and their correlations with absolute eosinophil count.

Methodology: This study was a cross sectional comparative research conducted at Medsol Clinical Lab, Blue Area, Islamabad. In this study, 40 pre-diagnosed SPA and 40 non-asthmatic adults were enrolled. Blood Absolute Eosinophil Count (AEC) was performed on haematology analyser (Mindray BC 50), FPG and Lipid Profile were measured by commercially available kits of spin react on Microlab 300, and Sd-LDL-C were measured by precipitating lipoproteins using heparin-$MnCl_2$ solution and measuring Sd-LDL-C from supernatant by spectrophotometric method in SPA and non-asthmatic adults. Data was analyzed by SPSS 20.2.

Results: Pair-wise comparison between SPA and non-asthmatic group was performed by two sample t-test. In SPA group, FPG (95 ± 8mg/dl), Triglycerides (162 ± 14mg/dl), LDL (97 ± 10mg/dl) and Sd-LDL-C (48 ± 4mg/dl) were significantly higher ($p < 0.05$) than non-asthmatic adults, while HLD in SPA (38 ± 4.4mg/dl) was significantly lower than non-asthmatic adults (42 ± 3.9mg/dl). We also observed strong positive association of FPG (0.54), Triglycerides (0.38) LDL (0.23) and Sd-LDL-C (0.60) with AEC of SPA group and strong negative correlation for HDL (0.50) and AEC in SPA.

Conclusion: Dyslipidaemia, hyperglycaemia and elevated levels of Sd-LDL-C are associated complication of severe persistent asthma and high levels of Sd-LDL-C in severe persistent asthma are a potential risk factor to induce atherosclerosis.

Keywords	*Address of Correspondence	Article info.
Asthma, Glucose, Lipid Profile, Respiratory syndrome, Small Dense-LDL, Cholestrol.	*4849487@gmail.com*	*Received: March 10, 2021* *Accepted: March 30, 2021*

Cite this article *Rashid HM, Awan N, Hassan H, Rashid A, Arshad R, Shoukat S. Comparison of Fasting Plasma Glucose, Lipid Profile and Small Dense Low Density Lipoprotein in Severe Persistent Asthmatic and Non-Asthmatic Adults. RADS J Biol Res Appl Sci. 2021; 12(2):128-134.*

INTRODUCTION

Asthma is an inflammatory respiratory syndrome that affects ~350 million people around the world every year[1]. Asthma is characterized by restricted airflow, airway inflammation, and airway hyper responsiveness, including symptoms like shortness of breath, wheezing, and cough[2]. On the basis of severity, it is classified in 4 classes (intermittent, mild persistent, moderate persistent and severe persistent) by National Asthma Education and Prevention Program (NAEPP), created on the individual's symptoms and spirometer data. Asthma prevalence has been increased by 50% every decade, and almost 100 million new asthma cases will be added to this asthmatic population till 2025[3].

As asthma is a chronic inflammatory condition of airways, it induces the production of pro-inflammatory cytokines and oxidative stress which results in osteoporosis, bruising, metabolic abnormalities and psychiatric disturbances[4]. Moreover, the most effective and commonly used controller therapy for asthma is an inhaled corticosteroid which inhibits the production of pro-inflammatory cytokines and reduces bronchial reactivity and frequency of exacerbations. Oral and parenteral corticosteroids are effective but are notorious for their side effects like contributing to increasing rates of related metabolic disorders, such as obesity and Type 2 diabetes[5].

Asthma induces a number of metabolic variations, but the variations in blood glucose and lipid profile are with conflicting results in various studies[6,7]. Similarly, the variations in Small Dense Low Density lipoprotein (Sd-LDL) which is the subclasses of Low Density Lipoprotein (LDL) is also controversial[6, 8]. Keeping in mind the correlation with various blood profile factors, we designed the current study to compare fasting glucose, lipid profile and Sd-LDL levels in pre-diagnosed Severe Persistent Asthmatic (SPA) and non-asthmatic adults, and their association with blood eosinophil count in SPA patients.

