Predictive value of lipoprotein a (Lp-a) as a screening test for dyslipidemia & obesity

Abstract

Objectives: Examining the significance of performing lipoprotein as a screening test for dyslipidaemia and cardiovascular risk factor and to find out the association of lipoprotein with the body mass index (BMI) and lipid profile.

Methods: A study was carried out at the Pak- Emirates Military Hospital and Army Medical College, Rawalpindi for a duration of 1 year. The ethical approval was obtained from the ethical review committee board of prior to conducting the study. The consent form was signed by the study participants after brief explanation of the study. A total of 60 participants were recruited for this study using the technique of non-probability convenience sampling. The demographic information of the study participants was collected at the time of the data collection. The age, height and weight of the study participants were recorded. The BMI and obesity levels were calculated. The serum samples collected from each of the study participants were analysed for the TC, TG, LDL-c, HDL-c and Lp (a) levels. The independent variable was Lipoprotein. The dependent variables were TC, TG, LDL-c, HDL-c. The statistical analysis was performed using the SPSS (version 24.0). The descriptive statistics and the correlation analysis were done to check the correlation between the Lp (a), BMI and other parameters.

Results: The results of the study indicated that there was no correlation or significantly negative correlation between the Lp (a) levels and the other studied parameters such as LDL-c, HDL-c, TC, TG levels. In addition, the results also suggested that there was no impact or effects of the BMI levels with the Lp (a) levels and there was no correlation between the Lp (a) with the lipid profiles and BMI.

These results obtained in the present study also demonstrated that the BMI, TC, TG, LDL-c, HDL-c concentrations are neither sensitive nor specific for Lp (a) levels.

Conclusion: The results of the study concluded that Lp (a) has no correlation with BMI and lipid profile parameters such as TC, TG, HDL-c, LDL-c and BMI. Therefore, a separate test for Lp (a) should be done for monitoring and assessment of the individuals for cardiovascular risk.

Key words: Lipoprotein, screening test, dyslipidemia, obesity, cardiovascular diseases, total cholesterol, body mass index, triglycerides.

Introduction

Dyslipidemia is referred to as the condition in which there is the formation of an abnormal amount of lipids in the blood. Different lipid contents formed in the blood including triglycerides (TG), fats, phospholipids and cholesterol[1]. The condition of dyslipidemia is associated with the hyperlipidemias particularly in the developed countries. Hyperlipidemia is the formation of more quantity of lipids in the blood due to intake of food with more lipid contents and a poor lifestyle[2]. Dyslipidemia referred to both high or low contents of lipids such as cholesterol, fats and TG contents in the blood. The study indicated that the most common causes of dyslipidemia were found to be an abnormal lifestyle, poor eating habits, genetic disorders or the use of drugs[3]. The cardiovascular disorders are amongst the higher cause of mortality in both the developed as well as developing countries. Statistics showed that only in the United States, 655,000 deaths are caused annually due to cardiovascular diseases[4]. In China, 40 percent of the deaths were found due to heart diseases or stroke. The high formation of lipids and cholesterol in the blood results in the formation of blood clots that prevent the blood flow from the heart to the other parts of the body and from arteries and veins to the heart[5].

Dyslipidemia or hyperlipidemia was also noticed as one of the risk factors for obesity[6]. According to the definition of WHO for obesity, it is defined as the individuals with the BMI greater than 25 kg/m^2. It was reported that the main contributory causes of obesity include physical inactivity, genetics, overeating, intake of foods with high cholesterol and fats, medications, psychological issues etc[7]. The enhanced concentrations of serum TG were due to the elevated formation of *"Very low-density lipoprotein cholesterol (VLDL)"* and the reduced clearance of the contents of TG with high lipoproteins[8].

The lipoprotein is one of the biochemical compounds whose main function is related to the transportation of fat molecules in the water, plasma or other fluids of the body[9]. Lipoproteins comprises the complex compounds that contain the esters of cholesterol and TG with the compounds of free cholesterol, apolipoproteins and phospholipids that enhances the synthesis of lipoproteins and their functioning in the body. It aids in the migration of cholesterol molecules to other tissues and organs of the body[10, 11]. The research studies indicated that dyslipidemia is one of the forms of lipoproteins disorders that contributed to the high risk of cardiovascular issues[12].

