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Study of Uveitic macular edema using Stratus OCT.

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***Abstract*- Objectives:** To describe the patterns of macular edema in uveitis using Stratus optical coherence tomography and know the correlation between tomographic features and visual acuity

Design: Hospital based, cross sectional, analytical retrospective study

Methods: 50 patients with uveitis with fundoscopic evidence of macular edema in at least one eye who visited vitreo retina department of minto ophthalmic hospital were considered for the study. Patients underwent complete ophthalmic examination including best corrected visual acuity using Snellen visual acuity chart, slit-lamp examination, fundus biomicroscopy, indirect ophthalmoscopy and optical coherence tomography. Fluorescein angiography was performed if needed. The patterns of macular edema were noted along with the central retinal thickness on OCT for each eye observed and the findings were correlated with the best corrected Snellen visual acuity. Any other significant findings observed during the examination and investigation were noted and described.

Results: Sixty eyes of 50 patients were found to have uveitic macular edema. 3 types of macular edema were found on OCT; namely, diffuse macular edema (DME), cystoid macular edema (CME) and serous retinal detachment (SRD). 4 eyes had epiretinal membrane (ERM). DME was seen in 44 eyes (72%), CME in 7 eyes (12 %) and SRD in 10 eyes (16%). The mean CMT was 313.13 +/- 144.84µ. Mean BCVA was 6/18 (Snellen). The CMT had a moderately strong correlation with BCVA (Pearson r 0.546; p <0.0001). The correlation was significant in the DME and SRD groups, not in CME group.

Conclusion:3 types of macular edema were found on OCT-CME, DME and SRD. CMT correlated negatively with BCVA.

***Index Terms*-** Uveitis; Macular edema; Optical coherence tomography; Visual acuity; Cystoid macular edema.

I. INTRODUCTION

Macular edema is a common and vision limiting complication of uveitis. Recent studies have shown that three different types of macular edema-cystoid macular edema (CME), diffuse macular edema (DME) and serous retinal detachment (SRD) can be made out on optical coherence tomography associated with uveitis.[1, 2]Cystoid macular edema is considered to be a common type causing visual loss in uveitis patients.[7] Until recently, fluorescein angiography was used to detect and confirm macular edema. It is an invasive technique and has rare serious side effects like anaphylaxis[1]. Detailed interpretation of OCT images can replace fluorescein angiography for detection and monitoring of macular edema, especially in uveitis cases.[5]Optical Coherence Tomography(OCT) has been shown to be a safe, non invasive and effective diagnostic modality for investigation of macular diseases by allowing morphological assessment of macular edema by producing two dimensional images of the retina. It can be used to quantify macular edema objectively.[1]It is not compromised by a low or medium degree of optical haze.[4] It is more sensitive than slit-lamp biomicroscopy to small changes in retinal thickness[6] and can be used to objectively monitor patients with macular edema. In patients with cystoid macular edema (CME), a potential for vision recovery has been identified. DME is associated with a poor visual prognosis and a poor prognosis for vision recovery. SRD is associated with a high probability of vision recovery when observed alone or underlying CME eyes.[2]Many studies of uveitic macular edema have shown moderate to strong correlations between macular thickness measured by OCT and visual acuity.[1, 2, 3] Hence, it is important to detect macular edema early in the course of the uveitis disease and to know the morphological type so that appropriate treatment can be initiated at the earliest. Also, it is important to be able to quantitatively follow up the macular edema to know the response to treatment. Here, OCT forms an invaluable tool. This study aims to evaluate the different morphologic patterns of uveitic macular edema using OCT and correlate the patterns of macular edema and central retinal thickness with visual acuity.

II. MATERIALS AND METHODS

Records of Patients with uveitis and fundoscopic evidence of macular edema attending vitreo retina department at Minto Ophthalmic Hospital during the period of November 2010 to October 2012.Fifty patients with uveitis with fundoscopic evidence of macular edema in at least one eye were considered for the study. Patients underwent systemic and complete ophthalmic examination including best corrected visual acuity, slit-lamp examination, fundus biomicroscopy, indirect ophthalmoscopy and optical coherence tomography. The patterns of macular edema were noted along with the central retinal thickness on STRATUS OCT for each eye observed and the findings were correlated with the best corrected visual acuity. Any other significant findings observed during the examination and investigation were noted and described. Pearson's correlation was used for correlation. Unpaired t test was used for comparing the means between the subgroups to test for statistical significances. NOVA was used where appropriate. Data were analyzed using GraphPad InStat version 3.10

III. SELECTION CRITERIA

Inclusion criteria: a).Patients with uveitic macular edema b).Adequate media clarity for fundus visualization.

Exclusion criteria:a).Presence of coexisting ocular disease limiting visual potential b).Posterior uveitis lesions involving foveola, Macular edema due to other causes.

IV. OPTICAL COHERENCE TOMOGRAPHY

All OCT scans were performed through a dilated pupil. The macula was scanned first with fast macular thickness scan protocol and then line scan protocol in horizontal and vertical meridians as appropriate. The scans were taken with 6 mm length centered through the fovea as confirmed by the red free image on the computer monitor of the OCT scanner .The central macular thickness was taken from the central 1mm of the OCT scans. The scans were analyzed using the retinal thickness volume tabular protocol using the fast macular scans. The fast macular scans provided normative data for age matched controls which is colour coded. For qualitative analysis various protocols like proportional, normalize+align, gaussian smoothing, scan profile was used as appropriate. These various patterns of uveitic macular edema were scored based on their unique appearance on OCT imaging:

(1) Diffuse macular edema as increased retinal thickness (defined as greater than 200µm) with reduced intraretinal reflectivity and expanded areas of lower reflectivity, especially in the outer retinal layers greater than 200 µm in width

(2) Cystoid macular edema was identified by the localization of intraretinal cystoid-like spaces that appeared as round or oval areas of low reflectivity with highly reflective septa separating the cystoid-like cavities

(3) Taut posterior hyaloid without retinal detachment was defined as a highly reflective signal arising from the inner retinal surface and extending towards the optic nerve or peripherally.