MATERIAL AND METHODS

It was a cross-sectional comparative study conducted at the Medsole Clinical Lab, Blue Area, Islamabad from Aug 2019 to Feb 2020. Ethical approval for the study was obtained from Ethical Board of Pakistan Institute of Medical Sciences (PIMS), Islamabad. We enrolled 40 pre-diagnosed severe persistent asthmatic and 40 non-asthmatic adults in this study. Fasting venous blood samples were collected in EDTA and plane tubes from SPA patients and non-asthmatic adults, after obtaining their consent. Blood Absolute Eosinophil Count (AEC) were measured on Mindray haematology analyser (BC50), FPG and lipid profile were measured on Mindray (240Pro) auto chemistry analyser, and Sd-LDL-C was were measured by spectrophotometric method[9] on Micro Lab 300. The data was entered and analyzed by using SPSS 20.0 to calculate frequencies, mean, and standard deviations. The pair-wise comparison of the parameters was carried out by two sample t-test and correlations were calculated by Pearson's correlation coefficient.

RESULTS

In the present study, 40 Severe Persistent Asthmatic (SPA) patients and 40 non-asthmatic adults were investigated. Out of 40 SPA patients, 24 (60%) were females and 16 (40%) were males; and amongst them 16% were active smokers and 9% were ex-smokers (smokers or ex-smokers 25%) however, 50% were from low socioeconomic class (Table **1**).

Pair-wise comparison was carried out with two sample t-test for all tested parameters between SPA patients and non-asthmatic group. AEC, FPG, Trig, LDL and Sd-LDL-C levels were significantly higher in SPA than non-asthmatic group. HDL levels were significantly lower in SPA patients as compared to non-asthmatic adults and there were no significant difference observed in Total Cholesterol of both groups (Table **2**).

Pearson Correlation coefficient was calculated for FPG, Trig, Total-Cholesterol, HDL, LDL and Sd LDL-C against absolute eosinophil count in SPA group. We observed a good positive association of FBG, Trig and Sd-LDL-C with absolute eosinophil count and strong negative association of HDL was observed with absolute eosinophil count in SPA group shown in (Table **3**).

Table 1. Demographic Characteristics of Severe Persistent Asthmatic Patients and Non-Asthmatic Adults Enrolled in the Study.

Variables	SPA (n = 40)	Non-Asthmatic Adults (n = 40)
Gender		
Males	16 (40%)	18 (45%)
Females	24 (60%)	22 (55%)
Age (Range) years	46.8 ± 7.2 (35-62)	46.6 ± 5.6 (36-56)
Smoking Status		
Non-Smokers	34 (85%)	12 (30%)
Smokers or Ex-Smokers	6 (15%)	28 (70%)
Socioeconomic Status		
Rich	6 (15%)	8 (20%)
Medium	14 (35%)	16 (40%)
Low	20 (50%)	16 (40%)

Table 2. Compression of Absolute Eosinophil Count, Lipid Profile and Small Dense LDL-C between Severe Persistent Asthmatic and Non-asthmatic Adults.

Variables	SPA (n = 40) (Mean ± SD)	Non-Asthmatic (n = 40) (Mean ± SD)	p-value
AEC (cells/µl)	546 ± 411	125 ± 64	<0.001
Fasting Blood Glucose (mg/dl)	95 ± 8	84 ± 7	<0.001
Triglycerides (mg/dl)	162 ± 14	154 ±18	0.029
Total Cholesterol (mg/dl)	168 ± 13	163 ± 16	0.12
HDL (mg/dl)	38 ± 4.4	42 ± 3.9	<0.001
LDL (mg/dl)	97 ± 10	95 ± 8	<0.001
Sd LDL-C (mg/dl)	48 ± 4	44 ± 3.5	<0.001

Table 3. Correlation FPG, Lipid profile and Sd-LDL-C with Absolute Eosinophil Count in Severe Persistent Asthmatic Patients.

Variables	Correlation Coefficient (Absolute Eosinophil Count)
FBG	0.54
Trig	0.38
T-Chol	0.10
HDL	0.50
LDL	0.23
Sd-LDL-C	0.60

Here, the negative correlation of FBG, Trig, T-Chol, HDL, LDL and Sd-LDL-C with AEC in SPA patients indicates that HDL levels are decreased with the increase in AEC, while positive correlation shows that FBG, Trig, LDL and Sd-LDL-C levels are increased with the increase of AEC.

DISCUSSION

Dyslipidemia, hyperglycemia and high levels of Sd-LDL-C are common risk factor for atherosclerosis. Asthma is an inflammatory lung disease and it is associated with metabolic variations. In present study, we tried to elaborate the variations in lipid profile, glucose and Sd-LDL-C in severe persistent asthmatic adults.

