



## MACULAR OEDEMA IN RURAL CENTRAL INDIAN POPULATION ETIOLOGY, VISUAL IMPACT AND ASSOCIATIONS AND OUTCOME OF TREATMENT

Bodhraj Dhawan, Vaishali Dhawan, Anand Saraswat

Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India

### ABSTRACT

**Background:** Macular edema is a result of diverse etiologies, Diabetes and Hypertension being the most prominent, manifesting as Diabetic Macular edema and macular edema secondary to retinal vein occlusion. Present study aims to evaluate the causes, visual impact and associations of macular edema and outcome of treatment, in rural Indian Population. **Methods-** This prospective evaluation is based on evaluation of 100 consecutive patients of Macular edema, aged 18 years or more, presenting to a tertiary care ophthalmic facility. They were ophthalmologically evaluated and treated as per established protocols. **Results-** Mean age in the study population with macular edema was  $55.20 \pm 7.84$  years; with Male to female ratio of 2.44:1. Diabetic retinopathy (seen in 58%) eyes was commonest cause of macular edema, followed by RVO ( seen in 20%) of eyes. 92% of the patients received intra -vitreal injections for the treatment of macular oedema. Additional laser photocoagulation for co- existent diabetic retinopathy as an additional treatment was done in 48% of the cases and 5% received surgical treatment in form of vitrectomy. Pre treatment visual acuity was 6/18 to 6/36 in 40%, 6/60 in 19% and  $<6/60$  in 41% of the patients. Post treatment, the acuity proportions improved to 31% between 6 /6 to 6/12, 45 in 6/18 to 6/36 and 13% had 6/60 and 11% had less than 6/60. **Conclusions-** Systemic disorders have important causation on macular edema which causes significant effect on the visual status and the treatment with established protocols helps in betterment of visual status of these cases.

**Keywords:** Macular edema; Diabetic retinopathy; Retinal vein Occlusion; Anti VEGF Therapy

### INTRODUCTION

Macular edema is a significant cause of visual impairment and blindness. Diabetes is seen in India in Pandemic proportions making us the Diabetic capital of the world [1]. Diabetes causes blindness mainly due to diabetic macular edema (DME) [2]. Diabetic retinopathy is seen in significant percentage of diabetics [3]. Hypertension is frequently related to retinal veinocclusion [4]. Macular edema is frequent in retinal vein occlusions [5]. Macular degeneration is the most common cause of legal blindness in elderly to the tune of 1-3 percent of population associated with macular edema in advanced disease 6. Life style related stress causing serous macular detachment associated with macular edema is a frequent finding in young stressed up personalities 7. The present study aims to understand the relative etiological affections of various disorders as a cause of macular edema and its impact on the visual status of the eyes and the outcome of the treatment. **Aim:** To study the Etiological factors, Visual status and systemic associations of macular edema in rural Indian population in central India.

### MATERIAL AND METHOD

An observational study was conducted in patients at-



eISSN: 2395-0471

tending the eye OPD in the Department of Ophthalmology of tertiary health care center. A total of 100 eyes of subjects aged 18 years or above with the macular oedema were included Patient's chief complaints were noted. Past history of Diabetes mellitus, Hypertension and Cardiovascular disease was recorded. Ocular history of any ocular trauma or ocular interventions like cataract surgery with duration and complications, Yag capsulotomy, prior laser photocoagulation, prior intra-vitreous injection for ocular conditions diagnosed elsewhere were recorded and a similar Family history was noted. Uncorrected and Best corrected visual acuity was recorded. A complete anterior segment slit lamp examination and a dilated fundus evaluation with slit lamp bio microscopy with 90Dioptre Convex lens and an indirect ophthalmoscopy with 20 Dioptre Convex lens was performed.

