ORIGINAL RESEARCH PAPER

Biochemistry

TO EVALUATE THE RELATIONSHIP BETWEEN LIPOPROTEIN (A) AND RETINOPATHY IN TYPE 2 DIABETES MELLITUS

KEY WORDS: Diabetes Mellitus, Diabetic retinopathy, lipoprotein(a) [Lp(a)], Fasting plasma sugar,HbA1c

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ABSTRACT

The study enrolled total 400 subjects: 200 subjects having diabetes mellitus (DM) without retinopathy as controls and 200 subjects having diabetic retinopathy (DR) as cases. Lipoprotein(a), Fasting plasma sugar, Total Cholesterol (TC), TG, HDL, LDL & HbA1c, was done for each patient. Statistically significant positive correlation between severity of DR with Lipoprotein(a) P=0.000(r = 0.712), TC P=0.000(r =0.972), LDL P = 0.000(r = 0.874), TG P = 0.000(r =0.917), was documented. DR was also strongly positively correlated with duration of diabetes P = .00001. There was strong inverse correlation of DR with HDL P = 0.001(r = -0.728). Serum lipoprotein(a) were significantly correlated with severity of DR.

INTRODUCTION

Diabetic patients are prone to developing microangiopathy, clinically manifested as diabetic nephropathy, neuropathy and retinopathy (American Diabetes Association, 2003). In developed countries, DR is the leading cause of vision loss in adults of working age (Jung, 2004). DR currently affects almost 100 million people worldwide and is set to become an ever-increasing health burden, with estimates between 1990 and 2010 showing that DR-related visual impairment and blindness increased by 64% and 27% respectively (Leasher,2016). Early identification and treatment are key priorities for reducing the morbidity of diabetic retinopathy DR. Population and family studies have shown the pathogenesis of DR due to the interaction of several environmental, nutritional, and genetic risk factors (Newfield, 1997). It has been demonstrated that atherogenic lipoproteins, such as total cholesterol, LDL cholesterol, oxidized low density lipoprotein, and triglycerides are associated with progression of retinopathy, and the development of macular oedema (Orchard, 1990; Davis, 1998; UÇgun, 2007). DR falls into 2 broad categories: the earlier stage of nonproliferative diabetic retinopathy (NPDR) and the advanced stage of proliferative diabetic retinopathy (PDR). Classification of NPDR is based on clinical findings manifested by visible features, including microaneurysms, retinal hemorrhages, intraretinal microvascular abnormalities (IRMA), and venous caliber changes, while PDR is characterized by the hallmark feature of pathologic preretinal neovascularization(Stitt,2016).

REVIEW OF LITERATURE

DR is the most common complication of DM and is a leading cause of blindness among working-age people worldwide (Whiting, 2011).Globally, it has been estimated that about 30% of people with DM have DR (Zheng, 2012). Park et al. reported that overall prevalence of any DR was 19%, and the prevalence of vision threatening DR was 5%. The presence of DR is strongly related to the duration of diabetes. In the Seoul Metropolitan City-Diabetes Prevention Program study, participants with duration of 10 years or greater, retinopathy was found in 55.2% compared with 12.6% in those with diabetes for a duration of 10 years or less (Park, 2012). In addition, there was an approximate 3-fold increase in vision-threatening DR in those who had diabetes for 10 years or more compared with those with diabetes for 10 years or less (Klein, 2008). Diabetic retinopathy is considered as the disease of eye associated with diabetes. It is caused by the blood vessels changes in the retina. After these blood vessels get damaged, the leaking of blood may occur resulting in the growth of fragile new vessels. These changes of cell damage leads to the impairment of vision. These changes can result in blurring of the vision, hemorrhage into the eye, or, if untreated, retinal detachment can also take place (Grunwald, 2012). Microaneurysms, Retinal edema and hard exudates, Cotton-wool spots, Dot and blot hemorrhages, Macular edema are some of the related causes of Diabetic retinopathy. Fluorescein angiography, Optical coherence tomography scanning and B-scan ultrasonography are the preferred diagnosis for Diabetic retinopathy. This is further classified as mild, moderate and severe depending on the presence of various deciding factors (Simó, 2009). Maintaining a regular exercise and a healthy diet, keeping blood sugar within the normal limits and the prescribed medications can be opted in the day to day life to prevent diabetic retinopathy (Ministry of Health Malaysia, 2011).

