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Original Research Article

ASSOCIATION OF BLOOD GLUCOSE, SERUM LIPIDS AND BODY MASS INDEX WITH RETINOPATHY IN OLDER ADULTS OF SOUTH KERALA

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Abstract

Background: Retinopathy, characterized by pathological changes in the retina, primarily affects the microvasculature and is commonly associated with conditions like Diabetes Mellitus. This study aims to investigate the relationships between blood glucose levels, serum lipid levels, body mass index (BMI), and the progression of retinopathy in patients attending a retinopathy clinic. **Materials and Methods:** A cross-sectional observational study was conducted in a tertiary care referral teaching hospital over a two-month period. A total of 263 patients aged over 60 years were included. Anthropometric measurements and blood profiles for glucose and lipids were recorded, and fundus examinations were performed to categorize patients into various grades of diabetic retinopathy according to the ETDRS classification. **Result:** The study found a high prevalence of diabetic retinopathy (75%) among diabetic patients, with duration of diabetes strongly correlated with the presence and severity of retinopathy. Hypertension was a common comorbidity, with significant association with diabetic retinopathy. Notably, patients with severe retinopathy showed both microalbuminuria and macroalbuminuria, indicating a potential predictive role of albuminuria in diabetic retinopathy. Higher triglyceride and cholesterol levels were associated with more severe retinopathy and maculopathy, while lower HDL levels and higher LDL levels were linked to increased retinopathy severity. However, no significant correlation was found between BMI and retinopathy grades. This suggests the need for further research with larger sample sizes to elucidate the relationship between BMI and retinopathy, in conjunction with established risk factors like blood glucose and lipid profiles. **Conclusion:** In conclusion, this study highlights the importance of duration of diabetes, hypertension, and lipid profile in the development and progression of diabetic retinopathy. Early detection and management of these risk factors may help mitigate the risk of vision loss associated with diabetic retinopathy.

INTRODUCTION

Retinopathy as the name suggests is pathophysiological change observed in the retina. It is multifactorial in origin which includes microvascular pathology. The microvasculature of the retina can be damaged in various disease conditions, most frequently associated with Diabetes Mellitus.[1] Other causes include systemic hypertension, pregnancy induced hypertension, retinopathy of prematurity in premature infants, sickle cell disease, anaemia, acute leukaemia etc.[2,3] The disease condition is progressive through different stages from asymptomatic to proliferative stage. Screening of the high-risk population helps in identifying the disease at a very early stage and can prevent vision loss by timely intervention.

Ninety-three million people are globally affected by diabetic retinopathy. Prevalence of diabetic retinopathy is 77.3% in type 1 diabetes patients and 25.1% in type 2 diabetes patients.[4] Several studies were carried out to estimate the prevalence of diabetic retinopathy among diabetic patients in India. All India Ophthalmological Society (AIOS) conducted a screening study in 2014, and reported the prevalence of diabetic retinopathy as 21.7%.[5] Study conducted by V. Narendran estimated the prevalence of diabetic retinopathy among diabetics aged 50 years or more as 26.8% in South India.[6,7] Several researchers have identified various risk factors in

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diabetic patients associated with retinopathy. Out of those, the most powerful factor is the duration and onset of diabetes.[6,7] Other factors are serum triglyceride level, systemic hypertension, age, sex, smoking, eating habits, sleeping patterns, ethnic variations, etc.[6-8] Incidence risk is higher in patients with high post prandial hyperglycemia when compared with those with elevated fasting plasma glucose levels.[8,9] Many epidemiological studies have been done to identify the association between serum lipid levels and micro vascular complications of diabetes but the results were inconclusive.[10,11] This may be due to selection of wide age groups or variation in ethnicity. Likewise, BMI (Body Mass Index) is identified as a risk factor in developing Diabetes Mellitus, but its association with Diabetic Retinopathy is not much conclusive.[11] While some studies identify association between diabetic retinopathy and body mass index, while others are inconclusive. So, through this hospital-based study, we would like to identify if there is any relation between serum lipid level and BMI with retinopathy, and how lipid levels and blood glucose of varying body mass index affects the progression in retinopathy in patients attending the retinopathy clinic.