In the all patients (with macular oedema), Optical Coherence tomography (OCT) and Fundus Fluorescein angiography (FFA) was done as per standard protocol. All the patients received intra-vitreous injections with NSAIDs, while laser photocoagulation therapy was given as an adjuvant in some patients. Patients with advanced retinopathy and tractional membranes were treated with surgical plan (Vitrectomy). All patients received a minimum of 1 intravitreal injection based on visual acuity and central macular thickness on OCT. Injections were repeated (maximum upto 3 doses) based on ocular response to the Anti Vegf, as per Indian Guidelines [3]. At the end of 6 months OCT scan was performed to see the CMT in all patients.

**Correspondence:** Bodhraj Dhawan. Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India

## RESULT

**Demographic details:** A total 100 cases were enrolled in the study during one year of the study period. Majority of the study subjects were in the age group of 50 to 60 years (46%) followed by 60 to 70 years (31%) and 40 to 50 years (19%). Mean age was  $55.20 \pm 7.84$  years; and range was 35 to 70 years out of 100 cases 71 were male and 29 were female. Male to female ratio was 2.44:1. In the present study, out of 100 cases, 57 subjects had left eye involvement and 43% had right eye involvement.

**II. Systemic associations:** Most common systemic association of macular edema was Diabetes Mellitus (53%) followed by Hypertension in 53 %. Amongst 59 patients, who had diabetes; 37.29% had diabetes for >10 years, 33.90 % for 5 to 10 years and 28.81% for 0 to 5 years. (Fig 1). Amongst 53 patients who had hypertension; 52.83% had hypertension for 0 to 5 years, 30.19% had for >10 years and 16.98 % for 5 to 10 years.

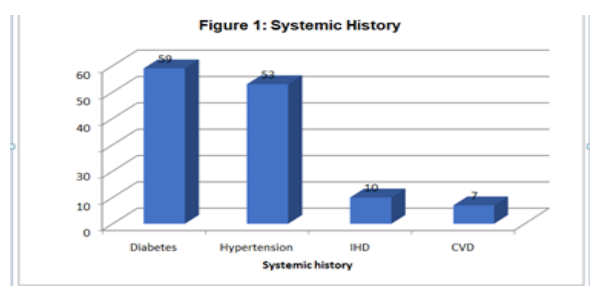


Fig 1: Distribution of systemic history

**III. Baseline visual status:** In the study population (n=100) 60% had the baseline visual acuity of 6/60 or less. However non of them on presentation had a visual acuity more than 6/18. This implies potential effect of macular oedema on baseline visual acuity causing blindness and visual impairment (Table 1).

Table1: Distribution of presenting visual acuity

| Visual acuity | Frequency |
|---------------|-----------|
| 6/18 to 6/36  | 40        |
| 6/60          | 19        |
| <6/60         | 41        |
| Total         | 100       |

**IV. Causes of macular edema:** In the study population (n=100), the leading cause of macular oedema was diabetic retinopathy (seen in 58%) eyes followed by RVO (seen in 20%) of eyes. CSR was the third common cause accounting for 12% of the eyes (Table 2).

**V. FFA findings:** All the study subjects (n=100) were subjected to FFA. Out of the 78 subjects with DME and RVO, the prevalence of focal, diffuse, mixed leaks and ischaemic maculopathy was seen in 30, 24, 21 and 3 eyes respectively. In ARMD (n=6), 2 eyes showed occult leak where as 4 eyes showed classical leak on FFA. In another 4 eyes, it showed unspecified leak. While in

4% ink-blot and 8% smoke-stack pattern noticed on FFA (Table 3).

