EPIDEMIOLOGICAL STUDY OF DIABETIC RETINOPATHY IN DIABETES MELLITUS PATIENTS IN TERTIARY CARE CENTRE

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ABSTRACT

OBJECTIVE

The study objective was to examine the effect of glycaemic control and variations on the incidence and progression of diabetic retinopathy (DR) among the diabetes mellitus patients visiting Medicine and Ophthalmology OPD Sapthagiri Medical college, Bangalore.

MATERIALS AND METHODS

10 patients with type 1 diabetes mellitus, and 70 persons with type 2 diabetes mellitus, visiting the Medicine OPD of Sapthagiri Medical College and referred to Ophthalmology department of the above to detect the Diabetic Retinopathy changes in a diabetes mellitus management programme conducted for 3 months in Bangalore, participated in the study. Patients who were followed up for 6 months the same above were also included in the study. Analyses were conducted to assess the relationship between the risk factors, incidence and progression of Diabetic Retinopathy among Diabetes Mellitus patients and management.

MAIN OUTCOME MEASURES

To determine the risk factors associated with it, stage of retinopathy diagnosed at presentation, management of it, and final visual outcome. The prevention is by strict glycaemic control, prompt use of anti-diabetic drugs and regular exercises. These included age and gender-adjusted prevalence of diabetes and diabetic retinopathy, [1] and correlation of prevalence with history-based risk factors.

RESULTS

The three months cumulative incidence of DR was 58 %in type I diabetes mellitus and 42 % among type II Diabetes mellitus. After controlling for known risk factors for DR,[1] a high baseline haemoglobin A_{1c} (HbA_{1c}), ethnicity, age, type of diabetes mellitus, duration were associated with the incidence of referable DR in patients with type 1 and type 2 diabetes mellitus. The age- and gender**-**adjusted prevalence rate of diabetes in urban Bangalore 28.2% (95% confidence interval [CI]), and the prevalence of diabetic retinopathy in general population was 3.5% (95% CI). The prevalence of diabetic retinopathy in the population with diabetes mellitus was 18.0% (95% CI). History-based variables that were significantly associated with increased risk of diabetic retinopathy included gender (women at greater risk 56.25%) use of insulin increases the probability of DR;[2] longer duration of diabetes 15 years showed increase of DR; and subjects with known family history of diabetes mellitus. Differences in the socioeconomic status[2] did not influence the occurrence of diabetic retinopathy.

CONCLUSION

It was revealed in the first study to report on the incidence and progression of DR in Bangalore that a high baseline $HbA_{1c,}$ ethnicity, and the presence of DR increased the risk of the development of other complications of the Diabetes mellitus among diabetics. The prevalence of diabetic retinopathy was 18% in an urban population with diabetes mellitus.

KEYWORDS

Diabetic Retinopathy, Diabetes Mellitus, Age incidence, Sex incidence, HbA1c, Duration of Diabetes, Smoking, type of diabetes, Hypertension, Hyperlipidaemia.

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INTRODUCTION: Diabetes mellitus (DM) is the metabolic disorder, primarily affecting the carbohydrate metabolism with secondary changes in the protein and fat metabolism.

History of DM is as old as medicine itself. Sushruta described it as "honey urine", since it is a chronic and progressive disorder, it is also known as melting of flesh in urine. Dobean in 1859, detected reducing substance sugar in the urine. Minkowsky in 1890 produced experimentally in

dog after pancreatectomy, a condition similar to DM. The whole life style of patient turned out to be magic wand in hands of Best, Banting and Charles in 1922 when they isolated insulin from B- cells of Langerhans in the pancreas.

Diabetic retinopathy (DR) is a major cause of blindness among the working age group as Diabetes holds the leading medical mystery. It is the bilateral ocular condition which is predictable but not preventable, runs a chronic and progressive course if untreated leads to total blindness. Wayn Jeger in 1869 first described the DR. Hiesberg in 1875 described the ophthalmoscopic changes in the fundus due to DR. Aston and Ballintoin in 1930 described in detail the histopathologic changes occurring in retinal vessels due to DR. Dobree in 1967 described the pathophysiology of PDR. According to the World Health Organization, India will become one of the major hubs of diabetic population during the next 2 decades; the number of cases of adult-onset diabetes mellitus will grow to nearly 80 million in 2030. Among people with diabetes, this translates to an overall prevalence of 34.6% for any DR, 7.0% for proliferative DR, 6.8% for Diabetic Macular Edema,[3] and 10.2% for sight-threatening DR.[4] Asians had the lowest prevalence and African Americans the highest noticed till now as DR was considered to be relatively infrequent in developing countries due to sectoral economics, diet and, longevity. In the Indian subcontinent, only limited data are available on the prevalence of DR in the general population. The Bangalore Urban Rural Epidemiology Study[5] reported the prevalence of DR in urban Bangalore to be 17.6% in diabetic population, and the study done in Sapthagiri Medical College reported the prevalence of DR (in self-reported subjects with diabetes) in urban South India to be 18%. Because diabetes and its complications are a public health problem, data on the prevalence of DR in diabetics will help in formulating primary and secondary prevention programmes for other complications associated with it namely neuropathy, cardiopathy, and nephropathy.

