ABSTRACT

Cystoid Macular Edema (CME) in its various forms can be considered one of the leading causes of central vision loss in the developed world. It is not a disease itself; it represents a common pathologic sequel of the retina and occurs in a variety of pathological conditions such as diabetic retinopathy, central or branch retinal vein occlusion, intraocular inflammation and following cataract extraction. This study was done to investigate the pattern of CME in patient attending Erbil Teaching Hospitals.

This is a hospital base prospective study that included 61 patients (75 eyes) conducted at Erbil Teaching Hospital and Rigor Teaching Hospital for six months. All patients underwent a comprehensive assessment including medical and ophthalmic history and detailed ophthalmic examination including slit lamp examination, intraocular pressure measurement (IOP), Best corrected visual acuity (BCVA), dilated fundus examination and Optical Coherence Tomography (OCT) examination.

It was found that of the 61 patients 32 (52.5%) were females and 29 (47.5%) were males. The mean age (56.4±10.8) years. Out of the 75 eyes included in the study, 41 eyes (54.66%) had diabetic retinopathy, 10 (13.34%) eyes had CME following cataract operation (Irvine-Gass syndrome), 8 eyes (10.67%) had BRVO, 6 eyes (8%) were had CRVO, 5 eyes (6.66%) had Age related Macular Degeneration, 3 eyes (4%) with uveitis, and 2 (2.67%) had Retinitis Pigmentosa. The average macular thickness was (415.6±107).
It was concluded that diabetic retinopathy is the most common predictive factor of CME, followed by cataract surgery. CME is more severe in diabetic retinopathy, CRVO and after cataract surgery.

**Keywords:** Cystoid Macular Edema, diabetic retinopathy, cataract surgery, retinal vascular diseases.
انماط وذمة الشائبة الصغراء الكيسية الشكل في اربيل

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الخلاصة

وذمة الشائبة الصغراء الكيسية الشكل بانواعها المختلفة، يمكن ان تعتبر واحدة من هم الأسباب التي تؤدي الى فقدان البصر المركزي في العالم المقدم. انها ليست مرضا بحد ذاته، وانما تعتبر ك Mahathma لامراض الشبكية الشائعة، وتحدث في العديد من الحالات المرضية كاعتلال الشبكية السكري وانسداد وريد الشبكية الرئيسي أو الفرعية والتهابات مقلة العين وبعد عمليات رفع ساد العين. هذه الدراسة اجريت لبحث انماط وذمة الشائبة الصغراء الكيسية الشكل في المرضى الذين برتانون المستشفى التعليمي في مدينة اربيل.

هذا البحث هو دراسة استطلاعية في المستشفيات وتضمنت 66 مريض (57 عين)، واجريت في مستشفى هولير التعليمي ومستشفى زكري التعليمي لمدة سنة اشهر، وفيها كل المرضى اخذ منهم تاريخ طبي شامل، واخذوا لفحوصات العيون والتي تضمن فحص العين بالمجهر وقياس ضغط العين وقياس حدة البصر وفحص الشبكية والعصب البصري بعد التوسيع والفحص بجهاز ( او سي تي) من الواحد والستون مريض الذين شملوا بهذه الدراسة 63.5% (51 مريض كانوا نساء و12.47%) مريض كانوا رجال، معدل العمر كان 43.05 4 (سنة. من هذه الخمسة وسبعون عين التي شملت بهذه الدراسة 44.4% (66.5٪ عين كانت مصابة باعتلال شبكية العين السكري 10، 32.6٪ عيون كان مصابات بوذمة الشائبة الصغراء الكيسية

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الشكل بعد عملية رفع ساد العين (أو ما يسمى بتلازمة إيرفين كاس) و ٨ (٦٧،١٠٪) عيون كان مصابات بانسداد وريد شبكية العين الفرعي و ٨ (٦٨٪) عيون كان مصابات بانسداد وريد شبكية العين الرئيسي و ٦٦،٤٦٪ عيون كان مصابات بانحلال شبكية العين الرئيسي والمتعلق بتقدم العمر وعينان (٦٧،٤٢٪) كانتا مصابتان بانحلال شبكية العين الصحيحة.

الشكل بعد عملية رفع ساد العين (أو ما يسمى بتلازمة إيرفين كاس) و ٨ (٦٧،١٠٪) عيون كان مصابات بانسداد وريد شبكية العين الفرعي و ٨ (٦٨٪) عيون كان مصابات بانسداد وريد شبكية العين الرئيسي و ٦٦،٤٦٪ عيون كان مصابات بانحلال شبكية العين الرئيسي والمتعلق بتقدم العمر وعينان (٦٧،٤٢٪) كانتا مصابتان بانحلال شبكية العين الصحيحة.