The data showed that the levels of lipoproteins were observed high among the population of Asian countries. It was also observed that dyslipidemia observed as the strongest contributor of cardiovascular issues among the Asian population with the 49.2 percent population at high risk due to this issue[13]. The screening test for the lipoproteins is used to determine the level of lipoprotein (a) in the blood of the individuals. This test showed the level of protein and fats contents in the body that is used to transport the high-density cholesterol (HDL) along with LDL in the blood[14]. The individuals with the LDL-C levels greater than 2.59 mmol/l were referred to as hypercholesteraemic[15]. The research studies suggested that the lipoprotein test (Lp (a)) was important to check along with the other parameters of the lipid profile that used to determine risk for cardiovascular disorders[16]. There were

limited research studies carried out on this aspect to determine the importance of screening tests of Lp (a).

There is a lack of baseline data with regard to checking the significance of performing the screening test of Lp (a) in the local populations. Therefore, this study was designed to examine the importance of performing the Lp (a) test as one of the screening tests for checking the condition of dyslipidemia and obesity. The study was also conducted to find out the association of Lp (a) with the body mass index (BMI) and the lipid profile along with the assessment of the requirement to conduct the separate test of Lp-a to find out the cardiovascular risk for the individuals. The hypothesis of the study was "The BMI and the concentrations of total cholesterol (TC), TG, LDL, HDL cholesterol concentrations are neither sensitive nor specific for Lp (a) levels".

Research Methodology

After designing the research proposal and description of the study, ethical approval was obtained from the ethical review committee (ERC) of the Pak- Emirates Military Hospital and Army Medical College, Rawalpindi, Pakistan for a duration of 1 year. The study was carried out within regulation of *"Good clinical practices"* as according with the policies of the hospitals and research institutions. All the participants of the study were presented as anonymous[17]. The information of each of the study participants was presented with the ID-no that was assigned to each of the study participants. All the personal information collected at the time of the data collection was kept confidential. Both the written and informed consent was obtained from the study participants prior to conducting the study[18].

The research design of the study was cross-sectional and it was carried out in the Military hospital and Army medical college Rawalpindi, Pakistan. This design was

selected in the present study because it was found helpful in the previous studies to examine the burden of the disease or to determine the health needs of the studied population. The cross-sectional survey was documented to be useful for the planning and allocation of health resources in the studied population. The study design was descriptive and useful to evaluate and understand the particular diseases in the population to be studied[19].

A total of 60 participants was recruited in this research study. The sample size of the study participants was estimated using the WHO calculator. The non-probability convenience sampling technique was employed to recruit the study participants. The rationale for selecting this sampling technique was due to its convenience, rapid and cost-effectiveness[20]. The participants taking the drugs or the specific medication were excluded from the study. The blood serum samples of the studied participants were collected at the time of the sample collection. The collected samples were stored properly until further chemical analysis.

The age of the study participants ranged from 20 to 82 years old. The data about the height, weight and BMI of each of the study participants were measured and recorded at the time of the data collection. The BMI of the study participants was measured by following the protocol[21]. The height and weight of the studied participants were measured by using the protocol of the World health organisation (WHO). The information about the obesity levels was also collected from each of the study participants. The obesity level was determined using the information provided by WHO. The obesity level was determined using the BMI parameters in which the height and weight data were used to calculate the BMI.

The independent variable of this study was the parameter of Lp (a). The dependent variables were BMI, TC, TG, LDL-c, HDL-c. The sensitivity and specificity of BMI, TC, TG, LDL-c, and HDL-c concentrations were examined for the Lp (a) levels. The Lp (a) is the key independent variable, and the dependence of other variables on Lp

(a) was examined and tested as part of the lipid profile because according to the research studies, Lp (a) can be considered as an important parameter just like the other parameters of lipid profile, to check the risk for obesity and cardiovascular risk.