(4) Foveal serous retinal detachment was defined as an accumulation of sub retinal fluid (which appeared dark) beneath a highly reflective elevation, resembling a dome, of the detached retina. The identification of the highly reflective posterior border of detached retina distinguished subretinal from intraretinal fluid; and

(5) Vitreo foveal traction or Vitreo-macular traction with detachment defined as a peak-shaped detachment of the retina.
The patients included in the study had the following 3 patterns as on STRATUS OCT

a). Diffuse macular edema b). . Cystoid macular edema c). Serous retinal detachment

Some patients also had epiretinal membrane (defined as hyper reflective band on the inner/anterior retinal surface with global or focal adhesions to the retinal surface[56]).

V. RESULTS

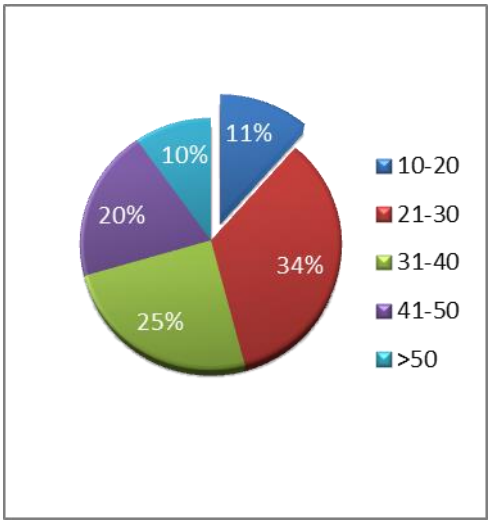


Fig (5.1): Age distribution of patients

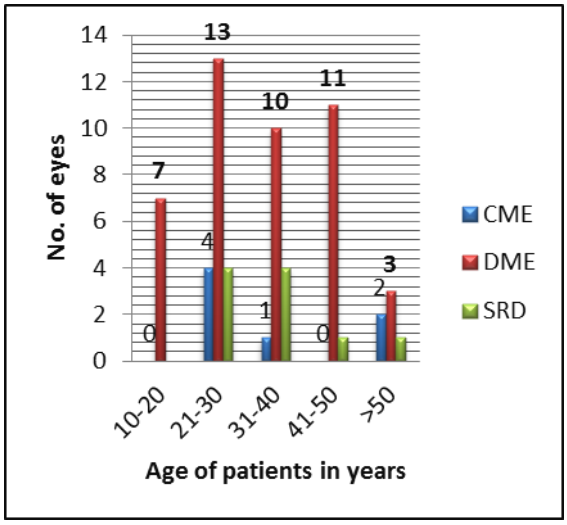


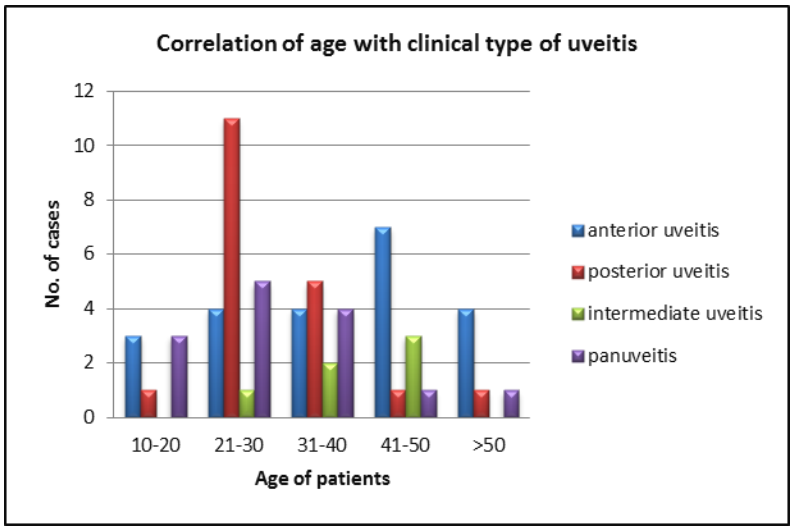
Fig (5.2): correlated with type of macular edema

Tab (5.1): Age of patients correlated with type of macular edema

Age (in years)	Number of eyes with CME	Number of eyes with DME	Number of eyes with SRD	No. of patients
10-20	0	7	0	5
21-30	4	13	4	17
31-40	1	10	4	13
41-50	0	11	1	10

>50	2	3	1	5
Total	7	44	10	50

Most of our patients in this study were between the age group of 21- 30 years. DME seems to be the most common type of macular edema irrespective of age of patients.



Fig(5.3): Correlation of age with clinical types of uveitis

Tab(5.2): Correlation of age with clinical type of uveitis

Age (in years)	**Anterior uveitis**	**Posterior uveitis**	**Intermediate uveitis**	**Panuveitis**	**Total**
10-20	3	1	0	3	7
21-30	4	11	1	5	21
31-40	4	5	2	4	15
41-50	7	1	3	1	12
>50	4	1	0	1	6
Total	**22**	**19**	**6**	**14**	**61**

Anterior uveitis seems to be more common in patients above age 40 years. Number of posterior uveitis cases was most in the age group of 21-30 years. Between the ages of 31-40 years, all types of uveitis cases were seen with almost equal distribution.

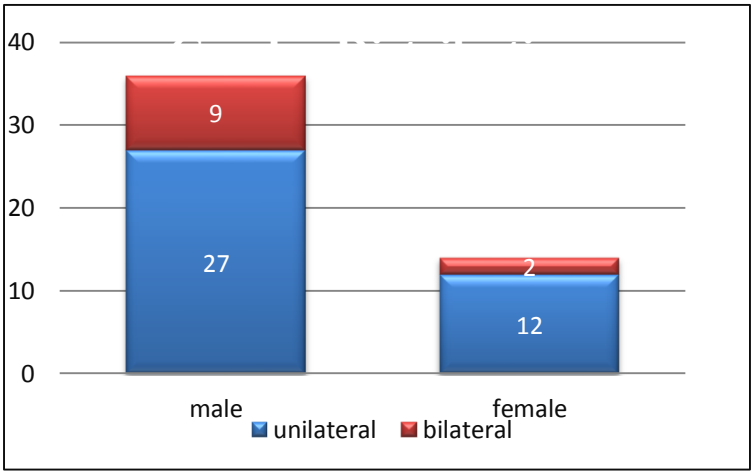
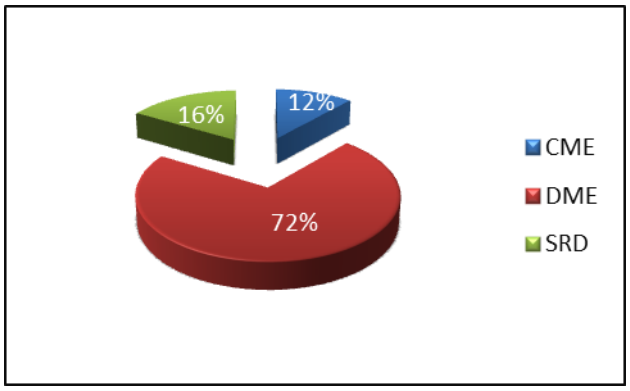