For this, we enrolled physician-diagnosed 40 SPA patients aged 35-62 years and 40 non-asthmatic adults aged 36-56 years (Table **1**). There are gender differences in the prevalence of asthma. Compared with adults men, adult women have a higher prevalence of asthma due to hormonal difference in both genders; specially low level of testosteron and high level of estrogen make the women more prone for getting Th-2 type asthma[10, 11]. Since, the females having SPA were at higher ratio than the males, therefeore, out of all the participants in our stdy, there were 16 (40%) males and 24 (60%) females in SPA group. However, the role of obesity, sex hormones and other gender-specific factors is yet unclear and may be responsible for such differences[11].

In the present study, the mean age of SPA patients was 46.8 ± 7.2 and range was (35-62 years). Throughout the rest of life after the age of 20, lung function is suppose to decline, and this decline rate is affected by air pollution, cigarette smoke exposure, urbanization and climate change. Aging is also associated with the increased chest wall stiffness, decreased lung elastic recoil and respiratory muscle weakness[12]. Here, we found that 50% of SPA patients come from low Socioeconomic Status (SES) and these findings are also consistent with previous studies, which concluded that the decrease of SES is linked with the increase in the incidence of asthma and asthma severity[13, 14].

Smoking can have harmful effects on different clinical aspects of asthma, such as accelerated lung function decline, weakened symptom control and weakened response to treatment[15]. Percentage of smokers with SPA was higher (20% current smokers, 24% ex-smokers and 2% electric ciggrate-smokers) than the general population in some of the countries[16]. But in our study, we observed that 15% SPA were current smokers or ex-smokers. The reason behind this controversial findings may be the higher ratio of females patients in our study due to consecutive sampling of asthmatic patients, and frequency of females smokers in Pakistan (2.8%)[17] is less than the world wide percentage of females smokers i.e. 4.3-23%[18]. Kitchen smoking or passive smoking have also significant role in the development of asthma[19], however these factors were not investigated in our study.

The role of eosinophils in asthma has been extensively studied. Increased numbers of eosinophils exist in the airways of most, but not all, persons who have asthma[20]. In our study we found significantly higher AEC (546 ± 411 cells/µl) in SPA than non-asthmatic adults (125 ± 64 cell/µl) p value < 0.001. Our results are consistent with the findings of Badar *et al*., 2010, where the absolute count of eosinophils found in SPA was 684.00 ± 75.58 cells/µl[21]. A study conducted in India in 2019 also reported similar findings regarding AEC (405 ± 83.16 cells/µl) in severe asthma[22].

We observed clinically significant higher fasting blood glucose levels in SPA groups and similar findings were reported by Koskela *et al.,* 2013, in which they proposed that medication used to control the asthma may cause hyperglycaemia[23]. This hyperglycemic effect have also been reported in different other studies on asthmatic patients[4, 24].

Triglycerides and LDL levels were higher and HDL levels were significantly lower in SPA group than non-asthmatic adults, while there was no significant difference in the levels of T-Cholesterol of both groups in present study. Our findings for high LDL and Triglyceride are in line with the findings of Ko *et al*., and Peng & Huang[6, 25]. T-cholesterol levels have no difference in both groups of our study and it is in accordance with the finding of Fang *et al.,* 2016[24]. Several studies have also reported high T-Cholesterol in SPA group than normal control while Low HDL levels were reported by various studies in asthmatic adults similar to our findings[26-28]. Sd-LDL-C is a sub-class of LDL and it is potential atherogenic cholesterol[29]. In SPA patients, we observed significantly raised levels of Sd-LDL-C and similar findings were reported by Scichilone *et al.,* 2013 periously in his study[8].

At present, the relationship between dyslipidemia and asthma or other allergic diseases is unclear. There are still some possible mechanisms; one of them may be the inflammatory link between asthma and dyslipidemia[30]. In

addition, dyslipidemia may also enhance eosinophil inflammation, which is related to other conditions in the pathophysiology of asthma, such as excessive mucus secretion, bronchial hyperresponsiveness, and subepithelial fibrosis[31].

