RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 5 | May 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Association Between Glycosylated Haemoglobin And Severity of Diabetic Retinopathy in Type 2 Diabetic Patients: A Hospital Based Study

KEYWORDS: Diabetic Retinopathy, HbA1c, Glycosylated haemoglobin

Adheesh P Shetty
Resident, KS Hegde Medical Academy, Deralakatte- 575018

Dr. Subrahmanya Bhat K
Additional Professor, KS Hegde Medical Academy, Deralakatte- 575018

ABSTRACT *Diabetic retinopathy (DR) is a major microvascular complication of diabetes mellitus. The Early Treatment Diabetic Retinopathy Study (ETDRS) identified HbA1c as one of the most important risk factors for the progression to high risk proliferative retinopathy.*

Aim was to study the association between Glycosylated Haemoglobin and Severity of Diabetic Retinopathy in Type 2 Diabetic patients

Methodology: It was cross sectional study wherein 500 type 2 diabetics with duration of diabetes >15years were included. Retinopathy was graded according to ETDRS and HbA1c assessed. Statistical analysis of the data was done by using SPSS software

Results: The mean HbA1c in patients with no DR, NPDR and PDR was 6.76 ±1.3, 8.99±1.89, and 11.045 ±1.53 respectively.

Conclusion: Elevated HbA1c is associated with higher prevalence of DR. We also found that the higher values of HbA1c is associated with increase in severity of retinopathy.

Introduction

Diabetic retinopathy (DR) is a major microvascular complication of diabetes mellitus. DR is the most frequent cause of new cases of loss of sight amongst adults aged 20-74years (Fong, D, 2003). There is a rise in prevalence of diabetes mellitus particularly in developing Asian countries like India and China (Yau, J. W. Y, 2012). According to latest IDF report, there are 387 million diabetics in the world and about 66.847 million diabetics in India (IDF. (n.d). There are about 11.587 million blind people in South East Asia region. Among them about 3% are caused by DR (Resnikoff S, 2004). Vision loss due to DR occurs through a variety of mechanisms, including capillary non-perfusion, macular oedema, vitreous haemorrhage, retinal detachment or associated neovascular glaucoma (Fong, D, 2003). Increase in glycosylated haemoglobin (HbA1c) is said to be associated with higher risk of NPDR, proliferative diabetic retinopathy (PDR), and diabetic macular oedema (DME). (Browning, D. J., 2010). The risk for progression to high-risk PDR is increased by approximately 60% when HbA1c increases from 9% to 12% (Davis, M. D, 1998). The Diabetes Control and Complications Trial (DCCT) showed marked reduction in risk of incidence of DR of approximately 50% in the rigorous therapy group compared to conventional group in the primary-prevention cohort and rigorous treatment reduced the risk of progression to severe NPDR or PDR by 47%. (Control, T. D, 1998). HbA1c has been known to predict the incidence and progression of DR (Raman. R, 2011). The severity and the duration of the inadequate glycaemic control have been seen to be correlated with a higher risk of increased severity of retinopathy, from non-proliferative to proliferative DR (Raman. R, 2011). The Early Treatment Diabetic Retinopathy Study (ETDRS) identified HbA1c as one of the most important risk factors for the progression to high risk proliferative retinopathy (Davis, M. D, 1998). Hence we conducted this study to know association of the HbA1c with the severity of diabetic retinopathy in in Type 2 diabetic patients.

METHODOLOGY

A hospital based cross sectional study was conducted on 500 adult patients diagnosed with type 2 diabetes mellitus, attending ophthalmology outpatient department of at KS Hegde hospital, conducted between December 2013 and October 2014.

Study participants included all type 2 diabetes mellitus patients referred to our out-patient department from various departments of KS Hegde hospital. Written, informed consent was obtained from all subjects and the study was performed in accordance with the tenets of the Declaration of Helsinki 2013. The Institutional ethical committee clearance was accorded from KS Hegde Medical College

Inclusion criteria:

All type 2 diabetes mellitus patients referred from various departments of KS Hegde hospital with duration of diabetes above 15yrs.

Exclusion criteria:

- Diabetic patients with coexisting vein occlusion or papillophlebitis
- Collagen disorders like DLE, PAN & SCLERODERMA
- Blood dyscrasias.
- Gestational diabetes
- Media opacities caused by lenticular and corneal opacities that obscure the fundus.
- Inflammatory diseases causing retinal ischemia and degenerative diseases of the retina.
- Local vascular malformations in the retina and radiation retinopathy.
- Patients with hemoglobin (Hb), total serum cholesterol (TC), high density lipoproteins (HDL), low-density lipoproteins (LDL), serum triglycerides (TG) and serum creatinine(SC) outside normal ranges were excluded from the study

Definitions:

A participant was considered diabetic if any of the fol-

Volume : 6 | Issue : 5 | May 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