Fig (5.4): Gender distribution

Tab(5.3): Gender Distribution of Patients

	Male	**Female**
Unilateral	27	12
Bilateral	9	2
total	36	14

Most of our patients were males. The bilaterality of uveitis also seems to be more in male patients.

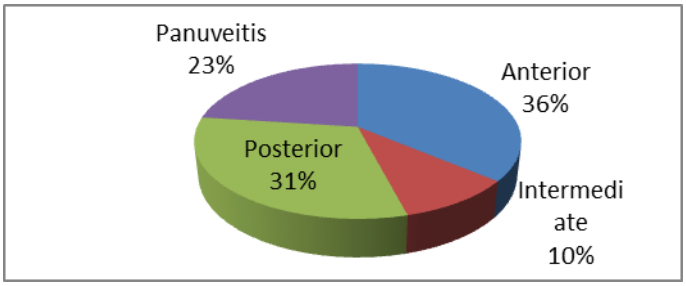


Fig(5.5): Types of macular edema on OCT

Table 5.4: Types of macular edema on OCT

Type of macular edema on OCT	**Number of eyes**
CME	7
DME	44
SRD	10
Total	61

DME was the most common type of macular edema that we saw on OCT (72%).



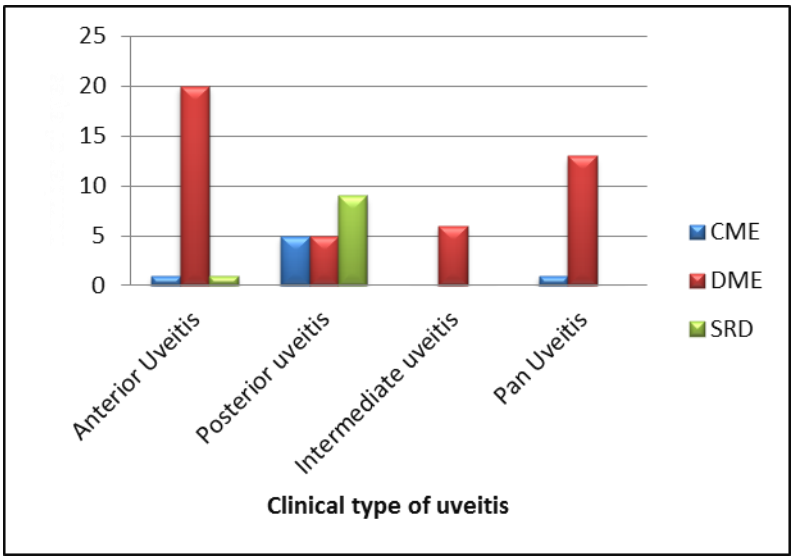
Fig(5.6): Anatomic types of uveitis

Anterior uveitis was the most common type of clinical uveitis in our study, followed by posterior uveitis.

Tab 5.5: Anatomic types of uveitis

Anatomic type of uveitis	Number of eyes	Percentage %
Anterior	22	36
Intermediate	6	10
Posterior	19	31
Panuveitis	14	23

Figure 5.7: Clinical types of uveitis correlated with type of macular edema

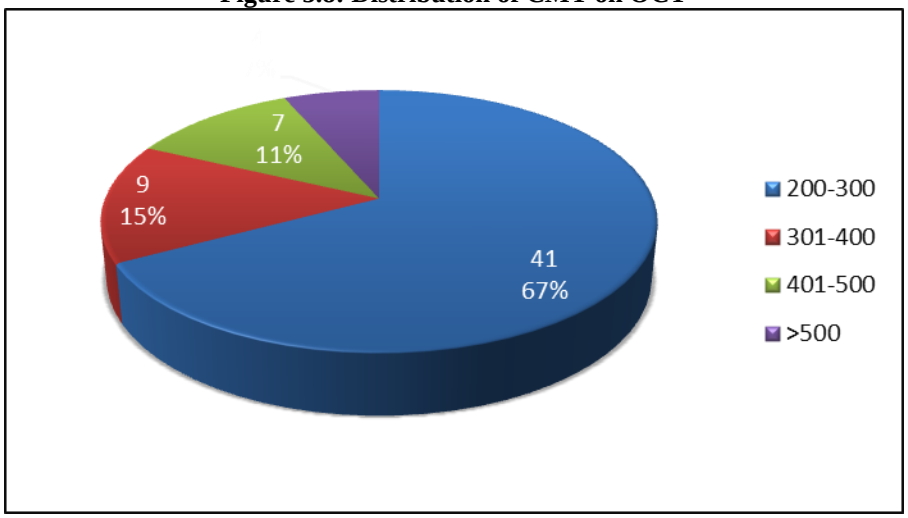


Tab 5.6: Clinical type of uveitis correlated with type of macular edema

	CME	DME	SRD
Anterior Uveitis	1	20	1
Posterior uveitis	5	5	9
Intermediate uveitis	0	6	0
Pan Uveitis	1	13	0
Total	7	44	10

Among anterior and panuveitis cases, diffuse macular edema was most commonly seen. In cases of posterior uveitis, SRD was the most common type of macular edema. It is interesting to note that in cases of intermediate uveitis, we found only DME and no other type of macular edema.

Figure 5.8: Distribution of CMT on OCT



Tab 5.7: Distribution of CMT on OCT

CMT in µ	number of eyes	Percentage %
200-300	41	67
301-400	9	15
401-500	7	11
>500	4	7

Most of our cases had CMT between 200-300 µ.