معدل سمك الشائبة الصفراء كان (١٦،٤١٪) ميكرومتر.

من أهم استنتاجات البحث ان مرض اعتلال شبكية العين السكري من أكثر العوامل المسببة لوذمة الشائبة الصفراء الكيسية الشكل وياتي بعدها عمليات رفع ساد العين، وكانت وذمة الشائبة الصفراء الكيسية الشكل أكثر حدة في حالات اعتلال شبكية العين السكري وحالات انسداد وريد شبكية العين الرئيسي وبعد عمليات رفع ساد العين.
1. Introduction

Cystoid Macular Edema (CME) in its various forms can be considered as one of the leading causes of central vision loss in the developed world [1]. Its first recognized and described in 1974 [2]. It is not a disease itself, rather the endpoint of a variety of processes that lead to the accumulation of fluid in the central retina [3], it represents a common pathologic sequel of the retina and occurs in a variety of pathological conditions such as; diabetic retinopathy, central or branch retinal vein occlusion, intraocular inflammation and following cataract extraction (Irvine-Gass) [4], approximately 20% of the patients who underwent uncomplicated phacoemulsification or extracapsular cataract extraction develop angiographically proven CME [5].

The inflammatory conditions in which CME may occur include intermediate uveitis, HLA B27 associated acute anterior uveitis, sarcoidosis, birdshot retinochoroidopathy, Behcet’s syndrome, toxoplasmosis, Eales’ disease, idiopathic vitritis, Vogt-Koyanagi-Harada syndrome, and posterior scleritis [6-10].

Other causes of CME like retinitis pigmentosa, gyrate atrophy, age related macular degenerations, viteromacular traction syndrome, macular epiretinal membranes, tumor’s such as hemangioblastoma and choroidal hemangioma and may caused by medications such as topical Adrenaline 2%, topical latanoprost and systemic nicotinic acid [11].

Cystoid Macular Edema is the result of accumulation of fluid in the outer plexiform and inner nuclear layers of the retina with the formation of fluid filled cyst like changes [11]. The pathologic process varied from transudation, exudation to liquefaction necrosis, disruption of the blood-retinal barrier at the retinal vasculature and retinal pigment epithelium were noted in CME. The possibility that disruption of the blood-retinal barrier and microinfarction play important roles in the formation of the macular cysts [12]. There are indications that Müller cell swelling may also contribute to CME development (particularly in cases without significant angiographic vascular leakage. Vascular leakage occurs after a breakdown of the blood-retinal barrier during traumatic, vascular, and inflammatory ocular diseases, and allows the serum to get into the retinal interstitium. Since intraretinal fluid distribution is restricted by two diffusion barriers, the inner and outer plexiform layers, serum leakage from intraretinal
vessels causes cysts mainly in the inner nuclear layer while leakage from choroid/pigment epithelium generates (in addition to subretinal fluid accumulation) cyst formation in the Henle fiber layer [13].

2. Materials and Methods

This hospital based, prospective, nonrandomized clinical study was carried out at Hawler and Rizgary Teaching Hospitals in Erbil between March 2013 and March 2014. The study protocol was in accordance with the Declaration of Hawler Medical University and was approved by ethic committee of Hawler medical University.

The patients were recruited into the study if they had significant CME (>320 μm) as measured by OCT (NIDEK, Model RS 3000 NAVIS-EX, Japan), as in Figure (2), decrease of visual acuity to 6/12 or more on snellen chart, and one of predictive factors of CME. The diagnosis of each patient was confirmed by OCT showing significant CME, as defined in the introduction.

The exclusion criteria were the absence of significant CME and any opaque media that prevent visualization of the retina by OCT (sever corneal scar, sever cataract and vitreous hemorrhage).

All the patients underwent ophthalmologic examinations, including measurements of best-corrected visual acuity (BCVA; Snellen chart at 6 m), intraocular pressure (IOP; GoldmannApplanation Tonometer, Model AT 900; Haag-Streit, Bern, Switzerland), slit-lamp examination of the anterior segment, dilated fundus examination by Volk lens +90 D or +78 D, and examination by OCT to prove the diagnosis of CME and to measure macular thickness.

Seventy five eyes of 61 patients with CME were recruited in to the study, Informed consent was obtained from all patients.