The study aimed at assessing the prevalence of DR in the urban South Indian general population of Bangalore. In type 1 diabetes, microaneurysms start to appear after 5 years in 25% of cases, affect half of cases at 10 years and nearly all patients after 20 years. Proliferative retinopathy, as defined by a formation of new vessels, appears after 10 years and affects about 40% after 20 years. Maculopathy[3] follows a similar pattern finally affecting 10-20% of cases. In type 2 diabetes, these changes may be found at diagnosis because subclinical hyperglycaemia may have been present for a prolonged preceding period. Over 25 years, there is a significant cumulative rate of progression to diabetic retinopathy (83%), to diabetic macular oedema (29%)[3] and clinically significant macular oedema (17%). Progression of retinopathy is associated with the severity and length of time hyperglycaemia exists, Hypertension and other cardiovascular risk. Renal disease, as evidenced by proteinuria and elevated urea/creatinine levels, is an excellent predictor of the presence of retinopathy.

MATERIALS AND METHODS:

Study Population: Every person known to have diabetes mellitus over the age of 12 years was referred to the Diabetic Retinopathy Screening Service organised by medicine department, Sapthagiri Medical College, apart from those excluded[6] on medical grounds (for example, those unable to attend screening owing to infirmity or comorbidity) or those already attending hospital based ophthalmology services because of retinopathy. Our three months retrospective analysis included data for all patients classified as having type 2 diabetes mellitus, diagnosed over the age of 12 years, and who attended screening between 1st Sept 2015 and 30th Nov 2015. Data were anonymised before undergoing statistical analysis.

Criteria for Selection

Inclusion Criteria:

1. Age: Between 12 years and 60 years.
2. Gender: Female are more prone.
3. Patients already diagnosed as DM (Type I or Type II) attending for routine ophthalmic check-up and inpatients admitted with various complications.
4. Diabetic with H/o Hypertension.
5. Diabetic with H/o Smoking.
6. Diabetic with Renal disease.
7. Diabetic with Obesity, BMI >30.
8. Pregnant women.

Exclusion Criteria:

1. All cases above 60 years.
2. Patients with acute complications of Diabetes like Hyperosmolar non-ketotic coma, ketoacidosis or acute infections.

Screening Procedure: After registration with the Diabetic Retinopathy Screening Service for Sapthagiri Medical College, each patient was investigated for blood: GRBS, FBS, PPBS, HbA1c, Blood urea, serum creatinine, and lipid profile. Urine routine investigation was also undertaken for detecting proteinuria and sugars. After thorough medical check-up patient was referred to ophthalmology department of the above College. A trained healthcare assistant assesses patients' current visual acuity in both eyes (achieved with or without glasses or with pinhole reading), using an illuminated 6 m Snellen chart. Tropicamide (1%) was then applied to each eye, and after about 15 minutes, two 45° digital retinal images per eye (one macular centred, and one nasal field) using a fundus camera was taken. The retinal images were graded then.

Diabetic Retinopathy Grading: The study participants were classified as type 1 or type 2 diabetes mellitus patients on clinical assessment, according to the American Diabetes Association.

Screening for DR was conducted with fundus camera with mydriasis, between 1st Sept 2015 and 30th Nov 2015. All retinal images were viewed and graded according to ETDRS classification. It classified DR as;

1. NPDR (Non Proliferative Diabetic Retinopathy): as mild, moderate and Severe.
2. PDR (Proliferative Diabetic Retinopathy): as mild, moderate and severe and among them as high risk PDR, Non High Risk PDR.