Fig(5.9): Correlation between CMT and type of macular edema

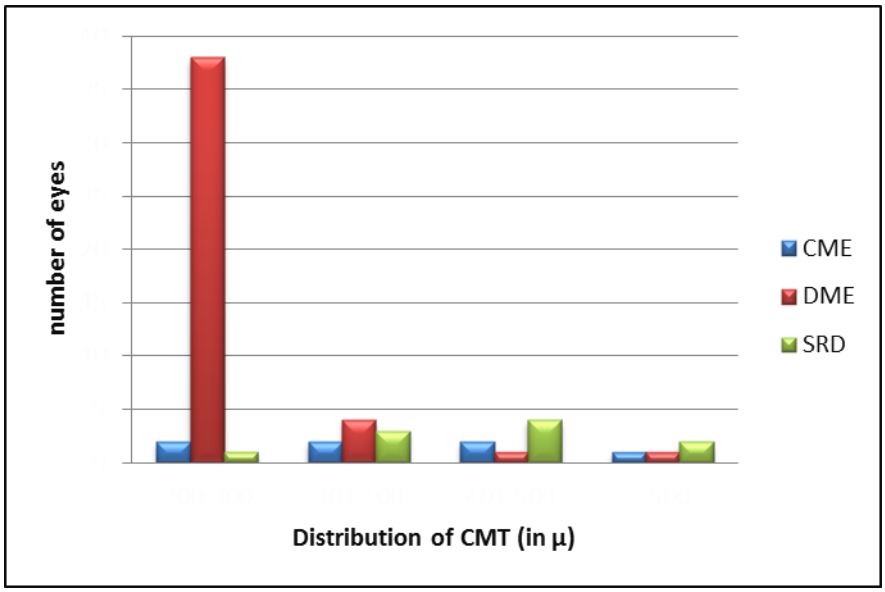
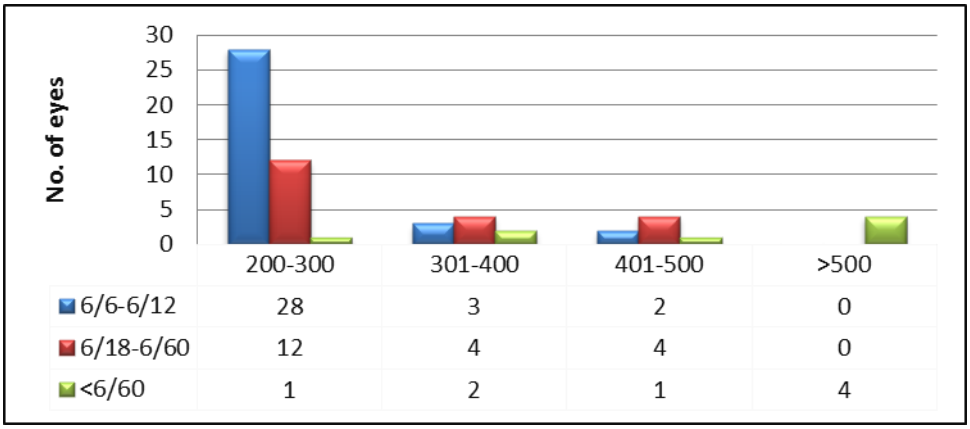


Table 5.8: Correlation of CMT with type of macular edema

CMT in µ	CME	DME	SRD
200-300	2	38	1
301-400	2	4	3
401-500	2	1	4
>500	1	1	2

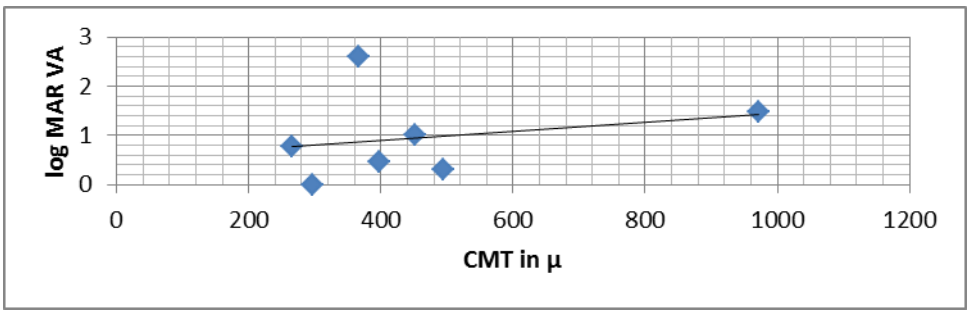
Most of our cases with CMT between 200-300µ had DME. The SRD cases had CMT most commonly between 300-500µ. The CME cases had almost equal distribution among all groups of CMT.

Fig 5.10 and Table 5.9: Correlation of CMT (in µ) with VA



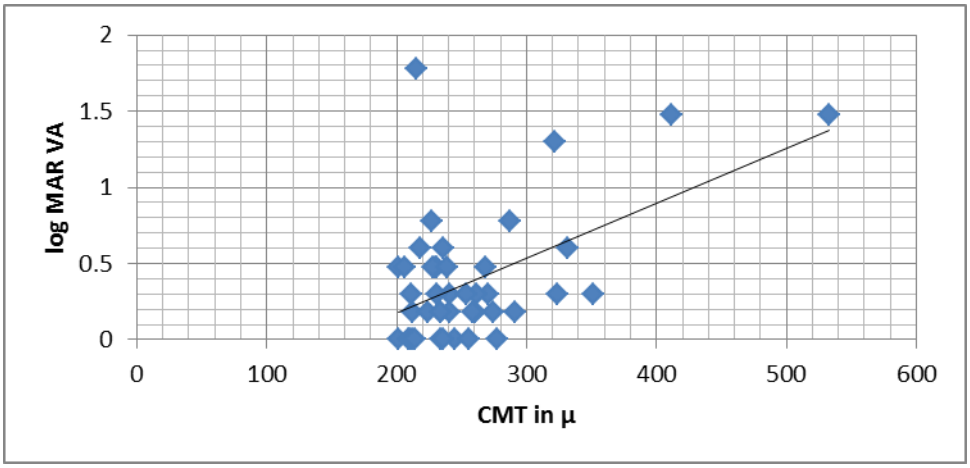
Most of our patients with CMT between 200-300 µ had good VA. As the CMT increased, the VA dropped. In fact, we found a moderately strong correlation between log MAR VA and CMT (Pearson's correlation r was 0.546).