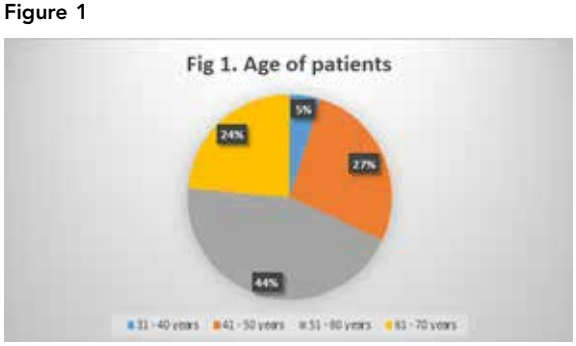
lowing criteria was met. Already diagnosed case of type 2 diabetes mellitus diagnosed by a physician or any history of treatment with oral hypoglycaemic agent or insulin. If diabetic changes were seen in the eye and patient was unaware of his diabetic status then any value of glycosylated haemoglobin above the normal 6.5% or Fasting blood sugar above 126mg/dl and post prandial blood sugar of 200mg/dl were considered as new cases.

Diabetic retinopathy was defined as the presence of 1 or more retinal microaneurysms or retinal blot haemorrhages with or without more severe lesions (hard exudates, soft exudates, intraretinal microvascular abnormalities, venous beading, retinal new vessels, preretinal and vitreous haemorrhage, and fibroproliferans) and was classified using the ETDRS grading as no DR, Very Mild non proliferative diabetic retinopathy(NPDR), Mild NPDR, Moderate NPDR, Severe NPDR , Very Severe NPDR and Proliferative diabetic retinopathy(PDR), and advanced PDR in either eyes and the worse eye was taken into consideration. Macular oedema was defined on the basis of presence or absence of CSME. Complete ocular examination was done. Visual acuity was recorded using Snellen chart. Detailed torch light examination and slit lamp examination was done. Direct ophthalmoscopy examination and Indirect ophthalmoscopy and Fundus examination with slit lamp bio microscopy with 78 D & 90 D Lenses and IOP was checked by Shiotz or applanation tonometer.Fundus Photography was taken for all patients with DR more severe than moderate NPDR, Fluorescein Angiography was done to differentiate exudative from ischemic maculopathy and to rule out neovascularisation in doubtful cases. Blood was collected under aseptic precautions and sent for HbA1c, Hb, TC, HDL, LDL, TG, SC. Statistical analysis of the data was done by SPSS software version 19 using Fischer exact test, chi square test and t test. ROC curve was drawn and area under it analysed for sensitivity and specificity of HbA1c.

RESULTS:

The total number of patients included in the study was 500 of whom 203(40.6%) were females and 297(59.4%) were males. The average age of females was 55.54 ± 8.61 years and that of males was 53.43 ± 8.57 and the age distribution was as shown in fig 1.

Figure 1



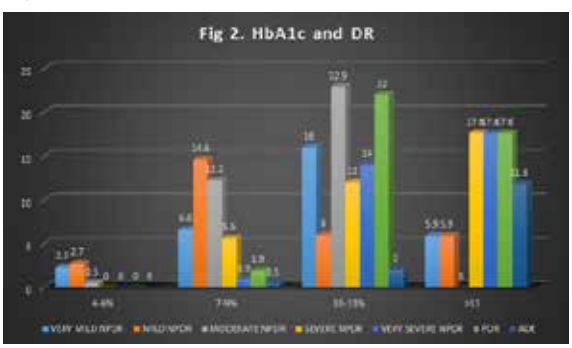
The mean ± SD of HbA1c in patients with no DR, NPDR and PDR was 6.76 ±1.3, 8.99±1.89, and 11.045 ±1.53 which was significant with a p-value 0.01. The prevalence of DR in diabetics with HbA1c of <4, 4-6, 7-9, 10-13, >13 were 0%, 5.5%, 42.3%, 88%,76.5% respectively and was statistically significant with p<0.01. The increase in HbA1c also showed an increase in the severity of the DR as shown in the figure 2 and the p-value was <0.001 which was highly significant. The ROC curve was plotted and a cut-off value of 7.45% was got with a sensitivity of 83% and a specificity of 85.9% above which the chances for retinopathy will be high in diabetics.

