# CLINICAL STUDY OF ASSOCIATION OF BMI WITH RETINOPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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**ABSTRACT**

**BACKGROUND**

Diabetes mellitus is known from the earliest times and its principal clinical symptoms were clearly recognised by the Hindus, Greeks and Arabians. Diabetes is a chronic illness characterised by either relative or absolute insulin deficiency leading to hyperglycaemia and other metabolic derangements. This is caused by the complex interaction of the genetic, environmental and lifestyle factors making the etiology multifactorial. Chronic hyperglycaemia will cause secondary pathophysiological changes in multiple organ systems and hence results in complications. Incidence and prevalence of diabetes increases with age in all ethnic groups. We wanted to study the association of BMI with retinopathy in patients with type 2 diabetes mellitus.

**METHODS**

We have studied a total of 50 patients of type 2 diabetes mellitus with respect to the various clinical presentations including visual disturbances. These patients are evaluated for duration of diabetes, changes in weight, central obesity, dietary habits & exercise pattern. Each patient was further evaluated with complete blood count, blood urea, creatinine, FBS, PPBS & fundus examination with direct ophthalmoscopy.

**RESULTS**

Out of 50 patients, 22 were having BMI of <25, of these, 6 patients have retinopathy and rest were having BMI of >25; of these, 13 patients were having retinopathy. 22 were male and 28 were females, out of 22 male patients, retinopathy was present in 4, whereas in females it is present in 15 members out of 28.

**CONCLUSIONS**

Our study results show that, retinopathy is noted in significant number i.e. 46.5% of obese patients (BMI >25 Kg/m$^{2)}$ of type 2 diabetes mellitus and females (i.e. 53.6%) are more affected than the males.

**KEYWORDS**

DM- Diabetes Mellitus, FBS- Fasting Blood Sugar, PPBS- Post Prandial Blood Sugar

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## BACKGROUND

Diabetes is chronic illness characterised by either relative or absolute insulin deficiency leading to hyperglycaemia and other metabolic derangements. This is caused by the complex interaction of the genetic, environmental and lifestyle factors making the etiology multifactorial. Chronic hyperglycaemia will cause secondary pathophysiological changes in multiple organ systems and hence results in complications. Incidence and prevalence of Diabetes increases with age in all ethnic groups.[1] There has been observed an increasing trend of shift of onset of diabetes to younger age in recent years.[2] This is attributable to the rise in childhood obesity.[3,4] This will add to the burden of Diabetes and its complications especially in developing countries. At the time of diagnosis of type 2 diabetes 8% of the patients already have cardiovascular disease, 18% have retinopathy of both eyes and 18% have micro albuminuria,[5] which is explained by the 4-7 year period of asymptomatic hyperglycaemia.[6] UKPDS and DCCT study findings suggest that intensive blood glucose control will lower the risk of eye diseases by 76%, kidney diseases by 50% and nerve diseases by 60%.[7-10] DM retinopathy is the leading cause of

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adult onset preventable blindness all over the world and important public health problem in India. Burden of DM nephropathy as cause of End Stage Renal Disease in US[11,12] and in India is high with prevalence of 30.3% compared to chronic interstitial nephritis (23%), chronic glomerulonephritis 17.7%.[13] Microalbuminuria in south Asian men and women was high by 1.2 to 1.7 times respectively compared to the Western world[14] Diabetic neuropathy is responsible for the sensory symptoms, non-traumatic foot amputations. Diabetic care involves addressing many issues beyond glycaemic Control. Obesity and Diabetes are the components of metabolic syndrome, which is the area of active research. Present study is intended to check the above reflections to our local population and to know the burden of diabetic micro vascular complications and obesity in patients attending the tertiary hospital. This may help in understanding the severity of problem and plan for appropriate steps needed to minimise these preventable complications.