Fig 5.11.a: Correlation between logMAR VA and CMT in eyes with CME



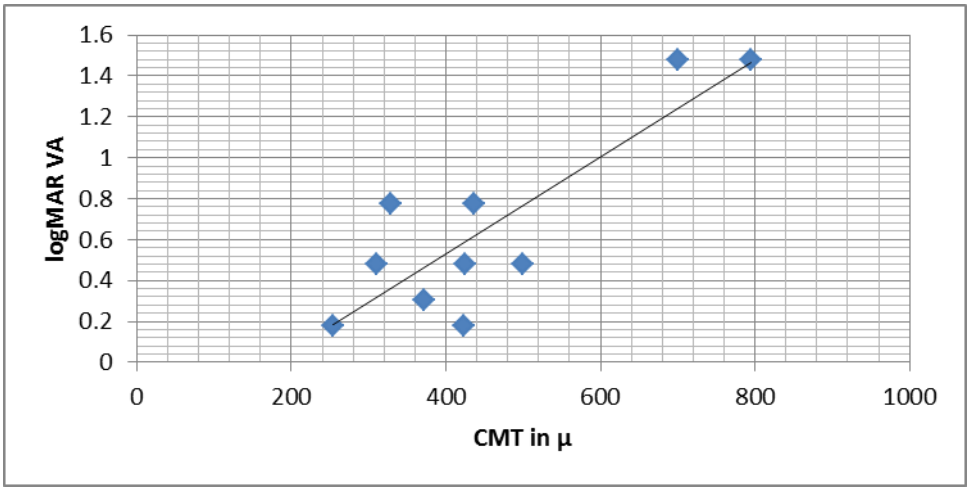
Correlation between CMT and logMAR VA in the CME group was not so significant (Pearson's r was 0.2).

Fig 5.11.b: Correlation between CMT and logMAR VA in DME group



The correlation between CMT and logMAR VA in DME group was significant (Pearson's r was 0.5181).

Fig 5.11.c: Correlation between CMT and logMAR VA in SRD group



The correlation between logMAR VA and CMT in SRD group was extremely significant (Pearson's r 0.851).

Tab 5.10.a: Comparison of means of CMT between RE and LE

	MEAN CMT (in µ)	STD. DEVIATION (in µ)
RE	339.64	180.12
LE	281.89	79.355

Difference in means between the 2 eyes was not statistically significant (p value 0.3581).

Table 5.10.b: Comparison of mean log MAR VA between RE and LE

	Mean log mar VA	Number of eyes
RE	0.5284+/-0.6073	33
LE	0.4534+/-0.4149	28

Difference in mean log MAR VA between the 2 eyes was not statistically significant (p value 0.5823).

