# Risk Factors for Clinically Significant Macular Edema in Patients with Diabetes in Clinical Population

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***Abstract:- Aim:*** **To determine the risk factors of Clinically Significant Macular Edema (CSME) in patients with diabetic retinopathy in a Indian clinical population Bangalore.**

***Methods:*** **This is a case control study in which 150 patients were recruited Nonproliferative diabetic retinopathy (NPDR) with clinically significant macular edema (CSME) and 150 patients were recruited Nonproliferative diabetic retinopathy (NPDR) with Non-CSME. Univariate logistic regression to find out the relation in between duration of DM, Obesity, Hypertension (HTN), Fasting blood sugar (FBS), postprandial blood sugar (PPBS), Glycated Hb( HbA1c) and Anemia between the two groups.**

***Results:*** **Both groups were matched in terms of age, gender, Anemia ,fasting blood sugar (FBS), postprandial blood sugar (PPBS), Glycated Hb ( HbA1c) , Hypertension(HTN) and duration of diabetes were significantly higher in the CSME group(P<0.05). There was no significant difference for body mass index (BMI). univariate logistic regression analysis showed that Anemia were significantly higher odds ratio in the CSME.**

***Conclusion:*** **The most risk factors for developing CSME are Anemia, Fasting blood sugar (FBS), postprandial blood sugar (PPBS), Glycated Hb ( HbA1c), Hypertension(HTN) and duration of DM.**

***Keywords***:- *Systemic factors; clinically significant macular edema; diabetes.*

## I. INTRODUCTION

The major cause of central vision loss is diabetic macular edema which can be clinically significant (CSME) usually bilateral. Approximately 20% Prevalence rate in patients with Insulin-Dependent Diabetes (Type 1).It is the leading cause of blindness in people aged 20 – 64 years old. It is caused partly by dysfunction at the level of the inner blood retinal barrier, abnormally permeable retinal capillary endothelial cells of micro aneurysms, capillaries and intra retinal micro vascular abnormalities (IRMA).

Macular edema is clinically defined only when retinal thickening is noted on slit-lamp bio microscopy during the clinical examination, either with a contact or hand-held lens. It is divided into two types.

*A. Focal macular edema*

- It derives from individual micro aneurysms or small clusters of micro aneurysms that histo-pathologically leak in more limited extent.
- These micro aneurysms are usually seen in association with streaks or sots of hard exudate or with strictly delineated circinate hard exudate rings.

*B. Diffuse macular edema*

- It derives from extensively damaged capillaries, micro aneurysms and arterioles in a capillary bed that appears to be generally dilated.
- These dilated vessels have extremely hyper permeable walls and leak co-extremely hyper permeable walls and leak copious amounts of fluid.
- The major risk factors for D.R are long duration of diabetes, poor glycaemic control, Hypertension, Obesity, Increased Cholesterol, Kidney disease and Low hemoglobin.

## II. RESEARCH DESIGN AND METHODS

This cross sectional study will be conducted at Dr. Agarwal's Eye Hospital Bangalore 300 Indian patients with D.R. out of 1000 Indian Diabetic patients will be selected in Dr. Agarwal's Eye Hospital. The patients are divided into two groups. Groups 1 are patients with CSME and groups 2 are patients without CSME. All subjects will have either T1 DM or T2DM. They will be matched with sex and age**.** Diabetic patients will be diagnosed according to the World Health Organization criteria. The patients are explained about the purpose of study and a voluntary informed Consent Form is obtained and enrolled in to study.

## III. CSME ASSESSMENT

*A.* It is based on the ETDRS study

Retinal photography will be performed according to standardized protocols to detect D.R.

- Visual acuity will be assessed in decimal system using a standardized Early Treatment Diabetic Retinopathy study (ETDRS) logarithmic chart.
- Retinal photographs will be obtained after pupillary dilation
- CSME (Clinically significant macular edema) is based on examination by slit-lamp stereo-bio microscopy using 78D lens.
- The retinal thickness (µm) is defined using OCT.
- Retinal thickening within 500µm of fovea
- Hard exudates within 500µm of centre of fovea associated with retinal thickening
- Retinal thickening >1500µm with any part within 1disc diameter of centre of fovea