The chemical analysis was performed for the measurement of TC, TG, LDL-C, HDL-C. and Lp (a) levels by using the serum samples of the study participants. These Lp (a) analysis of the serum samples was performed by following the procedure proposed[22]. Besides, the TG measurement was performed by following the protocol[23]. The levels of TC, LDL-C, and HDL-C of the serum samples of the study participants were determined by using the procedures[24].

The statistical analysis was performed by using the software of *"Statistical Package of Social Sciences (SPSS)"*[25]. The normality tests were performed to check the normal distribution of the data. The descriptive statistics were done to calculate the mean and standard deviation values of age, weight and height of the study participants. The correlation analysis was performed to check the relationship of Lp (a) with the BMI and lipid profiles. The p values were considered significant at the level of 0.05.

Results

The study provided the information about the demographic information of the study participants which were analysed further. In addition, the biochemical analysis was also performed in which the Lp (a) levels were measured along with the parameters of the lipid profiles such as TC, TG, LDL and HDL parameters. Figure 1 explained the normality distribution graph of the collected and analysed data. The results of the normality test demonstrated that the data was not normal. The further analyses

provided detailed information about the Tp (a) and BMI, TC, TG, LDL and HDL parameters.

Table 1 and Table provided the information about the descriptive statistics and correlation analysis. The descriptive statistics provided comprehensive information about the average and standard deviation values of the analysed parameters such as age, height, weight, BMI, and other lipid profile parameters. This analyses provided the overall picture of the range obtained for these analysed and measured parameters. Table 1 provided the information about the descriptive statistics in which the minimum and maximum values along with mean and standard deviation of age, height, weight, BMI, Lp (a), TC, TG, HDL, LDL parameters were documented. The average age of the included study participants was 41±14 years. The average height and the standard deviation of all of the study participants were 5.45±0.32 m.

The average weight of the included studied participants was 68±14 kgs. In addition, the results of the study also showed that the measured BMI was 24±4 kg/m^2. The average value of TC among all the studied parameters was 5.1±1.41 (mmol/l). The results of this study further suggested that the levels of TG were 1.78±1.04 (mmol/l) in the serum levels of the study participants. Besides, it was noticed that the HDL level was 1.40±0.54 (mmol/l).

The serum samples obtained from the studied participants were also analysed for LDL parameter. It was observed that the average value of LDL was 2.52±0.94 (mmol/l). The Lp (a) levels were determined and the average levels of Lp (a) was 21.32±7.80 (mg/dl) in the serum samples of the participants. Furthermore, it was observed from the findings of the study that the average BMI level was 24±4 kg/m^2. The results also indicated that the obesity level was also not influenced by the Lp (a) levels.

Correlation analysis was performed to check the hypothesis of the study in which the Lp (a) test and their correlation between the BMI and other lipid profile

parameters were examined such as TD, TC, LDL and HDL. This correlation analysis confirmed the information about the relationship between the Lp (a) and the studied parameters. The results of Table 2 presented the information about the correlation between the Lp (a) levels, BMI and other parameters used to determine the lipid contents such as TC, TG, HDL and LDL. The findings of the study indicated that Lp (a) had a significantly negative correlation (r= -0.405; *p=0.001*) with the BMI. In addition, the results demonstrated the correlation of Lp (a) with the other lipid profile parameters such as TC, TG, HDL and LDL. It was observed that there was a non-significant negative correlation (r= -0.216; *p=0.097*) between the Lp (a) and TC parameter analysed in the serum samples of the studied participants. Furthermore, the results indicated that there was a significant negative correlation (r= -0.281; *p=0.030*) observed between the Lp (a) and TG levels.

The correlation was also examined between the Lp (a) and HDL levels along with the LDL levels. The results of the study showed that there was a non-significant smaller correlation (r= 0.200; *p=0.125*) between the Lp (a) levels and HDL levels. Furthermore, it was also deduced from the obtained results that there was also a non-significant negative correlation (r= -0.191; *p=0.144*) between the Lp (a) and LDL levels within the serum samples of the studied population. Overall, it was observed that Lp (a) levels had a negative significant correlation with the BMI and TG levels. On the other hand, Lp (a) levels had a non-significant negative correlation with the TC levels, HDL and LDL levels. The study further demonstrated that there was no effect of the measurement of Lp (a) tests in the determination of the BMI, LDL, HDL, TG and TC levels. Therefore, the hypothesis of the study was in agreement with the outcomes of the study that indicated there must be a separate test of Lp (a) carried out to examine the risk of obesity, dyslipidemia and cardiovascular issues. Because there was no or negative correlation exists between the Lp (a) and other lipid profile parameters.