STATISTICAL ANALYSIS: We used descriptive analyses to characterise the study population and patterns of diabetic retinopathy, and used t tests and χ^2 tests to explore differences between patients without any retinopathy and those who developed any, background, or referable retinopathy. The presence or absence of diabetic retinopathy was determined after each screening event during the study period of 3 months. All data was anonymised before statistical analysis was conducted using SPSS® version 16. The population characteristics were described using means and standard deviations for continuous variables, and percentages for categorical variables. For people who developed retinopathy the time to development lay beat the screening time of 3 months were reviewed after 6 months for any progression of retinopathy changes.

We explored the effect of putative risk factors with available information (that is, age, sex, age at diagnosis, duration of diabetes mellitus, and treatment types) by incorporating them into this analysis. We did statistical analyses using SPSS version 16 and Stata version 10; evidence of significance was taken as $P<0.05$ unless otherwise stated. The results are reported with 95% confidence intervals (CIs).

RESULTS AND OBSERVATIONS:

1. DURATION OF DIABETES:

Duration of Diabetes in yrs.	Mild NPDR	Moderate NPDR	Severe NPDR	Non high Risk PDR	High risk PDR
< 5	2	-	-	-	-
5 -10	12	10	5	1	1
10-20	13	13	11	3	7
NEW	-	2	-	-	-

Table 1: Risk factors to diabetic retinopathy

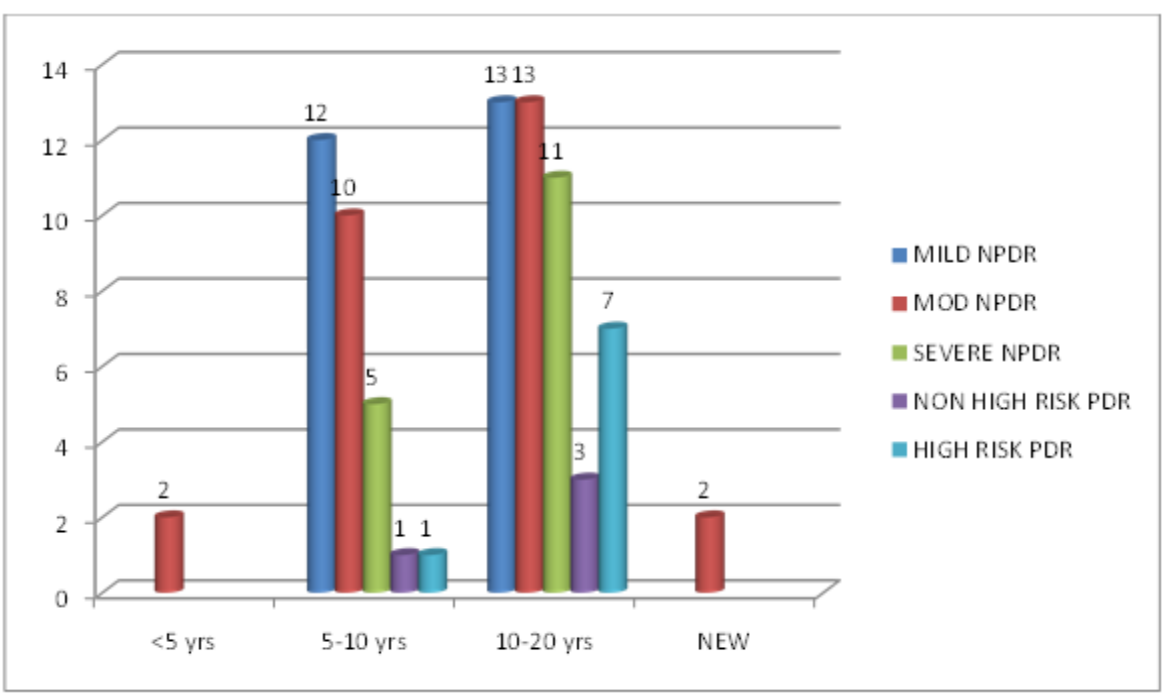

Figure 1

The prevalence of NPDR 15 to 20 years after the onset of NIDDM was high After 20 or more years, the cases of severe NPDR increased. PDR was more common among people with more than 15 years of DM. The duration of Diabetes remained the strongest predictor of any Diabetic retinopathy and its severity. Age at diagnosis of diabetes plays an important role as younger the patient at diagnosis of diabetes, longer the duration of diabetes before retinopathy becomes common.

2. **AGE OF ONSET OF DM:** Diabetes mellitus is more prevalent in the middle age group mainly between 30 to 50 years but DR is more prevalent in juvenile DM cases. The probability of developing the DR decreases after the age of 60 years as shown in our study.