*B. Systemic factors Assessment*

- Subjects with diabetes are identified based on the American Diabetes Association criteria [15].
- Systolic (SCBP) and diastolic (DCBP) will be measured on the left arm after 5 min rest in a sitting position using Sphygmomanometer. Hypertension will be defined in subjects with a Blood Pressure >140/90 mm of Hg.
- Nephropathy in patients with Type 1 or Type 2 Diabetes.
- Creatinine (Cr) is measured by kinetic method and its high levels are defined as >2mg/dl.
- HbA1c (Glycated Hb) is measured by Cyanmethemoglobin method. High HbA1c levels are defined as ≥7%.
- Low hemoglobin levels are defined as <13.5g/dL for male and <12g/dl for female.
- High urea levels are defined as >50 mg/dl.
- Patients will be considered to be newly diagnosed subjects with diabetes if fasting blood glucose level is above 130 mg/dl and postprandial blood sugar is above 180mg/dl.
- Total serum Cholesterol, high density lipoproteins (HDLs) and serum triglycerides (cholesterol oxidase-peroxidase) are estimated. Low serum HDL cholesterol levels are defined as <40mg/dl for men and <50 mg/dl for women. High serum triglycerides levels are defined as ≥150 mg/L. Total serum Cholesterol are categorized into levels Border line is 200-239 mg/dl and high≥240 mg/dl.
- Obesity will be categorized into levels. BMI will be mentioned as Obese Class I 30-35 Obese Class II 35-40 and Obese Class III >40.

*C. Inclusion criteria*

- All patients aged≥40 years of either sex with Type 1 and Type 2 DM will be screened for DR

*D. Exclusion criteria*

- Patients who have undergone any intraocular surgery in the past 3 months.
- patients undergone any intraocular laser treatment or intraocular injection in the past 3 months.
- patients with history of intake of drugs (corticosteroids, nephrotoxic) in the past 3 months or any non-diabetic renal disease.
- patients suffering from non-diabetic maculopathy (age-related macular degeneration/macular dystrophy)
- patients with chronic liver disease.
- patients with significant media haziness preventing adequate visualization of the fundus.

## IV. RESULTS

*A. Demographic Characteristics*

300 patients with DR out of 1000 Diabetic patients. There are 96 males (54%) and 54 females (44%) with CSME and 81 males (46%) and 69 females (56%) with Non-CSME. The prevalence of CSME at baseline is 15%.

*B. Demographic Data of Recruited Patients Included Gender*

| | Group | | | |
|---|---|---|---|---|
| Gender | CSME | Non CSME | Total | P-Value |
| Male | 96 (54%) | 81 (46%) | 177 | 0.078 |
| Female | 54 (44%) | 69 (56%) | 123 | |

Table shows there is no statistically significant difference in gender between the two groups.

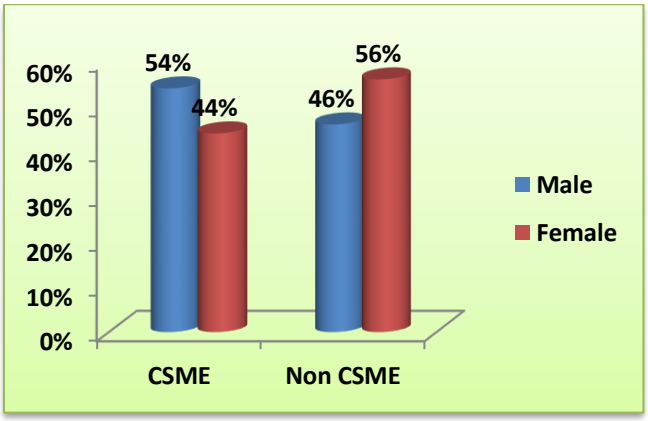


Fig 1:- Graph showing the difference in gender between the two groups

*C. Systemic factors in study groups*

- *Anaemia*

Table shows there is a statistically significant difference of CSME occurrence in Anemic.

| | Group | | | |
|---|---|---|---|---|
| | CSME | Non CSME | Total | P-Value |
| Anaemia | 61 (62%) | 37 (38%) | 98 | 0.003 |
| Non Anaemic | 89 (44%) | 113 (56%) | 202 | |