We observed a strong positive association of LDL and Sd LDL-C with AEC and strong negative association of HDL with AEC. Patients with decreased lung function have considerably high absolute eosinophil count[32]. Association of Triglycerides and HDL have been studied by Barochia *et al.,* 2017, and they concluded a positive correlation between HDL and AEC of SPA group. Eosinophilic inflammation in asthma is associated with variation of Triglyceride and HDL in asthmatic adults[33]. Sd-LDL-C association (r2=0.60) with eosinophilic inflammatory marker is reported for the first time in present study and further research work is required to validate this association.

CONCLUSION

From our study, it is concluded that dyslipidaemia, hyperglycaemia and elevated levels of Sd-LDL-C are associated complications of severe persistent asthma, and high levels of Sd-LDL-C in severe persistent asthma are a potential risk factor to induce atherosclerosis.

CONFLICTS OF INTEREST

None.

FUNDING SOURCE

Technical support and required instruments were provided by CEO Medsol clinical Lab, and other expenses were self-arranged by the authors.

ACKNOWLEDGMENTS

We are thankful to CEO of Medsol clinical Lab to provide testing facility and technical support.

LIST OF ABBREVIATIONS

AEC	Absolute eosinophil count
FBG	Fasting Blood Glucose
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
NAEPP	National Asthma Education and Prevention Program
Sd-LDL-C	Small dense Low Density Lipoprotein Cholesterol
SES	Socioeconomic Status
SPA	Severe persistent asthma

REFERENCES

1. Branco ACCC, Sato MN, Alberca RW. The possible dual role of the ACE2 receptor in asthma and coronavirus (SARS-CoV2) infection. Front Cell Infect Micro. 2020; 10-8.
2. Di Genova L, Penta L, Biscarini A, Di Cara G, Esposito S. Children with obesity and asthma: Which are the best options for their management? Nut. 2018; 10(11):1634-9.
3. Rashid HM, Khan M, Jamal M, Awan N, Waseem M. Association of serum sphingosine-1-phosphate with forced expiratory volume and absolute eosinophil count in asthma patients. Rawal Med J. 2020; 45(4):771-4.
4. Torres RM, Souza MDS, Coelho ACC, de Mello LM, Souza-Machado C. Association between asthma and type 2 Diabetes mellitus: Mechanisms and impact on asthma control-A literature review. Canadian Resp J. 2021; 1-13.
5. Dey L, Basu K, Sinha A, Maiti A, Chakraborty S. Effect of high dose inhaled steroids on blood glucose level and lipid profile in diabetic and non-diabetic subjects with asthma. Indian J Basic App Med Res. 2015; 4(4):231-8.
6. Scaduto F, Giglio RV, Benfante A, Nikolic D, Montalto G, Rizzo M, *et al*. Serum lipoproteins are not associated with the severity of asthma. Pulm Pharm Therap. 2018; 50:57-61.
7. Fenger R, Gonzalez-Quintela A, Linneberg A, Husemoen L, Thuesen B, Aadahl M, *et al*. The relationship of serum triglycerides, serum HDL, and obesity to the risk of wheezing in 85,555 adults. Resp Med. 2013; 107(6):816-24.
8. Scichilone N, Rizzo M, Benfante A, Catania R, Giglio RV, Nikolic D, *et al*. Serum low density lipoprotein subclasses in asthma. Resp Med. 2013; 107(12):1866-72.