MATERIALS AND METHODS

This cross-sectional comparative study was conducted in the department of Biochemistry in collaboration with the department of Regional Institute of Ophthalmology (RIO) at IGIMS, Patna from April'2017' to November '2018'. After approval by the hospital ethical review committee, informed written consent was taken from all subjects and details of procedure were explained to them in the local language prior to inclusion in the study. The present study enrolled total 400 subjects: 200 subjects having diabetes without retinopathy as controls and 200 subjects having diabetic retinopathy (DR) as cases.

Lipoprotein(a), Fasting plasma sugar, Total cholesterol (TC) low density lipoprotein (LDL), triglyceride level (TG), high density lipoprotein (HDL) and glycated hemoglobin (HbA1c) was done for each patient. Patients were divided in five groups according to retinopathy status based on early treatment DR study (ETDRS) disease severity level (ETDRS, 1991). Statistical analysis was performed with Statistical Packages for Social Sciences (SPSS) statistical software (version 17.0 for Windows).

RESULTS

The study enrolled total 400 subjects: 200 subjects had diabetes without retinopathy as controls and 200 subjects had diabetic retinopathy (DR) as cases. Out of 200 subjects of DR, 141(51.1%) were male and 59 (47.6 %) were female as shown in figure 1.There was statistically significant positive correlation between severity of DR with Lipoprotein(a) P=0.000(r = 0.712), TC P=0.000(r = 0.972), LDL P = 0.000(r = 0.874), TG P = 0.000(r = 0.917).There was strong negative correlation of DR with HDL P = 0.001(r = - 0.728) The results are summarized in Table1 and figure2.

Table 1
Level of LP(a) in cases & control group

Group	Mean ± S.D	Std. Error (Mean)	P. Value (sig- 2 tailed)	t- test	r-value
Case	43.32 ± 8.12	0.575	0.000	52.59	0.712
Control	15.88 ± 7.51	0.531			

Table 1

Table 1 shows there is statistically significant change in LP(a) of control and control in DR (p< .05).The mean value of LP(a) is 43.32 ± 8.12 Vs 15.88 ± 7.51 in cases and control respectively.

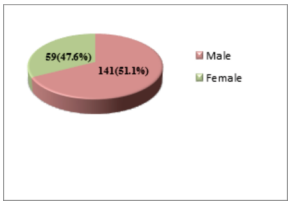

Figure 1. Gender wise distribution in cases.

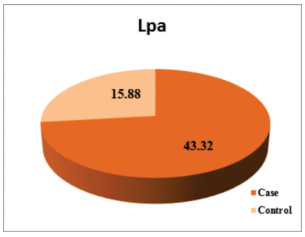

Figure 2. Level of LP(a) in cases & control group

DISCUSSION

In this study the average serum Lp(a) levels in patients with diabetic retinopathy were significantly higher than in those with no retinopathy. The mean value of LP(a) in current study was 43.32 ± 8.12 Vs 15.88 ± 7.51 in cases and control respectively. This study matches in accordance with the studies of Onuma et al., in 1994 conducted in Japan which reported high serum Lp(a) concentrations in type 2 diabetic patients with retinopathy. Maioli et al., in 2007 also reported raised serum apolipoprotein (a) levels in the active diabetic retinopathy group (severe NPDR and PDR) compared with no retinopathy group. Heesen et al.,in 1997 also reported higher prevalence of preproliferative retinopathy with increasing Lp(a) levels in type 2 diabetic patients. Verrotti et al.,in 1989 studied the serum lipids and lipoprotein concentrations in young adults with insulin-dependent DM and different degrees of retinopathy. They also reported significantly higher Lp(a) values in patients with preproliferative and PDR as compared to patients with background of DR.

CONCLUSION

The study concluded that DR was independently associated with the serum Lp(a) level in patients with type 2 diabetes. Lp(a) levels are significantly raised in patients with diabetic retinopathy as compared to patients with no retinopathy.