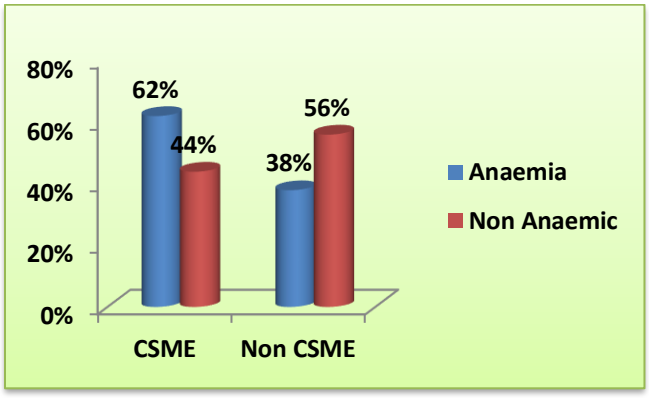


Fig 2:- Graph showing the difference of CSME occurrence in Anemic

- *Fasting blood sugar(FBS)*

| FBS | Group | | | |
|---|---|---|---|---|
| | CSME | Non CSME | Total | P-Value |
| ≥130 | 75 (65%) | 41 (35%) | 116 | <0.001 |
| <130 | 75 (41%) | 109 (59%) | 184 | |

Table shows there is a statistically significant difference of CSME occurrence in FBS level more or less than 130 mg/dl.

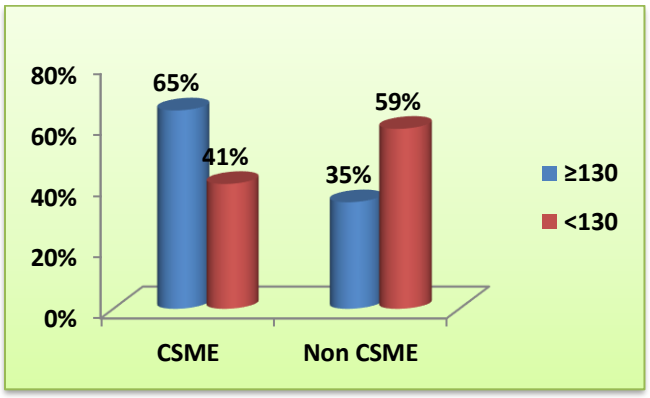


Fig 3:- Graph showing difference of CSME occurrence in FBS level more or less than 130 mg/dl.

- *Postprandial blood sugar(PPBS)*

| PPBS | Group | | | |
|---|---|---|---|---|
| | CSME | Non CSME | Total | P-Value |
| ≥180 | 112 (46%) | 132 (54%) | 244 | 0.003 |
| <180 | 18 (32%) | 38 (68%) | 56 | |

Table shows there is a statistically significant difference of CSME occurrence in PPBS level more or less than 180mg/dl

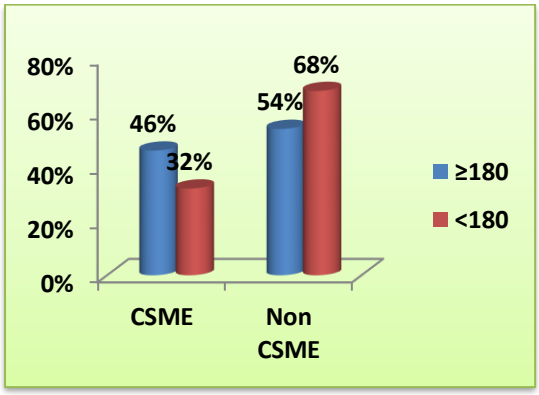


Fig 4:- Graph showing difference of CSME occurrence in PPBS level more or less than 180mg/dl

- *Glycated Hb (HbA1c)*

| HbA1c | Group | | | |
|---|---|---|---|---|
| | CSME | Non CSME | Total | P-Value |
| ≥7% | 99 (47%) | 110 (53%) | 209 | 0.156 |
| <7% | 40 (44%) | 51 (56%) | 91 | |

| HTN | Group | | | |
|---|---|---|---|---|
| | CSME | Non CSME | Total | P-Value |
| ≥140/90 | 91 (41%) | 129 (59%) | 220 | <0.001 |
| <140/90 | 21(26%) | 59 (74%) | 80 | |

Table shows there is no statistically significant difference of CSME occurrence in HbA1c level more or less than 7%.

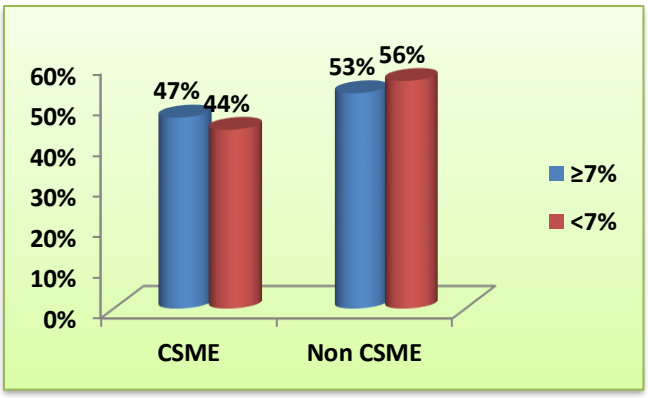


Fig 5:- Graph showing difference of CSME occurrence in HbA1c level more or less than 7%.