Review of Literature

Yau JW, Rogers SL, Kawasaki R, et al,[4] Studied population aged 20-79 years in a pooled data of 35 studies during the period of 1980-2008 determined overall prevalence was 34.6% (95% CI 34.5-34.8) for any diabetic retinopathy, 6.96% (6.87-7.04) for proliferative diabetic retinopathy, 6.81% (6.74-6.89) for diabetic macular oedema. They concluded that longer diabetes duration and poorer glycaemic and blood pressure control were strongly associated with diabetic retinopathy.

Narendran V, John RK, Raghuram A et al,[6] in a cross-sectional study conducted in northern Kerala, age-sex adjusted prevalence of diabetes among people aged 50 years and older was 5.1% (95% CI 3.9, 6.3, deff 4.33) and of diabetic retinopathy among the diabetics was 26.8% (95% CI: 19.2, 34.4, deff 1.99). Non-proliferative diabetic retinopathy (94.1%) was the most common form of retinopathy seen. Two eyes were blind (presenting vision <6/60) as a result of retinopathy. They suggested preventive strategies have to be evolved to ensure that blindness due to diabetic retinopathy does not become a public health problem in India.

Pradeepa R, Anitha B, Mohan V et al,[7] in a large cross-sectional study conducted in Chennai, South India included 1736 Type 2 diabetic subjects for the study logistic regression analysis revealed that male gender, duration of diabetes, blood glucose levels, macroalbuminuria and insulin therapy were significantly associated with severity of diabetic retinopathy. The risk for developing diabetic retinopathy was seven times for elevated postprandial plasma glucose levels.

Aims and Objectives

1. To observe variation in blood glucose level in progression of retinopathy
2. To observe relationship between serum lipid level and retinopathy
3. To observe relationship between BMI and retinopathy
4. To observe how lipid profile and BMI affect the progression in retinopathy.

MATERIALS AND METHODS

Study Design: Observational cross-sectional study

Study Setting: Tertiary care referral teaching hospital.

Study Duration: 2 months after obtaining permission from institution ethics committee

Sample Size: Assuming 95% confidence interval, 5% absolute precision, and based on the prevalence (21.7%) of retinopathy, the required minimum sample size is 261. The formula used is:

$n = Z1\text{-}\alpha/2\ 2 \times p \times (1\text{-}p) / d2$

n = sample size

P= prevalence

d = desired degree of precision

Z = standard normal value at the level confidence desired, usually at 95% confidence level.

Sampling method: Simple random sampling

Inclusion Criteria

Individuals over 60 years of age with retinopathy

Exclusion Criteria

Individuals aged less than 60 years

Study Tools and Procedure:

This study will be conducted in a tertiary care hospital using hospital and outpatient records. Patients of age 60 years and above will be recruited for the study and Informed consent will be taken from all the subjects. A case proforma will be used to collect the required data including the patient details, history of illness, treatment history, laboratory data, etc.

Biochemical parameters required includes:

- Plasma blood glucose level.
- HbA1c

Plasma glucose in a random sample ≥ 200 mg/dl or fasting plasma glucose ≥ 126 mg/dl or HbA1c ≥ 48 mmol/mol is considered diagnostic of diabetes.[2]

- Lipid profile: Serum triglycerides, HDL-Cholesterol and LDL-Cholesterol is calculated using the Friedewald formula: LDL-C = TC – HDL-C – (TG/5) mg/dl. The formula is unreliable in cases where TGs level exceeds 350 mg/dl, in that cases measuring non-HDLC or Apo B100 is more accurate in risk assessment.

Ocular Examination:

- Dilated Fundus Examination by Ophthalmoscopy
- Fundus photography will be carried out to identify patients with retinopathy.
- Fundus fluorescein Angiography if available is used to evaluate the retinal vascular status

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- Cases with diabetic retinopathy were graded into 5 classes on the basis of ETDRS classification.[12]

Analysis of results: Characteristics of the study population will be described using means for continuous variables and percentages for categorical variables. For continuous variables, Kruskal wallis test was used to find the association of continuous variables and Chi square test used for categorical variables.

Retinopathy by glucose level, lipid levels, and body mass index prevalence will be noted.