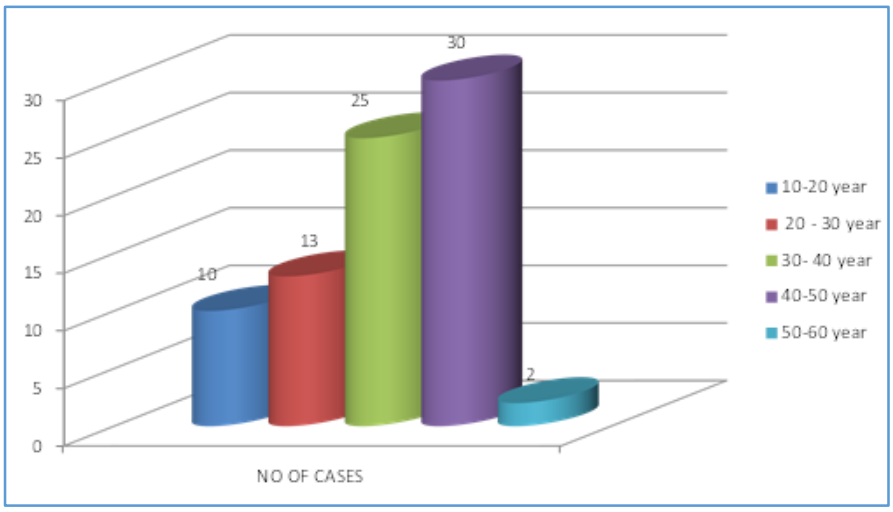

Figure 2

3. SMOKING:

Type of DR	No. of cases
Severe NPDR	10
Non high risk PDR	5
High risk PDR	7
DM	3
CSME	2
Table 2	

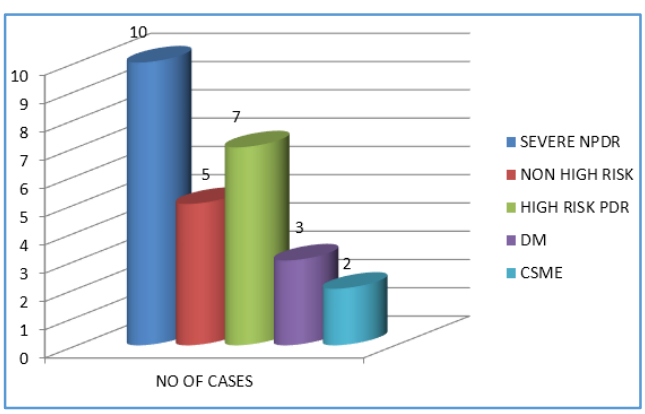

Figure 3

In this study, out of 80 patients, 29 patients have a known H/o of smoking, 6 patients have a longer H/o manifest with High risk PDR and 10 with severe NPDR as end products of tobacco increases hypercoagulable state in diabetic patients so number and duration of cigarettes smoked is important.

4. HYPERLIPIDEMIA:

Type of DR	No. of cases
Non high risk PDR	2
High risk PDR	4
Diffuse Maculopathy	6
Focal Maculopathy	3
Table 3	

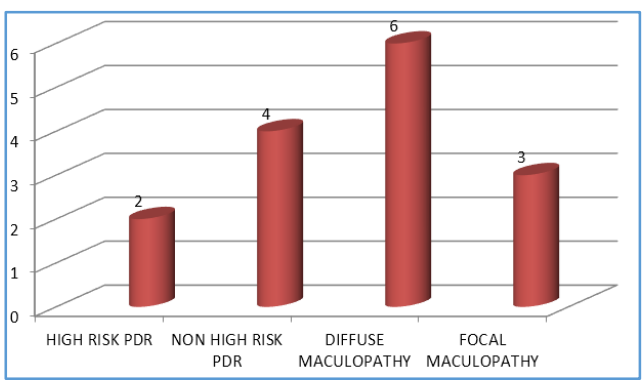

Figure 4

In this study out of 80 patients, 15 patients have elevated S. triglycerides and S. cholesterol, 6 patients manifest with diffuse maculopathy. Patients with elevated total cholesterol and LDL are likely to have diffuse hard exudates over macula leading to DR

5. HYPERTENSION:

Number of patients	Hypertensive	Normotensive
80	45	35
Hypertensive	**Mod-Severe NPDR**	**PDR**
45	33	12
Table 4		