Table 2: Causes of macular edema

| Final diagnosis (n=100)       | Frequency | %   |
|-------------------------------|-----------|-----|
| Diabetic retinopathy          | 58        | 58  |
| RVO                           | 20        | 20  |
| CSR                           | 12        | 12  |
| Uveitic CME                   | 1         | 1   |
| Exudative ARMD                | 6         | 6   |
| Retinitis pigmentosa with CME | 2         | 2   |
| Pseudo phakic CME             | 1         | 1   |
| Total                         | 100       | 100 |

Table 3: FFA findings

|                                | Frequency | %  |
|--------------------------------|-----------|----|
| Diabetic macular edema and RVO |           |    |
| Diffuse leak                   | 30        | 30 |
| Focal leak                     | 24        | 24 |
| Mixed leak                     | 21        | 21 |
| Ischaemic Maculopathy          | 3         | 3  |
| ARMD                           |           |    |
| Occult leak                    | 2         | 2  |
| Classical leak                 | 4         | 4  |
| Unspecified leak               | 4         | 4  |
| CSR                            |           |    |
| Ink-blot                       | 4         | 4  |
| Smoke-stack                    | 8         | 8  |

Table 4: Study of characteristic pattern visible on OCT

| Pattern on OCT                                              | No. of subjects |
|-------------------------------------------------------------|-----------------|
| Diffuse macular edema (Spongy macular edema)                | 21              |
| Cystoid macular edema                                       | 31              |
| Taut posterior hyloid without tractional retinal detachment | 6               |
| Foveal serous detachment                                    | 15              |
| Vitreo-foveal traction or Vitreo-macular traction           | 5               |

Table 5: Treatment given

| Intra-vitreous Anti-VEGF                      |   | No. patient |
|-----------------------------------------------|---|-------------|
| Number of injections                          | 1 | 4           |
|                                               | 2 | 2           |
|                                               | 3 | 86          |
| IVTA                                          |   | 7           |
| Systemic +Topical steroid                     |   | 1           |
| Total                                         |   | 100         |
| Additional treatment given                    |   |             |
| LASER/PRP                                     |   | 48          |
| Surgical treatment (for diabetic eye disease) |   | 5           |

VI. Pattern visible on OCT: Most of the study eyes with DME and RVO (n=78) had a cystoids pattern of macular oedema (31 eyes), it was followed by spongy macular oedema (21eyes). Neurosensory detachment was seen in 15 eyes. This is at par with the established clinical practices (Table 4).

VII. Treatment given: In the present study, about 92% of the patients received intravitreal injections of anti-VEGFs for the treatment of their macular oedema, out of which, 86 of them received 3 injections, 2 received 2 injections and 4 received single injection. We have also documented the use of intra vitreal steroids in 7% of the cases. About 1% of the cases also received systemic plus local steroid as a part of the treatment. About 48% of the cases had used LASER and 5% underwent surgical management (Table 5).

VIII. Visual acuity pre and post treatment: The visual acuity pre-operative was 6/18 to 6/36 in 40%, 6/60 in 19% and <6/60 in 41% of the patients. Post treatment, the acuity proportions improved to 31% between 6/6 to 6/18, 45 in 6/18 to 6/36 and 13% had 6/60 and 11% had less than 6/60. This difference was statistically significant. (Table 6).

Table 6: Visual acuity pre and post treatment

| Visual acuity        | Pre treatment     |     | Post treatment   |     | P value |
|----------------------|-------------------|-----|------------------|-----|---------|
|                      | No <sup>r</sup>   | %   | No <sup>r</sup>  | %   |         |
| 6/12 to 6/6          | 0                 | 0   | 31               | 31  | <0.001  |
| 6/18 to 6/36         | 40                | 40  | 45               | 45  |         |
| 6/60                 | 19                | 19  | 13               | 13  |         |
| <6/60                | 41                | 41  | 11               | 11  |         |
| Total                | 100               | 100 | 100              | 100 |         |
| CMT (µm)<br>Mean ±SD | 563.82±<br>227.42 |     | 296.46±<br>76.23 |     | <0.001  |

Treatment was effective in visual restoration in the study subjects. 76% of the study subject achieved a visual acuity better than 6/36 after treatment, there by signifying a positive prognosis (Fig 2).