Statistical analyses were performed using a commercially available statistical software package (SPSS for Windows, Version 16.0, SPSS, and Chicago, IL, USA). Visual acuity was converted into the logarithm of the minimum angle of resolution (logMAR) for statistical calculations. Univariate categorical analyses were performed using Student’s t-tests and Pearson's Chi-square tests, and a p-value of <0.05 was considered statistically significant.
3. RESULTES:

Out of sixty one patients (75 eyes) who were included in our study, 29 were males (47.5%) and 32 were females (52.5%) as in the table (1).

**Table 1** no. and percentage of sample by gender group

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>29</td>
<td>47.5</td>
<td>47.5</td>
<td>47.5</td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td>52.5</td>
<td>52.5</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Mean age of our sample was (56.43±10.8) years ranging from (17-72) years. The age grouping and distribution of study sample were shown in Figure (4) below.

![Fig. 1 frequency of age group of sample.](image)

Of the 61 patients, 14 (23%) patient had bilateral CME, 12 (85.76%) of them had Diabetic Retinopathy (regardless of stage).
Out of 61 patients 32 (52.7%) had diabetes mellitus and 29 patients were non diabetics, in those 61 patients included in this study, 35 (57.37%) patients had systemic hypertension.

Of the 61 patients, 14 (23%) patient had bilateral CME, 12 (85.76%) of them had Diabetic Retinopathy (regardless of stage), in those 61 patients included in this study, 35 (57.37%) patients had systemic hypertension. In the study sample, 17 (27.86%) patients had hyperlipidemia.

By studying the predictive factors of the 75 eyes that included in the study, 41 eyes (54.66%) were diagnosed to have diabetic retinopathy, which is the most common predictive factor for the development of CME, followed by 10 (13.34%) eyes cataract operation (Irvin Gass syndrome), then 8 eyes (10.67%) were diagnosed to have BRVO, 6 eyes (8%) were diagnosed to have CRVO, 5 eyes (6.66%) had Age related Macular Degeneration, 3 eyes (4%) with uveitis, and lastly 2 (2.67%) were had Retinitis Pigmentosa. Figure (2).

Fig. 2 the frequency of CME by predictive factors.
The mean average macular thickness at 6mm in eyes with Diabetic Retinopathy were (442.12 ± 123.66), in eyes with CRVO were (419.15 ± 121.74), in eyes with BRVO were (360.78 ± 42.43), in eyes with intermediate uveitis were (338 ± 8.17), in eyes with age related Macular Degeneration were (338.71 ± 68.56), in eyes with Retinitis Pigmentosa were (361.33 ± 62.93) and in eyes with CME after cataract surgery were (412.74 ± 57.33), and the p value (0.206) which is statistically not significant. Table (2).

**Table 2** Average Macular Thickness among predictive factors.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR</td>
<td>442.1165</td>
<td>123.66744</td>
</tr>
<tr>
<td>CRVO</td>
<td>419.1481</td>
<td>121.47642</td>
</tr>
<tr>
<td>Cataract operation</td>
<td>412.7444</td>
<td>57.33812</td>
</tr>
<tr>
<td>RP</td>
<td>380.8333</td>
<td>62.93250</td>
</tr>
<tr>
<td>BRVO</td>
<td>360.7778</td>
<td>42.43484</td>
</tr>
<tr>
<td>Uveitis</td>
<td>353.5556</td>
<td>14.65825</td>
</tr>
<tr>
<td>AMD</td>
<td>338.7111</td>
<td>68.56576</td>
</tr>
<tr>
<td>Total</td>
<td>415.6163</td>
<td>107.01552</td>
</tr>
</tbody>
</table>

**P value=0.206** The mean central thickness of macula at 1mm in eyes with Diabetic Retinopathy were (493.6 ± 176.77), in eyes with CRVO were (568 ± 170.78), in eyes with BRVO were (395 ± 92.79), in eyes with uveitis were (348 ± 34.03), in eyes with age related Macular Degeneration were (269.2 ± 125.314), in eyes with Retinitis pigmentosa were (478.5 ± 166.17) and in eyes with CME after cataract surgery were (499 ± 112.82). The mean thickness
of the macula in different sites of it, was centrally at 1mm (486.6 ± 166.1), which is the thickest area, superiorly at 3mm, (452.75 ± 115.1) and at 6mm, (386.05 ± 146.4), inferiorly at 3mm, (429.01 ± 150.9) and at 6mm, (368.97 ± 102.3). Nasally at 3mm, (444.49 ± 148.2) and at 6mm, (374.19 ± 125), temporally at 3mm (438.76 ± 156.3) and at 6mm, (377.72 ± 120.8). p value (0.001). Figure (10).