Figure 5.12: Comparison of logMAR VA between the 2 eyes

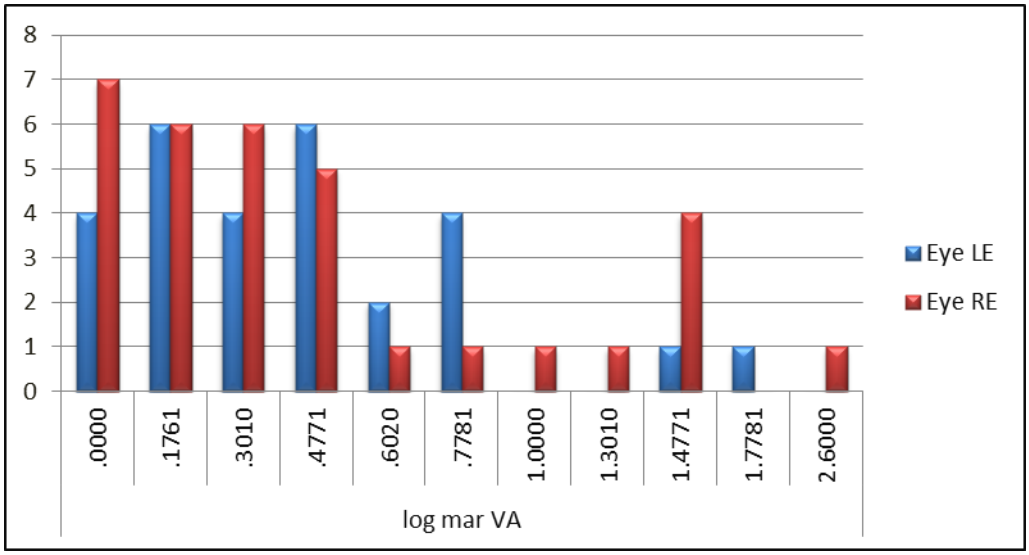


Figure 5.13: Distribution of VA

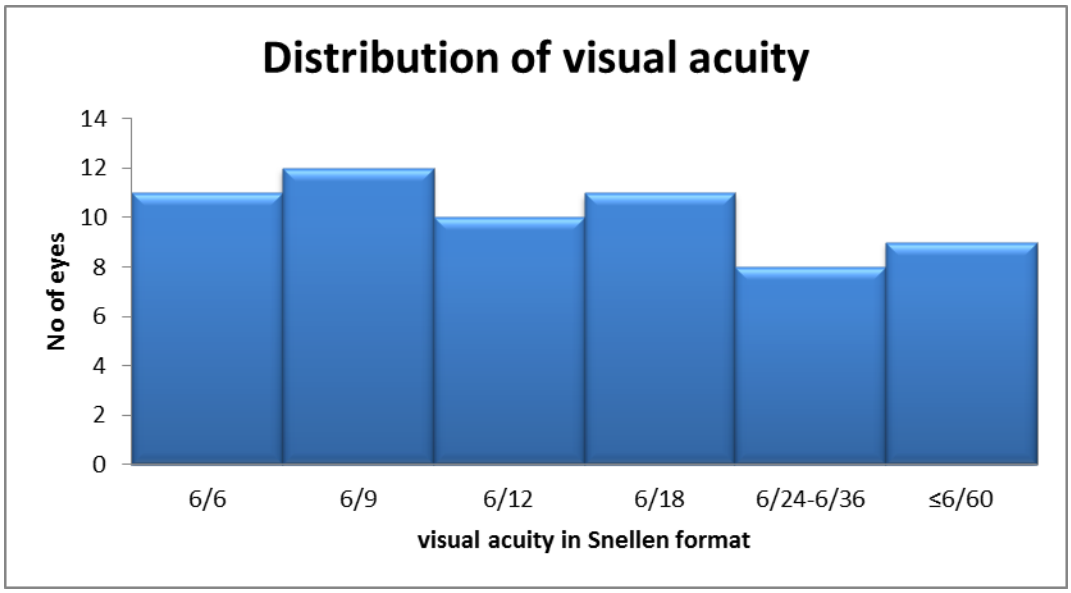


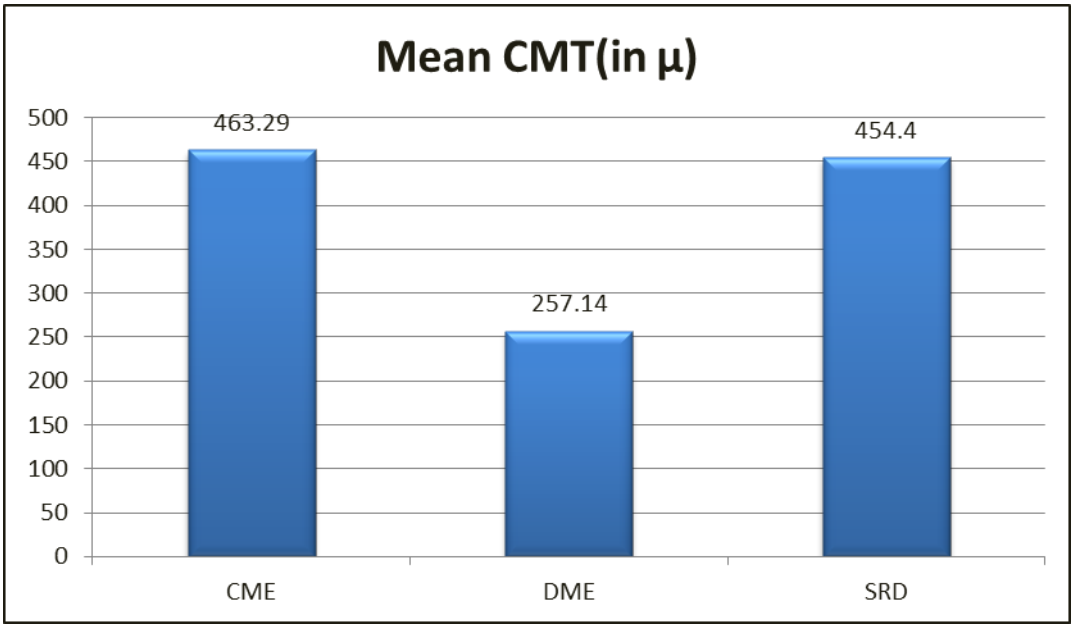
Table 5.11: Distribution of VA

Visual acuity	Number of eyes	Percentage %
6/6	11	18.12
6/9	12	19.6
6/12	10	16.4

6/18	11	18.12
6/24-6/36	8	13.1
≤6/60	9	14.75
total	61	100

The mean VA was 6/18. Distribution of visual acuity was even among the VA groups considered here.

Fig(5.14): Mean CMT of the 3 groups of macular edema



Tab(5.12): Overall mean CMT and VA

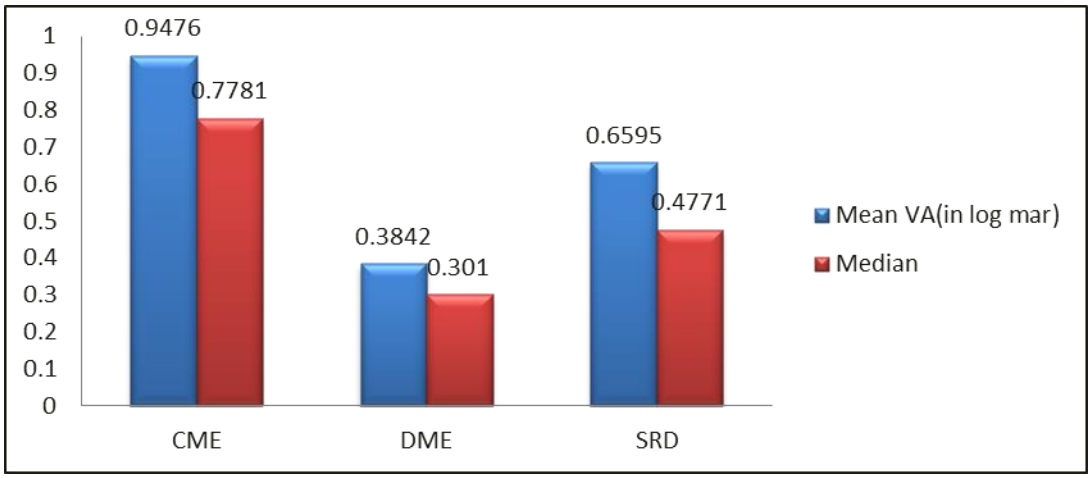
Variables	**Mean CMT (in µ)**	**Mean log mar VA**	**Approximate Mean VA in Snellen**
Overall (of all 61Eyes)	313.13+/-144.84	0.4854 +/- 0.4932	6/18

Table 5.13: Mean CMT and VA among the groups of macular edema

Variables	**Mean VA(in log mar)**	**Mean CMT**
CME	0.9476+/-0.87	463.29+/-238.34
DME	0.3842+/-0.42	257.14+/-60.909
SRD	0.6595+/-0.47	454.4+/-170.95