***Doctors Banting and Best***

Diabetes Mellitus is known from the earliest times and its principal clinical symptoms were clearly recognised by the Hindus, Greeks and Arabians.[15] The sweet taste of urine is called Madhumeha by the ancient Hindus, suggesting DM might have been present in India before 2500 B.C.[16-17] Aretaeces described it as "melting down of flesh and limbs into urine." In 1815 Cherrenl discovered that sugar eliminated in urine among his patients is grape sugar - glucose. Sir Petters discovered acetone in urine of diabetic patients. Two separate forms of diabetes - diabetes insipidus and mellitus were defined by John Peter Frank. The name Insulin suggested by Schaefer in 1916. Banting and best found that administration of pancreatic extracts will decrease glycosuria in experimental animals.[17] DM nephropathy was discovered by the British Physician Clifford Wilson and Paul Kimmelstiel. This was published for the first time in 1936. Distinctive lesions in retina of diabetic patients was first documented by Jaeger.[18] Micro aneurisms were demonstrated by Nettles up in 1988. Application of laser photocoagulation was first reported in 1969. Early treatment and strict glycaemic control is useful in preventing visual loss in both proliferative retinopathy and macular oedema. This was established in 1980.[19] The documentation of the same was given by DCCT research group.[20] Syndrome of profound fall in BP/SBP/DBP on standing leading to faintness and syncope was first described by Bradbury and Eggleston in 1925. Rundles in 1945 showed it to be a feature of DM neuropathy.[21] WHO predicts the burden of epidemic of Diabetes is on rise in developing countries in 21st century. Estimated 285 million people i.e. 6.4% of world's adult population live with DM in 2010. This is expected to grow to 438 million by 2030 i.e. 7.8% of adult population. 70% of the world's diabetic population is living in low- and middle-income countries. India stands first with an estimated 50.8 million people living with DM with china occupying second position i.e. 43.2 million in 2011.[22] Type II DM accounts for 85-95% of all diabetics in affluent countries and even more in developing countries. Number of DM people in India, 19 million in 1995 has doubled to 40.9 million in 2007 and the projected incidence is 69.9 million by 2025.[22] Age group affected by DM is between 40-59 by 2030 it moves to 60-79. Largest number of deaths attributable to DM has increased by 5.5% over the estimated rate for the year 2007.[23] Prevalence of diabetes in India among both rural and urban adults in 2004 was 62.4/1000.[24] Genetic predisposition, ethnicity, industrialisation, decreased physical activity and increased obesity are the main reasons attributed to increasing incidence of Diabetes in low income countries.[25] Type II DM is 3-4 times more common in South Asians than Europeans.[26]

Pathophysiology of Diabetic Retinopathy: Elevated blood glucose levels per se and the metabolic pathways directly related to hyperglycemia, such as the polyol and hexosamine pathways, activation of the diacylglycerol-protein kinase C pathway, and accumulation of advanced glycation end products, are involved in the pathophysiology of D.R. Inflammation, alteration of retinal blood flow autoregulation, and hemorheological factors also play an important role in the pathogenesis of D.R. Thickening of the basement membrane, pericyte loss, and disruption of inter-endothelial tight junctions are characteristic pathophysiological mechanisms in early stages of DR. Microaneurysm formation and fluid extravasation from the intravascular to the interstitial space can lead to retinal thickening and hard exudates. This first stage is called non-proliferative diabetic retinopathy (NPDR), or the so-called background DR (Figure 1).