REFERENCES

1. American Diabetes Association. (2003). Implications of the United Kingdom prospective diabetes study. Diabetes care, 26(suppl 1), s28-s32.
2. Chopra, R., Saramma, J. G., Mary, J., & Rebecca, A. (2007). Lipoprotein (a) as a risk factor for diabetic retinopathy in patients with type 2 diabetes mellitus. Indian Journal of Ophthalmology, 55(3), 195.
3. Davis, M. D. (1998).Worsening of diabetic retinopathy after improvement of glycemic control. Archives of Ophthalmology, 116(7), 931-932.
4. Early Treatment Diabetic Retinopathy Study Research Group. (1991). Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics: ETDRS report number 7. Ophthalmology, 98(5), 741-756.
5. Grunwald, J. E., Ying, G. S., Maguire, M., Pistilli, M., Daniel, E., Alexander, J., ... & Townsend, R. (2012). Association between retinopathy and cardiovascular disease in patients with chronic kidney disease (from the Chronic Renal Insufficiency Cohort [CRIC] Study). The American journal of cardiology, 110(2), 246-253.
6. Jung, D. S., & Park, K. P. (2004). Posttraumatic bilateral internuclear ophthalmoplegia with exotropia. Archives of neurology, 61(3), 429-429.
7. Klein, R., Knudtson, M. D., Lee, K. E., Gangnon, R., & Klein, B. E. (2008). The Wisconsin Epidemiologic Study of Diabetic Retinopathy XXII: the twenty-five-year progression of retinopathy in persons with type 1 diabetes. Ophthalmology, 115(11), 1859-1868.
8. Leasher, J. L., Bourne, R. R., Flaxman, S. R., Jonas, J. B., Keeffe, J., Naidoo, K., ... & Resnikoff, S. (2016). Global estimates on the number of people blind or visually impaired by diabetic retinopathy: a meta-analysis from 1990 to 2010. Diabetes care, 39(9), 1643-1649.
9. Ministry of Health Malaysia. (2011 ,June).Screening of diabetic retinopathy.Clinical practice guidelines. Retrieved from http://www.acadmed.org.my/index.cfm?&menuid=67
10. Newfield, R. S., Polak, M., Marchase, R., & Czernichow, P. (1997). Epidemiology and genetics of diabetic complications. Diabetologia, 40(3), B62-B64.
11. Orchard, T. J. (1990).Dyslipoproteinemia and diabetes. Endocrinology and Metabolism Clinics of North America, 19(2), 361-380.
12. Park, C. Y., Park, S. E., Bae, J. C., Kim, W. J., Park, S. W., Ha, M. M., & Song, S. J. (2012). Prevalence of and risk factors for diabetic retinopathy in Koreans with type II diabetes: baseline characteristics of Seoul Metropolitan City-Diabetes Prevention Program (SMC-DPP) participants. British Journal of Ophthalmology, 96(2), 151-155.
13. Simó, R., & Hernández, C. (2009). Advances in the medical treatment of diabetic retinopathy. Diabetes care, 32(8), 1556-1562.
14. Stitt, A. W., Curtis, T. M., Chen, M., Medina, R. J., McKay, G. J., Jenkins, A., ... & Lois, N. (2016). The progress in understanding and treatment of diabetic retinopathy. Progress in retinal and eye research, 51, 156-186.
15. UÇgun, N. I., Yildirim, Z., KiliÇ, N., & GÜrsel, E. (2007). The importance of serum lipids in exudative diabetic macular edema in type 2 diabetic patients. Annals of the New York Academy of Sciences, 1100(1), 213-217.
16. Utermann, G. (1989). The mysteries of lipoprotein(a). Science, 246(4932), 904-910.
17. Verrotti, A., Lobefalo, L., Chiarelli, F., Mastropasqua, L., Pallotta, R., Colangelo, L., & Gallenga, P. E. (1997). Lipids and lipoproteins in diabetic adolescents and young adults with retinopathy. Eye, 11(6), 876.
18. Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes research and clinical practice, 94(3), 311-321.
19. Zheng, Y., He, M., & Congdon, N. (2012). The worldwide epidemic of diabetic retinopathy. Indian journal of ophthalmology, 60(5), 428-431.