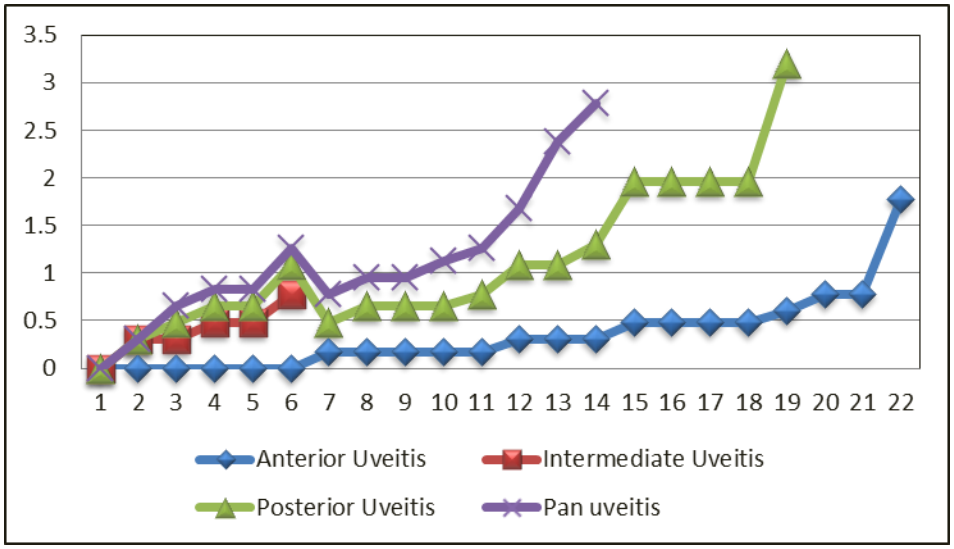
There was a significant difference in means of CMT between CME and DME groups and also between DME and SRD groups ($p < 0.001$), but not between CME and SRD groups (p 0.926).The difference in mean logMAR VA between the 3 groups was significant on ANOVA. Difference between CME and DME group was significant (p 0.0079); between DME and SRD group, it was not significant (p 0.1193). The difference between CME and SRD group was also not significant in terms of mean logMAR VA (p 0.3934).

Fig(5.15): Differences between the mean and median logMAR VA among the 3 groups



The mean logMAR VA of patients with DME seems to be the best. In fact, there is a statistically significant difference between the 3 groups on ANOVA, with DME group showing the best VA.

Fig(5.16): Comparison of VA among clinical types of uveitis



When the logMAR visual acuities were plotted in ascending order, it appears from the graph that patients of anterior uveitis seem to have the best vision.

VI. DISCUSSION

Optical Coherence Tomography(OCT) has been shown to be a safe, non invasive and effective diagnostic modality for investigation of macular diseases by allowing morphological assessment of macular edema by producing two dimensional images of the retina. It can be used to quantify macular edema objectively.[1]It is not compromised by a low or medium degree of optical haze.[4] It is more sensitive than slit-lamp biomicroscopy to small changes in retinal thickness[6] and can be used to objectively monitor patients with macular edema. Detailed interpretation of OCT images can replace fluorescein angiography for detection and monitoring of macular edema, especially in uveitis cases.[5] In this study, the morphologic patterns of uveitic macular edema were evaluated using OCT and the CMT was assessed for correlation with VA among the 3 sub types of macular edema

that were found on OCT. The patterns of macular edema that were found in this study are: diffuse macular edema (DME), cystoid macular edema (CME) and serous retinal detachment (SRD). DME was seen in 44 eyes (72%), CME in 7 eyes (12%) and SRD in 10 eyes (16%). Of the 10 SRD eyes, 5 were DME with SRD and 5 CME with SRD. In a study conducted by Markomichelakis et al[1], they found that DME was observed in 60.7 % cases, CME in 39.3% cases and RD in 20.2% cases (of 17 RD eyes, 5 were DME with SRD and 12 were CME with SRD). Of the 44 eyes with DME in our study, 4 eyes (9.1% cases of DME) had ERM and one had PVD. In the study by Markomichelakis, ERM was seen in 40.5% of cases of uveitic macular edema. The correlation of CMT with visual acuity was moderate in our study (using Pearson correlation r=0.5465, r^2=0.2986). Markomichelakis et al also found similar correlation (r^2=0.29). Among the sub groups of macular edema in our study, correlation was moderate in DME group (r^2=0.2684), very significant in SRD group (r^2=0.7241) and not so significant in CME group (r^2=0.0628). In our study, using multiple regression analysis, we found that age of the patient did not have a significant bearing on visual acuity (p value 0.1640) whereas CMT correlated significantly with VA (p < 0.0001). In the study by Markomichelakis et al, they found that age of the patient also correlated negatively with VA.The age distribution of patients in our study varied from 12 to 75 years with a mean age of 37 years. Most of the patients were aged between 21-30 years and 31-40 years with 17 and 13 patients (of the 50 patients) in the groups respectively. Only 5 patients were above the age of 50 years and 5 between 10- 20 years. Diffuse macular edema was the most common type of macular edema among all age groups; with diffuse macular edema being the only type of macular edema found in the 7 eyes of patients aged between 10-20 years. Between the ages of 10-20 years, anterior uveitis and panuveitis were seen in 3 eyes each. In the age group of 21-30 years, posterior uveitis was the most common type of uveitis seen with 11 eyes being diagnosed with posterior uveitis. The types of uveitis were evenly distributed in the age group of 31-40 years. Anterior uveitis was the more common type of uveitis seen in patients more than 40 years of age. Our study group consisted mostly of male patients- 36 of 50 patients were males. 27 of the 36 had unilateral uveitis; the other 9 patients had bilateral uveitis. 12 of the female patients had unilateral uveitis while the other 2 had bilateral uveitis. Among the anatomic types of uveitis seen in our study, anterior uveitis was seen most commonly- 36% (22 of 61 eyes had anterior uveitis), followed by posterior uveitis- 31% (19 of 61 eyes). Panuveitis and intermediate uveitis cases made up 23% (14 eyes) and 10% (6 eyes) respectively. It is interesting to note that a major chunk of eyes with OCT detected macular edema in our study had anterior uveitis as the anatomic diagnosis (36%).In eyes with anterior uveitis, DME was by far the most commonly seen type of macular edema (20 of 22 eyes). Among eyes with posterior uveitis, SRD was seen in 9 of 19 eyes and CME and DME seen in 5 eyes each. Interestingly, among the eyes with intermediate uveitis in our study, all 6 eyes had DME; in contrast to CME seen in most other studies. According to Malinowski et al[9], CME is clinically present in 28% to 64% of patients with intermediate uveitis and leads to permanent visual impairment in 8.5% of the cases.Among eyes with panuveitis, DME was seen in 13 of 14 eyes. In the study conducted by Markomichelakis et al[1], only 3 of their 60 patients had anterior uveitis, while 42 of 60 (70%) patients they studied had intermediate uveitis as their anatomic diagnosis. There have not been many reports of occurrence of macular edema in cases of anterior uveitis. In a study conducted in Pakistan, cystoid macular edema was seen in 8 of 46 eyes of anterior uveitis studied (17%).[57]