***Figure 1. Non-Proliferative Diabetic Retinopathy Showing Microaneurysms, Microhemorrhages, and Hard Exudates***

Loss of the capillary endothelium, thrombus formation, retinal leukostasis, and complete occlusion of the capillary lumen appear at later stages of the disease. Cotton-wool spots or soft exudates, reflecting infarct zones and intraretinal microcirculatory alterations, are hallmark features of pre-proliferative DR. (Figure 2). Basement membrane digestion by proteolytic enzymes is essential for angiogenesis (neovascularization). Degradation products and hypoxia are potent activators of angiogenesis. Hypoxia promotes vessel growth by upregulating multiple proangiogenic pathways, particularly the vascular endothelial growth factor (VEGF), which plays a pivotal role in the development of pathologic angiogenesis. This stage known as proliferative retinopathy (PDR) is characterized by growth of new vessels (Figure 3). The new vessels attached to the posterior hyaloid become fibrotic and may cause tractional retinal detachment. Vitreous haemorrhage may result from fragility and bleeding of neovascular vessels. Rupture of the inner or the outer blood retinal barriers leading to extravasation of the intravascular content and increased intravascular colloid osmotic pressure are early events in the pathogenesis of diabetic macular edema (DME). Proinflammatory cytokines and VEGF are involved in the breakdown of blood-retinal barrier. There is growing evidence suggesting that retinal neuro- degeneration is an early event in the pathogenesis of DR, which participates in the development of microvascular abnormalities.[27,28] This progressive degenerative process is characterized by neural apoptosis and reactive gliosis. Retinal neurodegeneration causes functional alterations, such as loss of color discrimination and reduced contrast sensitivity. Electrophysiological evaluation is the most sensitive method for detecting neurodegeneration. It is worth mentioning that electrophysiological abnormalities can appear even before that any impairment can be detected in the fundoscopic examination. Also, treatment based on neuroprotection opens up a new approach for preventing or arresting DR development. We wanted to study the association of B.M.I. with Retinopathy in patients with Type 2 Diabetes Mellitus, the prevalence of retinopathy in patients with diabetes mellitus.

***Figure 2. Proliferative Diabetic Retinopathy Showing the Presence of Neovascularization***

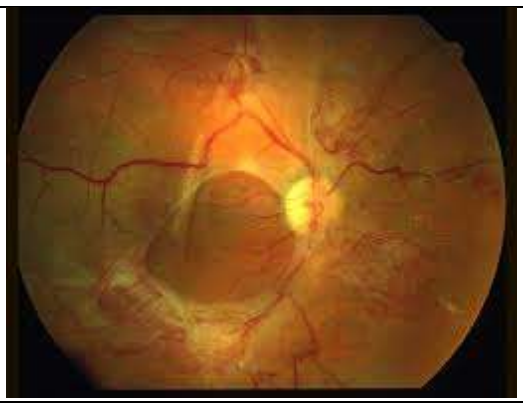


***Figure 3. Proliferative Diabetic Retinopathy and Tractional Retinal Detachment Caused by Fibrovascular Tissue***

## METHODS

### Study Design
Cross Sectional Observational Study.

### Setting
Patients attending medical OPD and those admitted as inpatients at Govt. Medical College Hospital, Anantapur.

### Study Period
October 2018 to March 2019.

### Sample Size
50 cases.

### Inclusion Criteria
All adult patients of age >20 yrs. with Type 2 Diabetes mellitus.

### Exclusion Criteria
Patients of type 2 diabetes mellitus with congestive heart failure, urinary tract infection, pregnancy, prostatomegaly, fever or known renal disease.

All patients who satisfies the inclusion criteria are thoroughly evaluated by clinical history and clinical examination for the microvascular complications and data recorded in the form of predesigned proforma. Anthropometric measurements are taken. BMI is calculated using the formula: Wt. in Kg ÷ Ht in $m^2$ - (ponderal index) BMI ≥25 are Obese and BMI <25 are non-obese (modified ATP III).

### Statistical Analysis
Analysis done in EXCEL using EPI Info software. Chi Square test was applied to know the statistical significance between the proportions. In all cases where Chi Square test can't be applied because the expected values in any of the cells is less than 5, Fisher's 1-Tailed corrected P values are used.

## RESULTS
Fundus examination done by using direct ophthalmoscope and findings confirmed by the Ophthalmologist and retinopathy graded as Non-Proliferative Diabetic Retinopathy (NPDR). Diabetic Maculopathy, Proliferative

Diabetic retinopathy, Advanced Diabetic Eye Disease. Other routine investigations including F.B.S., P.P.B.S, Serum cholesterol, R.F.T.,