9. Rashid HM, Hassan H, Khan M, Khan J, Khan H. Small dense low-density lipoprotein as risk factor for atherosclerosis in Type 2 Diabetes mellitus. RADS J Bio Res App Sci. 2020; 11(1):15-8.
10. Fuseini H, Newcomb DC. Mechanisms driving gender differences in asthma. Curr Allergy Asthma Rep. 2017; 17(3):1-9.
11. Tantisira K, Colvin R, Tonascia J, Strunk R, Weiss S, Fuhlbrigge A. Airway responsiveness in mild-to-moderate childhood asthma: Sex influence on the natural history. J Asthma. 2009; 46(6):632-9.
12. Zein JG, Dweik RA, Comhair SA, Bleecker ER, Moore WC, Peters SP, *et al*. Asthma is more severe in older adults. PLoS One. 2015; 10(7):e0133490.
13. Bråbäck L, Hjern A, Rasmussen F. Social class in asthma and allergic rhinitis: A national cohort study over three decades. Europ Resp J. 2005; 26(6):1064-8.
14. Li X, Sundquist J, Sundquist K. Socioeconomic and occupational groups and risk of asthma in Sweden. Occup Med. 2008; 58(3):161-8.
15. Boulet L-P, Boulay M-È, Dérival J-L, Milot J, Lepage J, Bilodeau L, *et al*. Asthma-COPD overlap phenotypes and smoking: comparative features of asthma in smoking or non-smoking patients with an incomplete reversibility of airway obstruction. COPD: J Chronic Obst Pulmon Dis. 2018; 15(2):130-8.
16. Katsaounou P, Odemyr M, Spranger O, Lindberg A, Hyland ME, Gasser M, *et al*. Smoking and severe persistent asthma. Eur Resp Soc; 2018; 1-7.
17. Saqib MAN, Rafique I, Qureshi H, Munir MA, Bashir R, Arif BW, *et al*. Burden of tobacco in Pakistan: Findings from global adult tobacco survey 2014. Nicot Tob Res. 2018; 20(9):1138-43.
18. Hitchman SC, Fong GT. Gender empowerment and female-to-male smoking prevalence ratios. Bulletin of the World Health Organization. 2011; 89:195-202.
19. Gautier C, Charpin D. Environmental triggers and avoidance in the management of asthma. J Asthma Allergy. 2017; 10:47-54.
20. Schleich FN, Zanella D, Stefanuto P-H, Bessonov K, Smolinska A, Dallinga JW, *et al*. Exhaled volatile organic compounds are able to discriminate between neutrophilic and eosinophilic asthma. American J Resp Crit Care Med. 2019; 200(4):444-53.
21. Badar A, Hussain MM, Saeed W, Aslam M. Correlation of eosinophil derived neurotoxin with airway resistance in asthmatics. JPMA. 2010; 60(2):97.
22. Lalrinpuia B, Naveen P. Study on absolute eoisinophil count correlation with severity of bronchial asthma. Int J Res Med Sci. 2019; 7:1229-32.
23. Koskela HO, Salonen PH, Niskanen L. Hyperglycaemia during exacerbations of asthma and chronic obstructive pulmonary disease. Clin Resp J. 2013; 7(4):382-9.
24. Mobaireek KF, Alshehri A, Alsadoun A, Alasmari A, Alashhab A, Alrumaih M, *et al*. Hyperglycemia in children hospitalized with acute asthma. Prog Med Res. Springer; 2018; 19-25.
25. Peng J, Huang Y. Meta-analysis of the association between asthma and serum levels of high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. Ann Allergy Asthma Immunol. 2017; 118(1):61-5.
26. Su X, Ren Y, Li M, Zhao X, Kong L, Kang J. Association between lipid profile and the prevalence of asthma: a meta-analysis and systemic review. Curr Med Rese Opin. 2018; 34(3):423-33.
27. Fang L-J, Huang C-S, Liu Y-C, Su Y-M, Wan K-S. The lipid profile in obese asthmatic children compared to non-obese asthmatic children. Allergologia Immunopathol. 2016; 44(4):346-50.
28. Ko SH, Jeong J, Baeg MK, Han KD, Kim HS, Yoon JS, *et al*. Lipid profiles in adolescents with and without asthma: Korea national health and nutrition examination survey data. Lipids Heal Dis. 2018; 17(1):1-7.
29. Liou L, Kaptoge S. Association of small, dense LDL-cholesterol concentration and lipoprotein particle characteristics with coronary heart disease: A systematic review and meta-analysis. PloS One. 2020; 15(11):e0241993.
30. Baumruker T, Csonga R, Pursch E, Pfeffer A, Urtz N, Sutton S, *et a*l. Activation of mast cells by incorporation of cholesterol into rafts. Int Immunol. 2003; 15(10):1207-18.
31. Pham T-H, Damera G, Newbold P, Ranade K. Reductions in eosinophil biomarkers by benralizumab in patients with asthma. Resp Med. 2016; 111:21-9.
32. Hancox RJ, Pavord ID, Sears MR. Associations between blood eosinophils and decline in lung function

among adults with and without asthma. Europ Resp J. 2018; 51(4).

33. Barochia AV, Gordon EM, Kaler M, Cuento RA, Theard P, Figueroa DM, *et al.* High density lipoproteins and type 2 inflammatory biomarkers are negatively correlated in atopic asthmatics. J Lip Res. 2017; 58(8):1713-21.