Figure 2 explained the information about the sensitivity of the Tp (a) test along with the other studied parameters such as BMI, TG, HDL, LDL and TC levels. It was found from the results and from the findings of the study that the sensitivity levels between the Tp (a) and TC were 0.83. In addition, the sensitivity levels between the Tp (a) with the TG level was 0.61. Furthermore, the sensitivity level observed between the Tp (a) and HDL was 0.91. The results of the study also showed that the sensitivity level between the Lp (a) and the LDL was 0.63. The sensitivity level of BMI with the Lp (a) levels was 1. The sensitivity was measured to examine the influence of Lp (a) parameters with the other studied parameters of the lipid profile The findings of the study indicated that there was little sensitivity observed between the Lp (a) and the other studied parameters. This indicated that tether was no impact on the screening test of Lp (a) with the other parameters. This study provided information about the sensitivity of the measured and analysed parameters to explore the relationship and effect of the Lp (a) test in the determination of the risk of obesity and cardiovascular issues.

Discussion

Obesity and dyslipidaemia are observed to be linked with an increased risk of cardiovascular diseases that are attributed by decreased high-density lipoprotein (HDL) cholesterol and increased triglycerides [26]. Several pre-screening tests have been introduced and studied to identify the best possible parameters for the detection of high-risk patients. Recently, Lp (a) screening test has gained significant attention to measure the risk of cardiovascular among individuals. A study has been conducted and showed evidence that Lp (a) plays significant role in assessing the risk for cardiac disease [27]. Moreover, this study has further identified the limitations of different screening methods for assessing cardiovascular risk and suggested that new methods need to be used because of lack of accurate sensitivities and specificities of

previously developed screening methods. Recently, Lp (a) is observed to be an important parameter as others to determine the risk of diseases such as obesity and dyslipidaemia.

In the recent study, a correlation analysis technique has been used to determine the relation of lipoprotein (a) with other variables, including body mass index (BMI), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL) as well as low-density lipoprotein (LDL) for the detection of cardiovascular risk among an individual. Based on the findings of this study, it has been found that LP (a) has a relation with BMI i.e. p= 0.001. This however, depicted that lipoprotein (a) could not be used as a separate parameter to be tested for the evaluation of an individual with CVD risk. Similar results have been observed in a study in which it was shown that through logistic regression analysis that lipoprotein (a) and BMI have a significant relationship and used to predict CVD risk in children [28].

In addition to this, the relationship between Lp (a) and total cholesterol has been tested and the outcomes of the current study showed insignificant difference between both the parameters i.e. p= 0.097. Hence, this outcome showed evidence that lipoprotein (a) has no relation with TC and could be tested independent of TC for the evaluation of CVD risks among individuals. In correspondence to these findings, the results of a study has also showed insignificant difference between lipid profile and Lp (a) [29]. On the contrary to this, the outcomes of the present study has also tested the relationship between lipoprotein (a) and triglycerides (TG) and a significant association has been found between two parameters. Based on this outcome, it can be said that Lp (a) could not be measured separately without the computation of lipid profile. Comparatively, it has been determined in a research that the concentrations of Lp (a) in the blood correlated positively with TC and negatively with TG [30]. Furthermore, a study has been conducted previously which also showed minimal dependence of TG on Lp (a) [31].