In another study conducted by Roesel et al[58], they correlated retinal thickness as measured by OCT with VA and found that VA correlated negatively with retinal thickness (r=0.38). Epiretinal membrane formation was seen in 70% of their cases. 36% of their 31 cases also had anterior uveitis as the anatomic diagnosis; which was similar to our study. Most of the patients in our study had a CMT between 200-300µ-41 eyes (67%). Of these 41 eyes, 38 eyes had diffuse macular edema, 2 eyes had CME and one had SRD.Eyes with SRD had CMT most commonly above 300µ (9 of 10 eyes with SRD), with 4 eyes with SRD having CMT between 400-500µ and 2 eyes above 500µ. Eyes with CME had CMT varying from 200 to > 500µ, with even distribution among the subgroups. The difference in means of CMT between the right and left eyes was not statistically significant, nor was the difference in means of log MAR VA between the 2 eyes. The overall mean CMT considering all 61 eyes was 313.13+/- 144.84 µ. Among the CME, DME and SRD groups it was 463.29 +/-238.34, 257.14 +/- 60.909 and 454.4 +/- 170.95 µ respectively. The difference in mean CMT among the subgroups was statistically significant on ANOVA (p <0.0001). The difference between CME and DME groups as well as the difference between the DME and SRD groups was statistically significant on doing unpaired t test (p <0.001). The difference in mean CMTs between SRD and CME groups was not statistically significant (p 0.926 on unpaired t test).

The differences in mean log MAR VA between the CME, DME and SRD groups was statistically significant on performing ANOVA. On unpaired t test, the difference between CME and DME groups was statistically significant (p value 0.0079). Difference between DME and SRD group was not significant (p value 0.1193). Difference between CME and SRD group was also not statistically significant (p value 0.3934). In spite of the differences not being statistically significant between the DME and SRD groups and between CME and SRD groups, patients with DME tended to have better visual acuities, compared to CME patients at least (p value 0.0079).

The overall mean CMT in our study was 313.13 +/- 144.84 µ and mean log MAR VA was 0.4854 +/- 0.4932. In the study conducted by Roesel M et al[58], the mean CMT was 369.4 +/- 161.4 µ and mean log MAR VA was 0.41 +/- 0.32. In the study by Markomichelakis et al[1], the mean log MAR VA was 0.2552 and mean CMT was 333 +/- 171µ. They also found that eyes with CME had significantly greater CMT than eyes with DME; a finding similar to our study.

Iannetti L et al[3] studied the use of OCT in macular edema in uveitis and found that both cystoid macular edema (CME) and diffuse macular edema (DME) correlated negatively with VA. Also that CME had higher mean foveal thickness than DME (p < .01). Negative correlation between foveal thickness and VA (p < .05) was observed. All these findings are similar to what we observed in our study. We were able to establish a diagnosis in 10 of our 50 patients (13 eyes). One patient had HIV immune

recovery uveitis, one had Toxoplasmosis and another had syphilitic granulomatous anterior uveitis. 7 patients had retinal vasculitis with choroiditis (Eales disease). In the other studies that we reviewed[1,58], there was no patient in whom syphilis had caused a uveitic reaction. In our study as well, only one patient had syphilis with granulomatous anterior uveitis of both eyes, with one eye having macular edema detectable on OCT. It seems to be a decreasingly rare cause of uveitis.

VII. CONCLUSION

Stratus OCT was used to evaluate the morphological patterns of uveitic macular edema and 3 patterns were found on OCT evaluation, namely diffuse macular edema (DME), cystoid macular edema (CME) and serous retinal detachment (SRD).

DME was the most common type of macular edema we found. Some cases of DME were associated with ERM and PVD. Not all cases of ERM were picked up clinically.

Overall, CMT had a moderate correlation with log MAR VA which was comparable to other studies. Also, we found that patients with CME and SRD tended to have worse VA than patients with DME.

A significant percentage of the cases we studied (36%) had anterior uveitis as their anatomic diagnosis; with most of these patients having DME. This may suggest that even in cases of anterior uveitis, macular edema may form a significant cause of visual morbidity. And that the macular edema may not always be seen clinically and may be picked up only on OCT evaluation. This needs to be recognized early to initiate appropriate treatment and prevent complications.

Further studies with larger sample sizes will be required to establish macular edema as a significant cause of visual morbidity in anterior uveitis cases. As macular edema is a common vision limiting complication of uveitis, it needs to be identified and quantified early to initiate appropriate treatment. OCT evaluation of uveitis cases helps in early detection of macular edema (including subclinical macular edema) and morphological assessment in an objective, reliable and non invasive way. This may lead to better prognostication, treatment and better visual outcome in uveitis cases.

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List of abbreviations used

AAU	Acute anterior uveitis
AIDS	Acquired immune deficiency syndrome
BCVA	Best Corrected Visual Acuity
BRB	Blood retinal barrier
CAU	Chronic anterior uveitis
CME	Cystoid macular edema
CMO	Cystoid macular oedema
CMT	Central Macular Thickness
DME	Diffuse Macular Edema
ERM	Epi retinal membrane
FA & FFA	Fluorescein angiography
HIV	Human immunodeficiency virus
HM	Hand movements
IOP	Intra ocular pressure

IU	Intermediate uveitis
KP	Keratic precipitates
LE	Left eye
LogMAR	Logarithm of Minimum Angle of Resolution
MS	Multiple sclerosis
NFL	Nerve fibre layer
OCT	Optical Coherence Tomography
PP	Pars planitis
PVD	Posterior vitreous detachment
RD	Retinal detachment
RE	Right Eye
RPE	Retinal Pigment Epithelium
SD	Standard Deviation
SRD	Serous retinal detachment
VA	Visual Acuity