Table 1

Table 1 .Comparison of HbA1c and severity of DR

			DR							
			No DR	MILD NPDR	MODERATE NPDR	PDR	SEVERE NPDR	VERY MILD NPDR	VERY SEVERE NPDR	Total
HbA1c	<4	Count	0	0	0	0	0	0	0	0
		% within HbA1c	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%
		% within DR	3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2%
	4 - 6	Count	207	6	5	1	0	3	0	219
		% within HbA1c	94.5%	2.7%	2.3%	0.5%	0.0%	1.4%	0.0%	100.0%
		% within DR	90.7%	4.0%	2.9%	0.8%	0.0%	17.6%	0.0%	43.8%
	7 - 9	Count	127	7	21	39	4	13	14	227
		% within HbA1c	57.7%	3.2%	14.6%	12.3%	1.8%	0.0%	6%	100.0%
		% within DR	30.1%	28.0%	75.6%	74.3%	22.2%	87.1%	50.0%	45.4%
	10 -	Count	9	1	0	8	11	0	4	33
		% within HbA1c	12.0%	3.0%	0.0%	10.0%	33.0%	12.5%	10.0%	14.9%
		% within DR	1.8%	20.0%	7.3%	22.9%	61.1%	23.6%	28.0%	10.3%
	13+	Count	4	2	1	0	3	1	2	17
		% within HbA1c	23.5%	11.8%	5.9%	0.0%	17.6%	5.9%	17.6%	100.0%
		% within DR	1.2%	10.0%	2.4%	0.0%	16.7%	14.3%	25.0%	3.4%
Total		Count	341	4	41	35	18	27	20	500
		% within HbA1c	68.2%	8%	8.2%	7.0%	3.6%	4.2%	2.4%	100.0%
		% within DR	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Figure 2



DISCUSSION

Diabetic retinopathy is a serious sight threatening condition which gradually and progressively leads to blindness if its natural course is not intervened. Our study was a hospital based study and our population included a large number of references from various departments including medicine and nephrology. A limitation in this study is we relied on self-reported cases of diabetics later confirmed by investigation and may have missed those cases who were actually diabetic but with no retinopathy changes and thus overestimated the prevalence. Also although diabetics with duration of diabetes >15years was taken the increase in duration might affect the prevalence to a certain extent. On analysing the correlation between glycated haemoglobin and DR and we found that the prevalence of retinopathy is increased in the higher HbA1c groups similar to findings in the Wisconsin epidemiologic study of diabetic retinopathy (WESDR) (Klein, R, 1984). The retinopathy was also increased in severity with higher HbA1c groups. We also obtained a cut-off value of 7.45% with a high sensitivity of 83% and specificity of 85.9% above which the chances for retinopathy will be high in diabetics. Rajiv Raman et al., concluded similar findings and showed that diabetics with HbA1c >8% would have a high chance of sight threatening retinopathy

CONCLUSION

Ours is a hospital based study with majority of our patients residing in towns along the Malabar Coast. Our study shows that an elevated HbA1c was associated with high prevalence of DR. Diabetes mellitus is increasing at an alarming rate in the developing countries and so are its

Volume : 6 | Issue : 5 | May 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

complications. Hence we need to screen these diabetics and maintain controlled blood sugars so as to prevent the further progression of this debilitating disease.

REFERENCES

1. Fong, D. S., Aiello, L., Gardner, T. W., King, G. L., Blankenship, G., Cavallerano, J. D., … American Diabetes Association. (2003). Diabetic retinopathy. Diabetes Care, 26 Suppl 1, S99–S102.
2. Yau, J. W. Y., Rogers, S. L., Kawasaki, R., Lamoureux, E. L., Kowalski, J. W., Bek, T., … Meta-Analysis for Eye Disease (META-EYE) Study Group. (2012). Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care, 35(3), 556–564. http://doi.org/10.2337/dc11-1909
3. International Diabetes Federation. (n.d.). Retrieved March 10, 2016, from http://www.idf.org/
4. Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, … Global data on visual impairment in the year 2002. (2004). Bull World Health Organ. Nov;82(11):844–51.
5. Browning, D. J. (2010). Diabetic Retinopathy: Evidence-Based Management. Springer Science & Business Media.
6. Davis, M. D., Fisher, M. R., Gangnon, R. E., Barton, F., Aiello, L. M., Chew, E. Y., … Knatterud, G. L. (1998). Risk factors for high-risk proliferative diabetic retinopathy and severe visual loss: Early Treatment Diabetic Retinopathy Study Report #18. Investigative Ophthalmology & Visual Science, 39(2), 233–252.
7. Control, T. D., & Group, C. T. R. (1993). The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus. New England Journal of Medicine, 329(14), 977–986. http://doi.org/10.1056/NEJM199309303291401
8. Raman, R., Verma, A., Pal, S. S., Gupta, A., Vaitheeswaran, K., & Sharma, T. (2011). Influence of glycosylated hemoglobin on sight-threatening diabetic retinopathy: a population-based study. Diabetes Research and Clinical Practice, 92(2), 168–173. http://doi.org/10.1016/j.diabres.2011.01.006
9. Klein, R., Klein, B. E., Moss, S. E., Davis, M. D., & DeMets, D. L. (1984). The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years. Archives of Ophthalmology (Chicago, Ill.: 1960), 102(4), 527–532.