FIGURE 2: Visual acuity pre and post treatment

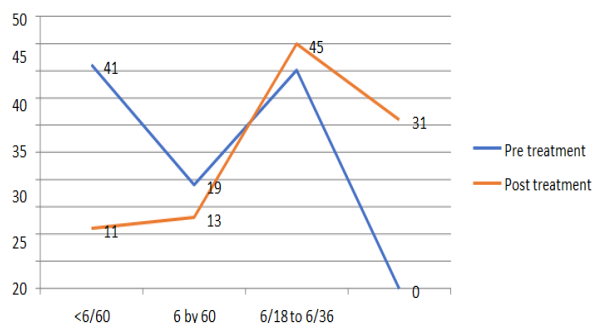


Fig 2: Visual acuity pre and post treatment

## DISCUSSION

Mean age in the study population with macular edema was  $55.20 \pm 7.84$  years; and range was 35 to 70 years.

Similar results have been reported elsewhere in literature with mean ages 54 years 8 and 57 years<sup>9</sup>. Out of 100 cases 71 were male and 29 were female. Male to female ratio was 2.44:1. We attribute this to probably more number of males seeking health care facility compared to females in Indian rural setting. Venkatesh P et al studied subjects who were 62% males and 38% females [8].

Systemic History revealed Diabetes Mellitus being the commonest association. This is attributable to high prevalence of diabetes in this age group and prolonged duration of systemic illness. Similar data has been published by Niazi MK et al, who reported the majority of the subjects were having duration of diabetes in the range of 5 to 10 years followed by more than 10 years in their study. They also reported that patients without retinopathy had macular edema in 21.1% cases, with mild to moderate retinopathy 28.2% had macular edema and 63.9% of advanced retinopathycases had macular edema [10].

Leading cause of macular oedema in our study was diabetic retinopathy (seen in 58%) eyes followed by RVO (seen in 20%) of eyes. CSR was the third common cause accounting for 12% of the eyes. Trichonas G et al summarized that the more frequent causes of macular edema are diabetic retinopathy, age related macular degeneration, venous occlusion, hypertensive retinopathy, central serous retinopathy [11]. Management Protocol in the present study, about 92% of the patients received intra-vitreous injections for the treatment of macular oedema. Additional laser photocoagulation for co-existent diabetic retinopathy as an additional treatment was done in 48% of the cases and 5% received surgical treatment in form of vitrectomy. This is accordance with established treatment protocols with special reference to Diabetic retinopathy [3].

On comparing Visual acuity and OCT thickness as markers of outcome of treatment it was observed that the Pre treatment visual acuity was 6/18 to 6/36 in 40%, 6/60 in 19% and <6/60 in 41% of the patients. Post treatment, the acuity proportions improved to 31% between 6/6 to 6/12, 45 in 6/18 to 6/36 and 13% had 6/60 and 11% had less than 6/60.

In the study population (n=100) 60% had the baseline visual acuity of 6/60 or less. However none of them on presentation had a visual acuity more than 6/18. This implies potential effect of macular oedema on baseline visual acuity causing blindness and visual impairment. Treatment was effective in visual restoration in the study subjects. 76% of the study subject achieved a visual acuity better than 6/36 after treatment, there by signifying a positive prognosis. The pre treatment OCT thickness was  $563.82 \pm 227.42$  and post treatment it was  $296.46 \pm 76.23$  and this difference was statistically significant. This concludes that the with existing treatment algorithm there is significant anatomical outcome in terms of reduction of foveal thickness as documented on serial OCT scans. This is in line with the suggested clinical protocol [12].

## CONCLUSION

Macular edema is a consequence of many ocular and systemic conditions. Anti-VEGFs therapy with or without lasers is the most accepted treatment protocol followed for macular oedema with reasonably good results as documented with gains in the vision and resolution of macular oedema based on OCT. Thorough systemic and ocular assessment in combination with good metabolic control and proper ocular treatment in cases of macular oedema leads to good functional and anatomical results.