RESULTS

263 patients were screened for retinopathy and their anthropometric measurements and blood profile for glucose and lipid profile determined. It was noted that 24% of the sample screened were non-diabetic and rest all patients were diabetic and among them nearly 21% of them were having additional comorbidity of hypertension along with diabetes. It was noted that 43% of the studied population had no changes of retinopathy and only 3.8% had Proliferative Diabetic Retinopathy changes (PDR). 9.5% of population had maculopathy. All the baseline characteristics and variables are shown in [Table 1-2].

In [Table 3] the association of all anthropometrics, blood parameters and disease condition to retinopathy changes. Our results indicated signification correlation of diabetic retinopathic changes with duration of diabetic condition and all parameters of lipid levels. But our results could not establish any significant association of diabetic changes with reference to body mass index (BMI).

Table 1: Descriptive statistics of continuous variables.

Variables	Mean	Std. Deviation	Median	25th Percentile	75th Percentile
Age (years)	64.65	4.48	64.00	61.00	67.00
Height (m)	1.60	0.07	1.59	1.53	1.63
Weight (kg)	67.23	10.11	68.00	60.00	74.00
BMI (kg/m2)	26.50	4.27	26.84	23.53	29.43
FBS (mg/dl)	140.05	63.81	130.00	85.00	174.00
Blood Urea (mg/dl)	33.19	11.94	32.00	26.00	36.00
Serum Creatinine (mg/dl)	1.09	0.70	1.00	0.80	1.20
Total cholesterol (mg/dl)	164.05	45.32	148.00	130.00	200.00
HDL (mg/dl)	49.54	13.11	47.00	39.00	57.00
LDL (mg/dl)	81.37	25.91	74.00	63.00	91.00
Triglycerides (mg/dl)	123.85	77.15	107.00	77.00	130.00
Micro albuminuria (mg/l)	72.33	100.68	23.00	18.00	78.00
HbA1c	7.57	2.15	7.60	5.60	8.80
Diabetic duration (years)	5.42	5.15	4.00	1.00	9.00

Table 2: Descriptive statistics of categorical variables

Gender	Frequency (%)
Female	111 (42.2)
Male	152 (57.8)
TREATMENT PROFILE	
Non- diabetic	63 (24)
No therapy	36 (13.7)
Oral hypoglycaemic agent	105 (39.9)
Insulin	59 (22.4)
GRADE OF RETINOPATHY	
Within Normal Limit (WNL)	113 (43)
Mild NPDR	96 (36.5)
Moderate NPDR	33 (12.5)
Severe NPDR	7 (2.7)
Very Severe NPDR	4 (1.5)
PDR	10 (3.8)
HYPERTENSIVE	
YES	55 (20.9)
NO	208 (79.1)
MACULOPATHY	
YES	25 (9.5)
NO	238 (90.5)

NPDR – Non-Proliferative Diabetic Retinopathy

PDR- Proliferative Diabetic Retinopathy

Table 3: Association of various factors with the grades of retinopathy

	Grade of Retinopathy						P value
	WNL (113)	Mild NPDR (96)	Moderate NPDR (33)	Severe NPDR (7)	Very Severe NPDR (4)	PDR (10)	
Age	64.35±4.3	64.60±4.53	65.97±5.37	64.71±2.81	64.25±2.87	64.20±3.73	0.569
Gender							0.575
Female	45(40.5)	44(39.6)	16(14.4)	3(2.7)	1(0.9)	2(1.8)	
Male	68(44.7)	52(34.2)	17(11.2)	4(2.6)	3(2)	8(5.3)	