## V. HYPERTENSION (HTN)

Table shows there is a statistically significant difference of CSME occurrence in HTN

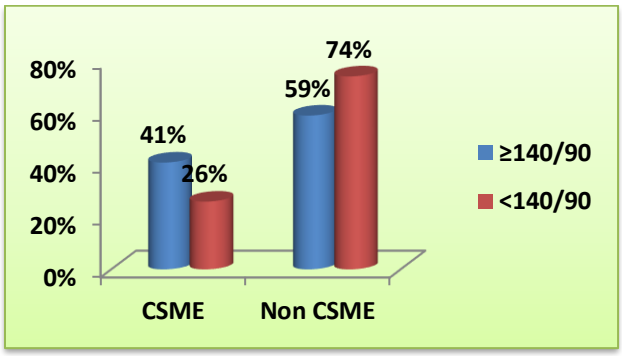


Fig 6:- Graph showing difference of CSME occurrence in HTN.

➢ *Duration of DM*

| Duration of DM | Group | | | |
|---|---|---|---|---|
| | CSME | Non CSME | Total | P-Value |
| >5 Years | 121 (53%) | 106 (47%) | 227 | <0.001 |
| ≤ 5 Years | 29 (40%) | 44 (60%) | 73 | |

Table shows there is a statistically significant difference of CSME occurrence in duration of DM.

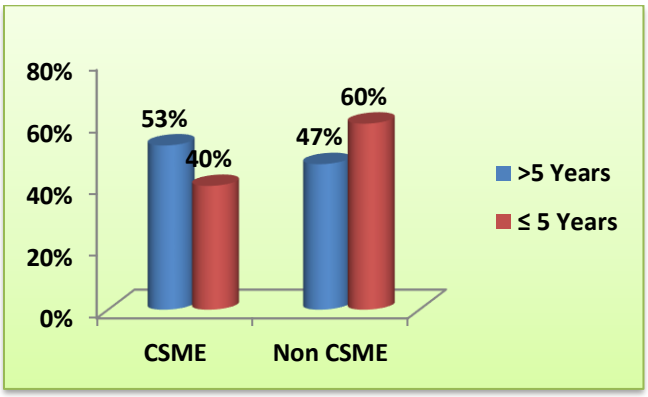


Fig 7:- Graph showing difference of CSME occurrence in duration of DM.

➢ *Obesity*

| | Group | | | |
|---|---|---|---|---|
| BMI | CSME | Non CSME | Total | P-Value |
| >30 | 1 (25%) | 3 (75%) | 4 | 0.314 |
| ≤30 | 149 (50%) | 147 (50%) | 296 | |

Table shows there is no statistically significant difference of CSME occurrence in Obesity

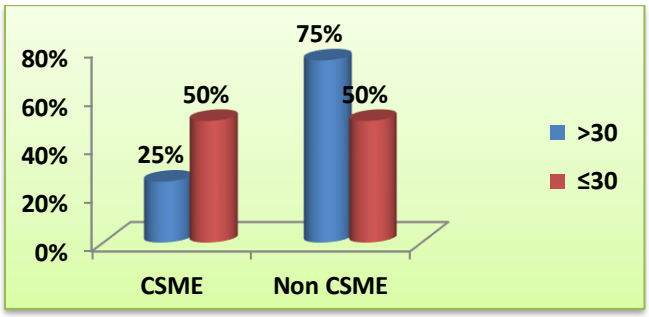


Fig 8:- Graph showing difference of CSME occurrence in Obesity

## VI. ODDS RATIO OF RISK FACTORS ASSOCIATED WITH CSME

*A. Univariate logistic regression for odds*

Age, gender, duration of diabetes, hemoglobin, FBS, PPBS and HbA1c is included in the regression analysis.

| | Univariate analysis | | |
|---|---|---|---|
| Factors | Odds ratio | 95% C.I | P-Value |
| Duration of DM >5 years | 1.73 | 1.01 – 2.96 | 0.045 |
| Anemia | 2.09 | 1.28 – 3.43 | 0.003 |
| FBS ≥ 130 | 0.37 | 0.23 – 0.61 | <0.001 |
| PPBS ≥180 | 0.40 | 0.22 – 0.74 | 0.004 |
| HbA1C ≥7% | 0.71 | 0.43 – 1.15 | 0.168 |