**Competing interests:** The authors declare that they have no competing interests.

## REFERENCES

1. Sychareun V, Rowlands L, Vilay P, Durham J, Ghosal S, Batin M. The diabetes epidemic in India: where we stand and future projections. *J Indian Med Assoc.* 2013;111(11):751-4. PMID:24968484.
2. Klaver CCW, Wolfs RCW, Vingerling JR, Hofman A, de Jong PTVM. Age-specific prevalence and causes of blindness and visual impairment in an older population: The Rotterdam Study. *Arch Ophthalmol.* 1998;116(5):653-8. doi:10.1001/archophth.116.5.653.
3. Giridhar S, Verma L, Rajendran A, Bhende M, Goyal M, Ramasamy K, et al. Diabetic macular edema treatment guidelines in India: All India Ophthalmological Society Diabetic Retinopathy Task Force and Vitreoretinal Society of India consensus statement. *Indian J Ophthalmol.* 2021;69(11):3076-86. doi:10.4103/ijo.IJO\_1469\_21. PMID:34708746; PMCID: PMC8725123.
4. Noh GM, Lee H, Kwak HD, Kim HW, Lee SJ. Non-dipping pattern of nocturnal blood pressure as a risk factor for macular ischemia in branch retinal vein occlusion. *Sci Rep.* 2021;11(1):10505. doi:10.1038/s41598-021-89915-9. PMID:34006916; PMCID: PMC8131356.
5. Ang JL, Ah-Moye S, Kim LN, Nguyen V, Hunt A, Barthelmes D, et al. A systematic review of real-world evidence of the management of macular oedema secondary to branch retinal vein occlusion. *Eye (Lond).* 2020;34(10):1770-86. doi:10.1038/s41433-020-0861-9. PMID:32313172; PMCID: PMC7608462.
6. Heesterbeek TJ, Lorés-Motta L, Hoyng CB, Lechanteur YTE, den Hollander AI. Risk factors for progression of age-related macular degeneration. *Ophthalmic Physiol Opt.* 2020;40(2):140-70. doi:10.1111/opo.12675. PMID:32100327; PMCID:PMC7155063.
7. Park JB, Kim K, Kang MS, Kim ES, Yu SY. Central serous chorioretinopathy: Treatment. *Taiwan J Ophthalmol.* 2022;12(4):394-408. doi:10.4103/2211-5056.362040. PMID:36660123; PMCID: PMC9843567.
8. Venkatesh P, Tibrewal S, Bhowmik D, Tripathi M, Ramakrishnan S, Vashist N, et al. Prevalence of systemic co-morbidities in patients with various grades of diabetic retinopathy. *Indian J Med Res.* 2014;140(1):77-83. PMID:25222781; PMCID: PMC4181164.
9. Sander B, Larsen M, Engler C, Strøm C, Moldow B, Larsen N, et al. Diabetic macular oedema: a comparison of vitreous fluorometry, angiography, and retinopathy. *Br J Ophthalmol.* 2002;86(3):316-20. doi:10.1136/bjo.86.3.316. PMID:11864891; PMCID: PMC1771034.
10. Niazi MK, Ameen SS, Saeed K, Yaqub MA, Khan MD. Retinopathy risk factors among diabetics in a tertiary care military hospital. *Pak Armed Forces Med J.* 2011;1(1):38.
11. Trichonas G, Kaiser PK. Optical coherence tomography imaging of macular oedema. *Br J Ophthalmol.* 2014;98 Suppl 2:ii24-9. doi:10.1136/bjophthalmol-2014-305305. PMID:24934220; PMCID:PMC4208347.
12. Nguyen QD, Brown DM, Marcus DM, Boyer DS, Patel S, Feiner L, et al.; RISE and RIDE Research Group. Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE. *Ophthalmology.* 2012;119(4):789-801. doi:10.1016/j.ophtha.2011.12.039. PMID:22330964