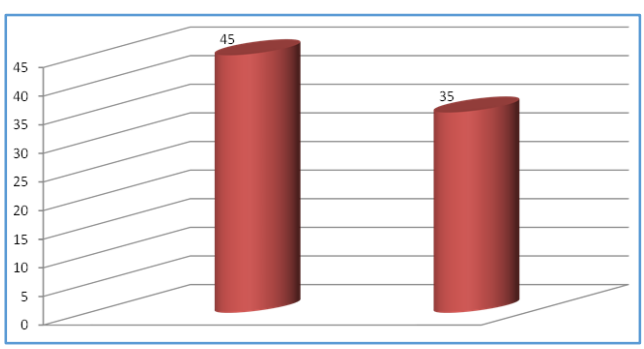

Figure 5

In this study, out of 80 patients, 45 patients have Systemic hypertension, out of which uncontrolled cases usually have proliferative retinopathy. In type 1 diabetes the development of diabetic nephropathy may play a major role in the subsequent development of hypertension since microalbuminuria is present in about 80% of type 1 diabetic subjects before the onset of hypertension in contrast to type 2 DM where already hypertension causes complication of DM.

6. SEX DISTRIBUTION:

Sex	Number of Patients with DM having DR	Percentage
Male	35	56.25
Female	45	43.75
Total	**80**	**100**

Table 5

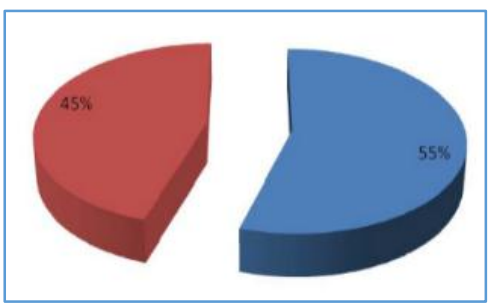

Figure 6

In the present study of 80 cases, 35 cases (43.75%) were males and 45 cases (56%) were females giving the picture that DR is more prevalent in females as DM is more prevalent in them.

7. EFFECT OF CONTROL OF BLOOD SUGAR LEVELS:

Elevated levels of glycosylated haemoglobin (HbA1C) in all the patients indicates the state of chronic uncontrolled hyperglycaemia which leads to the progression of background retinopathy to a state of proliferative retinopathy. Most of the patients under study have a value of HbA1C >7.2%.

The association of HbA1C with cardiovascular diseases and other diabetic microvascular complications is very much evident with our study. HAb1C normal values range from5.2% to 7.8%.

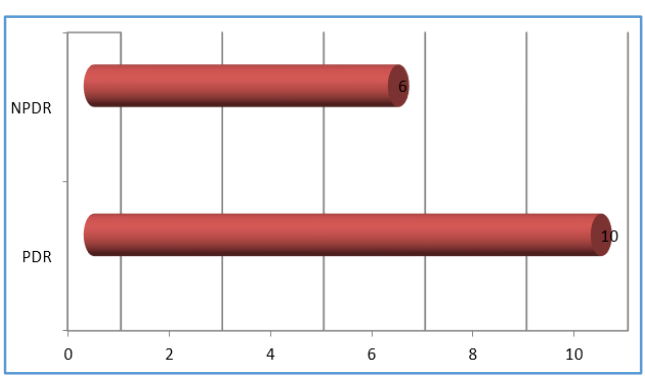

Figure 7

DISCUSSION: The seven-year cumulative incidence of any DR in persons with type 2 diabetes mellitus without previous DR was reported in two previous studies. There have been no similar studies with respect to type 1 diabetes mellitus. The seven-year incidence of any DR in persons without previous DR in the present study 80 cases was higher than that in a Shankar Nethralaya study[7] at 17%.The incidence rates of referable DR reported in this study are very similar to those previously reported in populations undergoing systematic screening in the UK.

It has been demonstrated in evidence from clinical trials that tight control of glycaemia reduced the risk of the incidence and progression of DR. Therefore, after controlling for other putative risk factors, baseline HbA_{1c} was a stronger predictor of the development of referable DR than the changing HbA_{1c} during the study. Also, there was an increased risk of developing referable DR in both type 1 and type 2 diabetes mellitus patients for every 1% increase in HbA_{1c} at baseline. Non-Caucasians were at an increased risk of developing DR (both type 1 and type 2 diabetes mellitus patients) when adjusting for other putative risk factors, including glycaemic control, which has previously been shown in prevalence studies in South Africa.[8,9] There is some evidence that HbA_{1c} may vary independently of glycaemia in people of different ethnicities.[10] Other possible explanations include ethnic differences in response to chronic glycaemia, as well as factors unrelated to glycaemia, such as the erythrocyte turnover or the rate of protein glycation, anaemia, haemolytic anaemia, thalassaemia and sickle cell anaemia. Therefore, whether the increased risk in incidence of referable DR in non-Caucasians is owing to differences in the underlying risk factors, or some sort of genetic propensity for DR, remains unknown. Clearly, achieving good glycaemic, blood pressure control, decrease in LDL, and increase in HDL is the first step in reducing the risk of the development and progression of DR. Duration of DM and DR plays a significant role in progression of DR.