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Height (m)	1.59±0.07	1.60±0.06	1.57±0.06	1.59±0.07	1.65±0.06	1.57±0.05	0.085
Weight (kg)	67.80±10.	68.25±9.94	64.00±10.61	61.57±10.75	70.75±9.5	64.13±7.40	0.076
BMI (kg/m2)	26.73±4.4	26.65±4.14	25.96±4.31	24.31±3.62	25.90±3.76	25.83±3.48	0.580
Diabetic duration (years)	3.09±2.62	5.96±5.46	7.48±5.64	12.86±3.89	11±4.24	12.30±6.70	<0.001*
FBS (mg/dl)	138±55.03	135.36±72.26	143.27±61.87	181.71±76.17	152±58.19	163.60±68.89	0.213
Blood Urea (mg/dl)	28.75±6.31	33.59±12.37	39.91±17.64	41.71±6.67	44.25±8.65	46.80±12.03	<0.001*
Serum Creatinine (mg/dl)	0.88±0.25	1.18±1.02	1.19±0.44	1.31±0.30	1.70±0.41	1.77±0.46	<0.001
T. Cholesterol (mg/dl)	149.22±33	164.77±45.8	186.64±53.63	208.71±54.0	251±25.11	184.10±33.14	<0.001
HDL (mg/dl)	50.82±11	48.76±13.1	49.03±16.49	50.43±15.06	36.50±4.65	48.90±16.97	0.121
LDL (mg/dl)	72.98±18	84.39±23.7	96.03±36.44	87.43±45.56	99±37.57	87.50±24.55	<0.001*
Triglycerides (mg/dl)	109.46±70	120.90±68.6	155.88±104.6	156±76.40	211±89.64	214.60±63.24	0.003*
Microalbuminuria (mg/l)	29.66±40	72.34±100.5	104.85±92.87	190.85±108.4	291±144.02	279±129.61	<0.001*
HbA1C	7.65±2.12	7.25±2.22	7.95±2.34	7.98±1.99	9.05±1.50	7.62±0.55	0.231
Treatment							
Insulin	6(10.2)	25(42.4)	10(16.9)	6(10.2)	3(5.1)	9(15.3)	<0.001*
Non-Diabetic	21(33.3)	34(54)	8(12.7)	0(0)	0(0)	0(0)	
No Therapy	30(83.3)	4(11.1)	1(2.8)	0(0)	0(0)	1(2.8)	
Oral Hypoglycaemic	56(53.3)	33(31.4)	14(13.3)	1(1)	1(1)	0(0)	
Hypertension							0.405
YES	85(40.9)	81(38.9)	27(13)	5(2.4)	2(1)	8(3.8)	
NO	28(50.9)	15(27.3)	6(10.9)	2(3.6)	2(3.6)	2(3.6)	
Maculopathy							<0.001*
YES	0(0)	14(56)	5(20)	3(12)	3(12)	0(0)	
NO	113(47.5)	82(24.5)	28(11.8)	4(1.7)	1(0.4)	10(4.2)	

DISCUSSION

In the present study 263 patients in the age group of more than 60 years visiting the Ophthalmology OPD were included in the study. Initially basic anthropometric parameters were recorded and later subjected for fundus examination and were categorized in to various grades of diabetic retinopathy according to ETDRS classification. The fundoscopic changes were correlated with Body Mass Index (BMI) and various biochemical parameters namely HbA1c, microalbuminuria and serum lipid profile. In the present study the prevalence of diabetic retinopathy among diabetics was 75%. In the study conducted by Kalk et al the prevalence was 39.3%.[13] The CURES -1 study showed a prevalence of 17.2%.[14] The high prevalence may be accounted as the hospital is a tertiary centre and the cases following up in OPD are usually diagnosed at a later stage and are having uncontrolled blood glucose levels.

In our study average duration of diabetes was 5 years and standard deviation of 5 years suggesting more than 10 years and retinopathy was a consistent feature among these patients. The association of duration of diabetes and retinopathy is well established in our study. Winconsin epidemiological study of diabetic retinopathy also found that risk of diabetic retinopathy directly related to the duration of disease.[15] The CURES-2 study revealed that the risk of development of retinopathy increases by 1.89 times every 5 years.[16]

Hypertension commonly co exists with diabetic retinopathy. In our study about 51% cases were hypertensives. The prevalence of diabetic retinopathy among hypertensives was 40.9%. The prevalence of albuminuria among hypertensive patients was 42.2%. Kalk et al reported significant association between high systolic BP and diabetic retinopathy. Our study was in coherence with the findings of Kalk et al.[13]

In our study 75% cases showed normoalbuminuria and 25% showed microalbuminuria with no retinopathy 6.9 % of cases had microalbuminuria with mild NPDR, 7.4% had microalbuminuria with moderate NPDR. 7.5% and 2.5% cases of severe NPDR and 0.7% of PDR had macroalbuminuria respectively. In PDR and severe NPDR and very severe cases had both microalbuminuria and macroalbuminuria. None of the cases had normal albumin excretion. Serter et al study concluded that there is a good correlation between diabetic retinopathy & proteinuria and albuminuria is important indicator of early diabetic microangiopathy.[17]