- *Systemic factors odds ratio in recruited patients*

Table shows there is a statistically significance difference of CSME occurrence in duration of DM (OR, 1.73**,** **95**% CI 1.01 – 2.96, P=0.045), Anemia (OR, 2.09, 95% CI 1.28 – 3.43, P=0.003), FBS (OR, 0.37, 95% C.I 0.23 – 0.61, P=<0.001) and PPBS (OR, 0.40, 95% C.I 0.22 – 0.74, P=0.004)

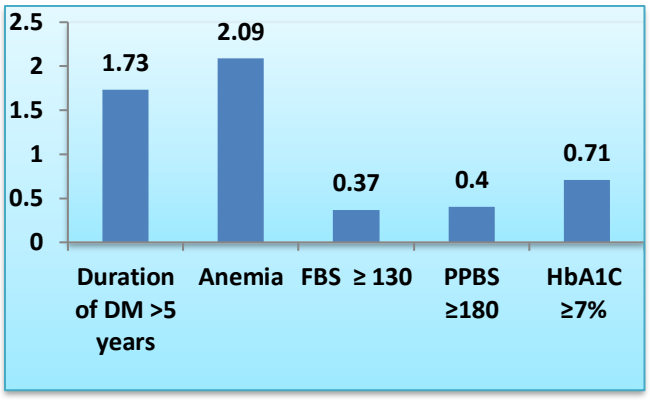


Fig 9:- Graph showing univariate logistic regression for odds

- *Systemic factors in study groups*

Significance difference of CSME and Non CSME occurrence in HbA1c (7.64 ± 1.73) and (7.14 ± 0.91)

## VII. DISCUSSION

This case control study is to evaluate the risk factors for CSME. The patients examined are Indian with Diabetes mellitus who had regular examination of fundus both clinically and using OCT. This study is designed so that only subjects with NPDR in both eyes are selected. We found that subjects with type2 diabetes with suboptimal (PPBS>180mg/dl), FBS>130mg/dl, HbA1c>7%, Anemia and Hypertension are statistically significant factors for CSME. It is also evident that poor glycemic control is the immediate cause for DR complication. Normally, blood glucose levels increase slightly after eating. This increase causes the pancreas to release insulin, which assists the body in removing glucose from the blood and storing it for energy. People with diabetes may not produce or respond

| | CSME | Non CSME | Total |
|---|---|---|---|
| Factors | Mean ± SD | Mean ± SD | |
| Hemoglobin | 12.16 ± 2.39 | 12.01 ± 1.85 | 0.679 |
| Fasting Blood sugar | 132.52 ± 44.15 | 139.76 ± 41.24 | 0.207 |
| Post Prandial Blood sugar | 205.67 ± 63.72 | 201.40 ± 49.68 | 0.585 |
| HbA1c | 7.64 ± 1.73 | 7.14 ± 0.91 | 0.029 |
| Central foveal thickness | 415.96 ± 56.64 | 227.40 ± 18.34 | <0.001 |

properly to insulin, which causes their blood glucose to remain elevated. Blood glucose levels that remain high over time can cause Thickening of capillary basement membranes. The United kingdom prospective Diabetes Study (UKPDS), which involved newly diagnosed patients with type 2 diabetes mellitus, revealed that the risk of retinopathy is reduced both improved glycemic control and blood pressure control. A 1% reduction in HbA1c reduced the risk for retinopathy by 31% and a 10 mm Hg reduction in systolic blood pressure reduced photocoagulation by 11%.

## VIII. CONCLUSIONS

Type 2 diabetes with suboptimal glycemic control and long –term hyperglycemia is probably responsible for the development of DR. and also observed an association of DR with Hypertension and Anemia. Diabetes mellitus, in general and diabetic retinopathy, in particular are progressive conditions, so regular follow-up care with a physician is crucial for detection of any systemic factors that may benefit from treatment

## IX. LIMITATIONS & FUTURE DIRECTIONS

There are cases where in spite of the risk factor being in control the patient has manifested with CSME and inverse holds true; patient with uncontrolled systemic factors presented with no evidence of CSME and to evaluate further as to how this happened with respect to confounding variables and other risk factors which were beyond the scope of the study. Future studies can be done: to compare between controlled and uncontrolled DM for Risk of CSME.

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