The relationship between Lp (a) and high-density along with low-density lipoproteins (HDL and LDL) have been determined in the present study. As a result, insignificant association of Lp (a) with both HDL and LDL have been found i.e., p= 0.125 and 0.144, respectively. This however, exhibited that Lp (a) could be tested independent of HDL and LDL. Thus, it can be predicted that lipoprotein (a) and BMI are closely related to each other and could be used in relation to each other for the evaluation of cardiovascular risk factors among individuals. On the other hand, lipoprotein (a) and lipid profile were observed to have no relation with each other and so Lp (a) can be understood as a separate predictive parameter for the detection of CVD risks. Notwithstanding the fact, a study has been conducted in which the association between lipoprotein (a) and other risk factors of CVD such as body fatness along with plasma lipoprotein concentrations among obese individuals have been determined. With the use of cross-sectional analysis, the findings of this study found evidence that Lp (a) has a positively significant relation with both total cholesterol and HDL whereas, insignificant relationship was observed between Lp (a) and TG. Furthermore, this study claimed that lipoprotein (a) has been strongly related with HDL but it has no relation with other lipid parameters [32].

Moreover, a study has been conducted that aimed to determine the association between lipoprotein (a) and LDL in premature acute coronary syndrome. By adopting a case-control research design, this study has found strong association between lipoprotein (a) and LDL with $p< 0.001$. This study further depicted that an individual with high levels of lipoprotein (a) has increased levels of LDL [33]. On the other side, another research has been taken into consideration to support the evidences obtained in the present study that aimed to determine the relationship of lipoprotein (a) with other parameters including BMI among individuals with risk of obesity, diabetes and CVD. The outcomes of this study showed that females who were obese exhibited increased levels of lipoprotein (a) as compared to males.

Furthermore, this study has found that the levels of lipoprotein (a) has a significantly positively relation TC. This study claimed that BMI and Lp (a) showed the risk of CVD and obesity among both adults and children however, it has no association with TC [34]. Similarly, a study has been proposed which showed that in obese young girls the increased levels of Lp (a) have association with severe diabetes and CVD [35].

In accordance with the findings of a research, lipoprotein (a) has been recognised as an independent parameter for the evaluation of cardiovascular risks among individuals, particularly those who found to be overweight or obese. In addition to this, this study observed no significant association between lipoprotein (a) levels and age of an individual, HDL cholesterol, insulin, BMI, triglycerides and TC. On the other hand, this study has determined a positive correlation between glucose and Lp (a) levels i.e. $p < 0.05$. The findings of this study observed to be contradicted with the present study in which the relationship between Lp (a) and HDL as well as LDL was determined to be insignificant. Based on this discussion, it can be evaluated that lipoprotein (a) has to be tested with BMI to analyse the risks of cardiovascular and diabetes among both obese and non-obese individuals. Whereas, the testing of lipid profile with Lp (a) would not be necessary as per the findings of this study. Due to several uncertainties related to the association of lipoprotein (a) levels with other parameters, including LDL, HDL, TC and TG further investigation is required as contradiction has been developed between the findings of present study and that or pre-existing researches. Since, this study has shown significantly positive relationship between Lp (a) and TG so it could be predicted that there might be some association between lipoprotein (a) and lipid profile that would be tested for the evaluation of CVD risks among individuals.

Conclusion

This research has been conducted to determine the predictive value of lipoprotein (a) as a screening test for dyslipidaemia and obesity. The key variable selected in this study was lipoprotein (a) and dependence of other variables on Lp (a) has to be determined for the evaluation of CVD risks among an individual. The prime aim of this study was to prove that Lp (a) could be used as a separate parameter and not in association with body mass index and lipid profile. Primary data has been gathered in this study and analysed using correlation statistical analysis along with normality analysis to determine the relationship of Lp (a) with BMI, HDL, LDL, TG as well as TC. Based on the outcomes of this study, it has been observed that lipoprotein (a) can be tested separately from lipid profile but it has a strong relationship with BMI. Hence, it can be concluded from this analysis that the null hypothesis formulated in this study has been rejected while, the alternative hypothesis was accepted as the relationship between BMI and Lp (a) was determined. Supporting evidences have also exhibited that BMI and Lp (a) are associated with each other and tested together to evaluate the risks of both diabetes and CVD among obese individuals. Furthermore, this study has shown association with TG only thus, ot can be concluded that there might be some association between Lp (a) and lipid profile but due to insignificant differences with other lipid parameters has left the study with uncertainty about the relationship between Lp (a) and lipid profile.

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Table 1: Descriptive statistics shows the minimum and maximum values along with mean and standard deviation of age, height, weight, BMI, Lp (a), TC, TG, HDL, LDL parameters.