Klein R et al did a population-based study in Winconsin to examine relationship between gross proteinuria and proliferative diabetic retinopathy. They concluded that gross proteinuria is a risk indicator of proliferative retinopathy in younger onset individuals.[18]

Only 18.9 % of individuals with no retinopathy had normal levels (<6%) of HbA1c, 52.4% of mild NPDR cases and 62.8% of moderate NPDR cases had HbA1c more than 8% and only 12.8% of very severe NPDR cases and PDR cases had HbA1c > 8%. Klein R Ronald et al in a population-based cohort study on 996 IDDM patients, suggested that glycosylated Hb level were strongly related to incidence and progression of diabetic retinopathy and incidence of

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gross proteinuria.[19] Data from the WESDR showed that lower glycosylated haemoglobin at any stage of retinopathy prior to proliferative phase and any duration of diabetes was associated with lower incidence of retinopathy and progression of retinopathy.[20]

In our study, 78.2% had normal triglyceride levels with no retinopathy, 65.2% of mild NPDR cases had normal triglyceride levels, 69% of severe NPDR cases showed very high triglyceride levels and only 19% of PDR cases showed very high triglyceride levels. EURODIAB prospective study with sample size of 3250 in 31-euro diabetic centres showed triglycerides is significant risk factors for moderate to severe NPDR and PDR after adjusting for age, duration of disease, HbA1c and albumin excretion.[21]

The present study also attempted to compare BMI parameters to varying degrees of retinopathy, the analysis could not establish any significant correlation to the compared variables. Hence, we need a larger sample to study the varying effects of BMI with respect to retinopathy changes along with established contributing risk factors like blood glucose levels and altered lipid profile or dyslipidaemia.

CONCLUSION

Despite of the high prevalence of type 2 diabetes mellitus the incidence of high grade /severe diabetic retinopathy is less in South East Asia but the increase in mean age of survival in this region due to improved medical facilities the incidence of high-grade retinopathy might increase in coming years. The study revealed a strong association between duration of disease, hypertension and diabetic retinopathy. It was found that higher grade retinopathies severe NPDR, very severe NPDR and PDR showed to have both macroalbuminuria and microalbuminuria. But none of the above patients had normoalbuminuria. The cases with no retinopathy (excluding hypertensive cases) showed microalbuminuria suggesting that microalbuminuria can be early predictor of diabetic retinopathy.

The study showed strong association of microalbuminuria with retinopathy but was not correlating with grade of retinopathy. HbA1c levels were higher both in lower and higher grade of diabetic retinopathies. This might be partly attributed to the association of diabetic retinopathy and HbA1c but also fact that some patients were on either irregular treatment or on no treatment.

Serum triglyceride and serum cholesterol levels correlated with severity of grade of retinopathy and hard exudates. The study pointed out that higher triglyceride levels associated with more incidence of maculopathy. Serum HDL levels showed study decline against the severity of retinopathy. Serum LDL levels were high with increasing severity of retinopathy.

Summary: The study comprised of screening of 263 patients at tertiary centre during the period of two months for presence and grading of diabetic retinopathy. The patients were categorized into various grades of diabetic retinopathy according to the ETDRS classification. The fundus findings were correlated to the anthropometric and biochemical parameters namely serum lipid profile, HbA1c (glycosylated haemoglobin) and urine albumin excretion. The microalbuminuria was estimated by nephelometric method, serum lipids by oxidase – peroxidase and HbA1c by enzymatic microcolumn method.

The study showed there is strong correlation between systemic hypertension, duration of disease and severity of diabetic retinopathy. Patients with severe NPDR, very severe NPDR and PDR showed both microalbuminuria and macroalbuminuria. The cases with no retinopathy (excluding hypertensive cases) showed microalbuminuria suggesting that microalbuminuria can be early predictor of diabetic retinopathy HbA1c levels were high irrespective of the grade of retinopathy. Higher triglyceride levels and cholesterol levels showed association with higher grade retinopathy and maculopathy. Lower HDL levels showed an inclination towards higher grade retinopathy whereas higher LDL levels were associated with increased severity of retinopathy. However, one of the parameters under investigation the BMI and grades of retinopathy were not related as per our observation.