The diagnosis of DR was made either clinically, using indirect ophthalmoscopy, or was made using fundus photographs. Regardless of the method used to detect DR, the prevalence of DR in India, inclusive of the present study, was 12% to 22.4%. In one study, however, the prevalence was high (26.2%), because the estimation was performed in a population with self-reported diabetes. Even the neighbouring Asian countries showed a similar trend (approximately 15%), except for Japan (38%, with a self-reported population with diabetes). In other countries such as the United States, the United Kingdom, Australia, and the West Indies, [11] the prevalence of DR was estimated to range from 28.5% to 50.3%; Although the exact reasons for these ethnic differences are not known, the likely reasons may be interaction of genetic susceptibility and protective factors in the population or lesser duration of diabetes, in reported series, in the Indian population. The mean duration of diabetes in the Wisconsin study was 11.8 years, as compared with 6.7 years in the present study.

CONCLUSION: In medicine department of tertiary care center of Sapthagiri Hospital, to conduct an epidemiological study of DR in DM cases for a period of 3 months from 1st September to 30th November 2015 in association with ophthalmological department we come to following conclusion;

As DM is more prevalent in middle age group of 30-50 years mainly type II the prevalence of DR is also seen in the particular age group more as duration of diabetes plays a crucial role in progression and development of DR as patients with 10-15 years of DM showed that 26 patients had NPDR changes and 21 had PDR changes. 15 patients in our study had high triglyceride levels of which most of them (9) went into maculopathy rest 6 had PDR changes. Hypertension also plays an important role in development of PDR and last but not the least the most important factor for chronic DM control (HbA1c) showed linear association with development of DR as 10 patients had PDR and 6 patients had NPDR changes among 16 patients with HbA1c levels high.

It is important to have screening camps like this to control DM and decrease the incidence of complication of DM.

REFERENCES:

1. Ramandeep Singh, Kim Ramasamy, Chandran Abraham, et al. Diabetic retinopathy: An update. Indian J Ophthalmol 2008;56(3):179–188.
2. Viswanath K, Murray Mc Gavin DD. Diabetic retinopathy: Clinical findings and management. Community Eye Health Journal 2003;16(46):21–24.
3. Jost B Jonas, Ingrid Kreissig, Antje Söfker, et al. Intravitreal injection of triamcinolone for diffuse diabetic macular edema. Arch Ophthalmol 2003;121(1):57-61. doi:10.1001/archopht.121.1.57.
4. Eye Diseases Prevalence Research Group. The prevalence of diabetic retinopathy among adults in the United States. Arch Ophthalmol 2004;122:552-63.
5. Eye Diseases Prevalence Research Group. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477– 85.
6. Van Spall HG, Toren A, Kiss A, et al. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: A systematic sampling review. JAMA 2007;297(11):1233-40.
7. Ramachandran A, Jali MV, Mohan V, et al. High prevalence of diabetes in an urban population in South India. BMJ 1988;297:587–90.
8. Cockburn N, Steven D, Lecuona K. Prevalence, causes and socio-economic determinants of vision loss in Cape town, South Africa. PLoS One. 2012;7(2):e30718. 10.1371/journal.pone.0030718 [CrossRef], [PubMed], [Web of Science ®].
9. Levy J, Jotkowitz AB. Diabetes in Africa: Screening for diabetic retinopathy. E J Internal Med 2010;21:145–6. 10.1016/j.ejim.2010.02.010 [CrossRef], [PubMed], [Web of Science ®].
10. Thomas RL, Distiller L, Luzio SD. Ethnic differences in the prevalence of diabetic retinopathy in persons with diabetes when first presenting at a diabetes clinic in South Africa. Diabetes Care 2013;36(2):336-41. 10.2337/dc12-0683 [CrossRef], [PubMed], [Web of Science ®].
11. Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27(5):1047–53.