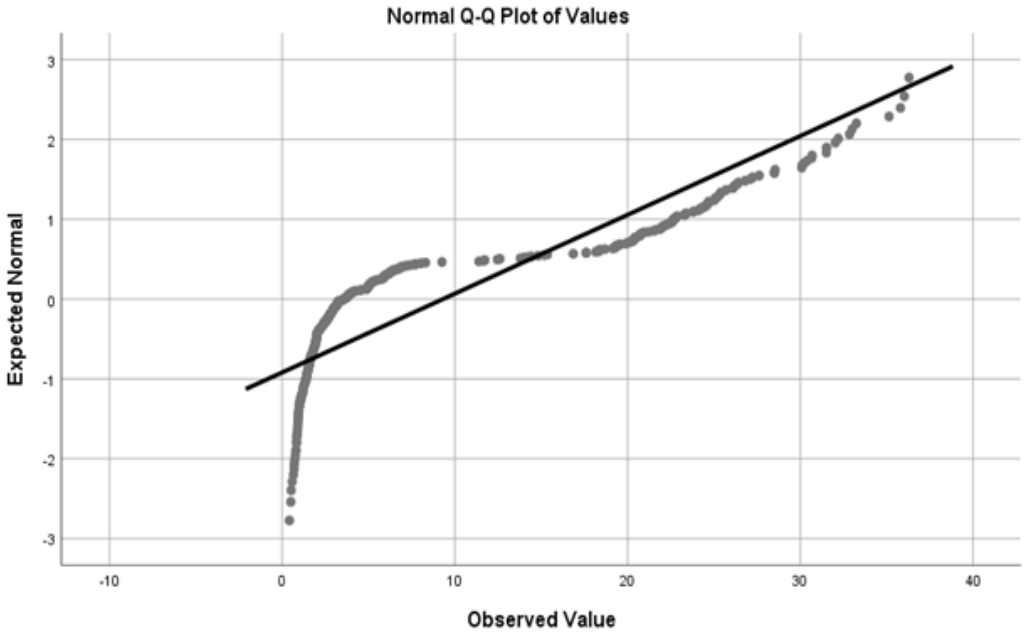
	N	Minimum	Maximum	Mean	Std. Deviation
Lpa	60	6.03	36.02	21.3273	7.80627
BMI	60	17.60	36.30	23.6943	3.96130
TC	60	2.20	8.02	5.1162	1.41446
TG	60	.58	6.39	1.7885	1.04273
HDL	60	.42	2.56	1.4035	.54266
LDL	60	1.25	6.70	2.5277	.94012
Age	60	20.00	82.00	41.8500	14.37256
Height	60	5.00	6.30	5.4560	.32434
Weight	60	45.00	110.00	67.6500	14.10472
Valid N (listwise)	60				

Table 2. Correlation between the Lp (a) levels, BMI and other parameters such as TC, TG, HDL and LDL.

		Lpa	BMI	TC	TG	HDL	LDL
Lpa	Pearson Correlation	1	-.405**	-.216	-.281*	.200	-.191
	Sig. (2-tailed)		.001	.097	.030	.125	.144
	N	60	60	60	60	60	60
BMI	Pearson Correlation	-.405**	1	.377**	.541**	-.336**	.577**
	Sig. (2-tailed)	.001		.003	.000	.009	.000
	N	60	60	60	60	60	60
TC	Pearson Correlation	-.216	.377**	1	.652**	-.335**	.637**
	Sig. (2-tailed)	.097	.003		.000	.009	.000
	N	60	60	60	60	60	60
TG	Pearson Correlation	-.281*	.541**	.652**	1	-.392**	.686**
	Sig. (2-tailed)	.030	.000	.000		.002	.000
	N	60	60	60	60	60	60
HDL	Pearson Correlation	.200	-.336**	-.335**	-.392**	1	-.331**
	Sig. (2-tailed)	.125	.009	.009	.002		.010
	N	60	60	60	60	60	60
LDL	Pearson Correlation	-.191	.577**	.637**	.686**	-.331**	1
	Sig. (2-tailed)	.144	.000	.000	.000	.010	
	N	60	60	60	60	60	60

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).