## DISCUSSION

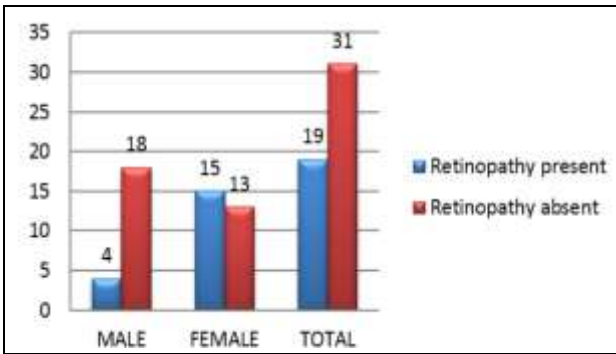
Type 2 diabetes is, because of its high incidence and high risk of diabetic microvascular complications, one of the potentially most damaging diseases. Diabetic eye disease and its complications, especially diabetic retinopathy which leads to macular edema and retinal neovascularization, are a leading cause of blindness and visual dysfunction in adults in economically developed societies.[29-30] Many epidemiological studies have already shown that the frequency of microvascular complications in diabetes is clearly correlated to duration of diabetes, quality of metabolic control and systolic blood pressure.[31] As the onset of type 2 diabetes occurs at least 4 to 7 years before clinical diagnosis and at the time of diagnosis many patients already have microvascular complications, the period of undiagnosed disease is considered to be even more harmful.[32] Therefore screening for diabetic late complications in type 2 diabetes is performed from the time of its diagnosis. The strict metabolic control in both, type 1 and type 2, diabetes unequivocally and significantly delays the onset and slows the progression of diabetic retinopathy.[33] Aggressive treatment of even mild-to-moderate hypertension also reduces significantly the risk of microvascular complications.[34] Besides those well-known risk factors, overweight and obesity are also very frequently found in type 2 diabetic patients. Obesity is a chronic, stigmatized disease whose incidence has increased nearly 50% in the past decade.[25-26] In our study increase in BMI associated with increase in retinopathy similarly seen in Damir Katsuk et al.,[28] where along with increase in BMI other parameters such as deterioration of HbA1c and significant increase in blood pressures associated with diabetic retinopathy, since our population is less, we concentrated mainly on BMI. Similar results were also found in Raman et al,[27] where it has been showed that obesity and waist hip ratio are independent risk factors for retinopathy in Type 2 diabetes mellitus and also it concludes that, isolated abdominal obesity and higher WHR in women are associated with diabetic retinopathy, and higher BMI offers a protective role. Thus, for assessing the risk of diabetic retinopathy, multiple obesity indices such as WC, WHR and BMI in combination seem to play a greater role rather than a single obesity index. In our study it is observed that females with high BMI develop more retinopathy as compared to their male counterparts with high BMI, in contrast to Mohamed Dirani et al,[26] where male population is more affected with retinopathy than the females, the difference may be because of higher study sample of the study and higher male patients got selected because the patient selection is done from retinal clinic where as in our study selection of the patient from medicine department. 38% of the total study population, 53.5% of females and 18.1% of males have retinopathy.

| BMI | Retinopathy Present | Retinopathy Absent |
|---|---|---|
| Series 1- <25 (n=22) | 6 | 16 |
| Series 2- >25 (n=28) | 13 | 15 |
| Total (n=50) | 19 (38%) | 31 |

***Table 1. Retinopathy with Respect to BMI***

| | Male | Female | Total | Percentage |
|---|---|---|---|---|
| Retinopathy present | 4 | 15 | 19 | 38% |
| Retinopathy absent | 18 | 13 | 31 | 62% |

***Table 2. Retinopathy in Patients with Type 2 DM (Gender Wise Distribution)***




***Graph 2. Bars Showing Retinopathy in Male & Female Patients with Type 2 DM***

***Figure 4. Retinopathy with Cotton Wool Spots***

## CONCLUSIONS

In conclusion, DR is a complex disease with several known and proposed risk factors. We have shown that BMI and sex are associated with DR in a clinical sample of diabetic patients. Our study results show that, retinopathy is noted in significant number i.e. 46.5% of obese patients (BMI >25 $Kg/m^{2)}$ of type 2 diabetes mellitus and females (i.e. 53.6%) are more affected than the males.

### Limitations

Prevalence of Retinopathy in study population is high compared to the population-based studies as this study is conducted in a tertiary hospital which is a referral centre.

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