REFERENCES

1. Shukla UV, Tripathy K. Diabetic Retinopathy. StatPearls Publishing; 2021.
2. Ralston SH, Penman I, Strachan MWJ, Hobson R, editors. Davidson's principles and practice of medicine. 23rd ed. London, England: Elsevier Health Sciences; 2021
3. Sihota, Tandon R. Parsons' diseases of the eye. 23rd ed. New Delhi, India: Elsevier; 2019.
4. Yau JW, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care 2012; 35:556–64
5. Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: The All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2014. Indian J Ophthalmol 2016; 64: 38–44
6. Narendran V, John RK, Raghuram A, Ravindran RD, Nirmalan PK, Thulasiraj RD. Diabetic retinopathy among self-reported diabetics in Southern India: A population-based assessment. Br J Ophthalmol. 2002; 86:1014–8
7. Pradeepa R, Anitha B, Mohan V, Ganesan A, Rema M. Risk factors for diabetic retinopathy in a South Indian type 2 diabetic population – The Chennai urban rural epidemiology study (CURES) eye study 4. Diabet Med. 2008; 25:536–42
8. Kelly M West, Linda J Erdreich, Judy A Stober; A Detailed Study of Risk Factors for Retinopathy and Nephropathy in Diabetes. Diabetes 1 July 1980; 29 (7): 501–508.
9. Chang YC & Wu WC. (2013): Dyslipidemia and diabetic retinopathy. Rev Diabet Stud, 10: 121–132.
10. Idiculla J, Nithyanandam S, Joseph M, Mohan VA, Vasu U, Sadiq M. Serum lipids and diabetic retinopathy: A cross-sectional study. Indian J Endocrinol Metab. 2012;16(Suppl 2):S492-S494.
11. Zhou Y, Zhang Y, Shi K, Wang C. Body mass index and risk of diabetic retinopathy: A meta-analysis and systematic review. Medicine (Baltimore). 2017;96(22):e6754.

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12. Helen K. Li, Larry D. Hubbard, Ronald P. Danis, Adol Esquivel, Jose F. Florez-Arango, Nicola J. Ferrier, Elizabeth A. Krupinski; Digital versus Film Fundus Photography for Research Grading of Diabetic Retinopathy Severity. Invest. Ophthalmol. Vis. Sci. 2010;51(11):5846-5852
13. Kalk W J,Joannou J , S.Nteserco, P.Mohanlal. Ethnic differences in the clinical and laboratory associations with retinopathy in adult-onset diabetes'. Journal of Internal medicine1997; 241:31-37.
14. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: The Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci. 2005 Jul;46(7): 2328-33.
15. Klein BE, Moss SE, Klein R et al. The Winconsin epidemiological study of DR. XIII. Relationship of serum cholesterol and retinopathy to hard exudates. Ophthalmology 1991; 98:1261-65.
16. Rema M, Srivastava BK, Anitha B, Deepa R, Mohan V. Association of serum lipids with diabetic retinopathy in urban south Indians - The Chennai Urban Rural Epidemiology Study (CURES) Eye Study-2. Diab Med 2005; 23: 1029-36.
17. Rusty Serter, Sema Aral, Necdet Unuvar. Assement of early microangiopathic complications inn NIDDM '. Turk J med res 1993;11(3):140-45.
18. Klein R, Moss SE, Klein BE. Is gross proteinuria a risk factor for incidence of proliferative diabetic retinopathy? Ophthalmology, 1993 Aug;100(8):1140-1146.
19. Klein Ronald, Babera, Moss Scott. Relation of glycemic control to diabetic microvascular complications in Diabetes Mellitus'. Annals of Internal Medicine 1997; 241:31-37.
20. Tudor SM, Hamman RF, Boron A et al. Incidence and progression of diabetic retinopathy in Hispanics and non-Hispanics with type 2 diabetes mellitus. San Luis valley diabetic study, Colorado Diabetic care 1998;21:53-61.
21. Sjolie AK, Stephenson J, Aldington S et al. Retinopathy and vision loss in insulin dependent diabetes in Europe. The EURODIAB IDDM complications study: ophthalmology 1997 Feb;104(2):252-60

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