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465 Figure 1. Normality plot of the studied parameters of this study.

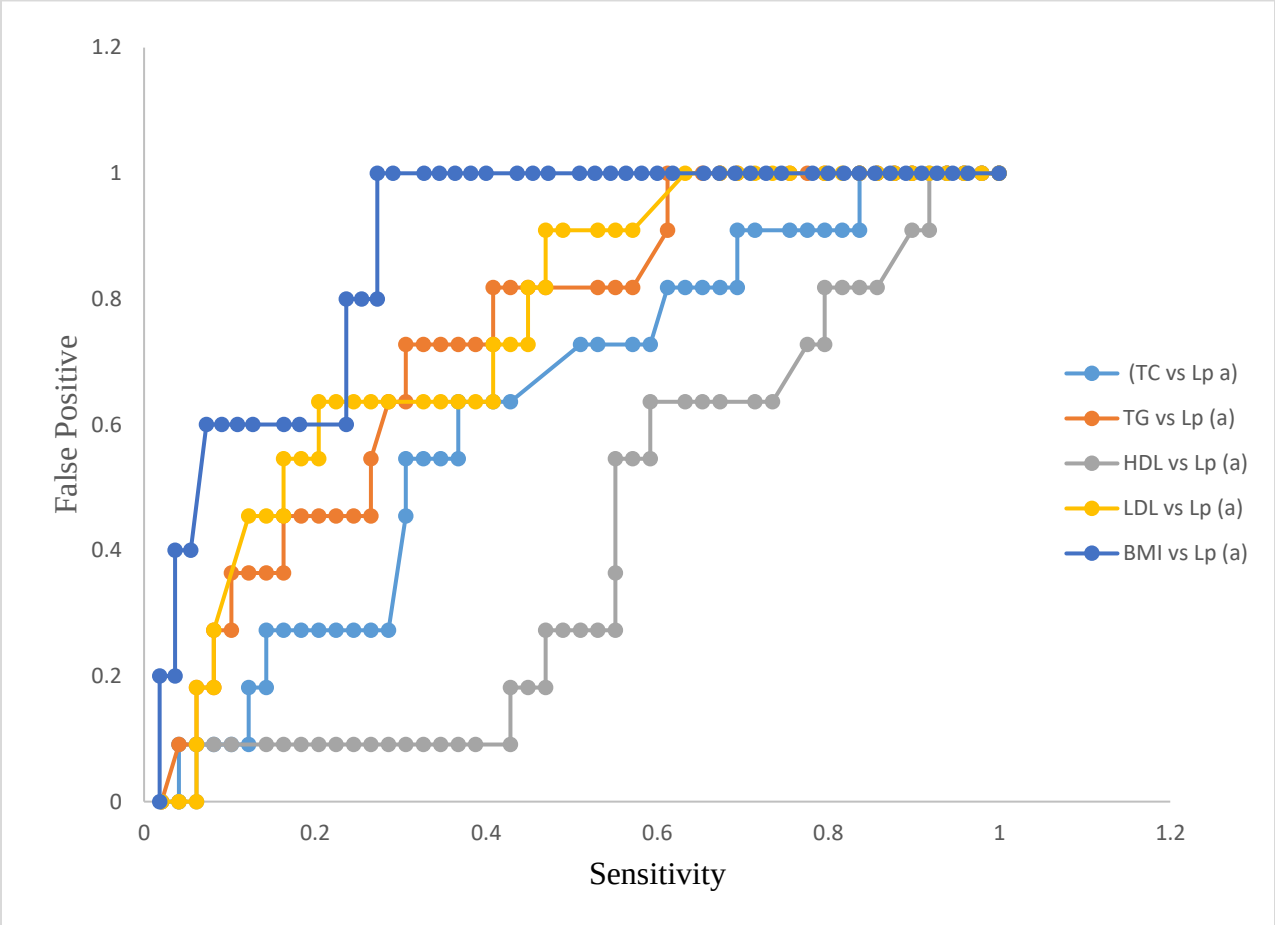

Figure 2. Sensitivity values of Tp (a) levels with the other parameters.