4. DISCUSSION:

Cystoid Macular edema is a condition of enormous medical and socioeconomic importance because of its high prevalence and occurrence in a large number of pathologic conditions. It is the endpoint of a variety of pathophysiologic processes that can be effectively managed by recognizing and addressing the pathogenic factors that are operative in a given clinical setting.

The present hospital based prospective study which was done in Erbil city show the mean age of patients with CME was 56 years, and around this age, DM, and systemic hypertension, that cause diabetic retinopathy and hypertensive retinopathy respectively, that represent common risk factors for the development of CME, and this finding was reported by a study done in Iran [14].

Regarding gender difference, 47.5% of patients were males and 52.5% of patients were females, the prevalence of CME was higher in females than males. The possible explanation could be that female sex is a significant risk factor for the development of diabetic maculopathy as reported by English town study [15], also hypertensive retinopathy seen more in females than males as reported by a study done in Iran [14] where 45.8% of females and 32.6% of males had retinopathy, and study done in Jordan [16] (48% of females and 42% of males had retinopathy).

Diabetes mellitus was present in 32 (52.5%) of the study patients, and about 41 (54.66%) of eyes with diabetic retinopathy, and 12 (37.5%) of diabetic patients with bilateral CME. This match a study done in Erbil city by Mustafa [17] in 2011 revealed that the prevalence of diabetic retinopathy was high (15%) among diabetic patients and about (20%) of them develop CME.
In this study 35 (57.37%) patients had systemic hypertension. This could be explained by high prevalence of hypertensive retinopathy (48.5%) in Erbil city based on a study done in the city at 2012 by Said [18], also arterial hyper tension is a risk factor for development of central and branch retinal vein occlusion, central retinal artery occlusion and retinal hemorrhage, that are predictive factors of CME.

Hyperlipidemia was found only in 17 (27.86%) of the patients with CME, this was consistent with United Kingdom study [15] that showed no significant association between serum cholesterol and maculopathy, but this finding didn’t match the Germany study [19], that showed significant association between maculopathy and high serum cholesterol. The possible explanation could be due to low attendance of those patients with CME and high serum cholesterol, and unreliable laboratory results with inappropriate preparation of patients for the biochemical investigation.

In the present study the frequency distribution of the 75 eyes of CME which were included in the study among the predictive factors was as following; 41 eyes (54.66%) were diagnosed as diabetic retinopathy, which is the most common predictive factor for development of CME, followed by 10 (13.34%) eyes with CME following cataract operation (Irven Gass syndrome), then 8 eyes (10.67%) were diagnosed as BRVO, 6 eyes (8%) were diagnosed as CRVO, 5 eyes (6.66%) were diagnosed as age related macular Degeneration, 3 eyes (4%) had uveitis, and lastly 2 (2.67%) had Retinitis Pigmentosa. It’s known that diabetes mellitus is a common disease, and the prevalence of diabetic retinopathy is high (15%) of the diabetic patients and (20%) of patients with diabetic retinopathy had developed CME as shown in a previous study done in Erbil city by Mustafa [17] in 2011.

Colin J. [20] (2007) and Cable M. [21] (2012) postulate that, Cystoid macular edema (CME) is one of the most common causes of vision loss after cataract surgery. Its pathogenesis is likely multifactorial, but inflammation caused by surgical manipulations appears to be a major cause. In this study 10 (13.34%) CME occurred after cataract extraction, and this is consistent with previous studies done by Eriksson U. et al [22], in 2011, Perente I [23] et al, in 2007, and Kim SJ. et [24] al , in 2008 showed that between 4% and 20% of healthy eyes develop CME (diagnosed by OCT) after cataract surgery, but most patients experience little or no reduction in visual acuity.
Measurement of macular thickness in the study patients, revealed that, the average macular thickness was higher in diabetic retinopathy, it was statistically nonsignificant, but the values of retinal thickness in diabetic retinopathy were consistent with the values of previous study done in Erbil city at 2012 by Ahmed [25].

In the present study, the macular thickness measured at 1mm (central), 3mm (superior, inferior, nasal and temporal) and 6mm (superior, inferior, nasal and temporal) using spectral domain OCT, and found that the severity of macular edema was more centrally, and lessen gradually as it’s goes peripherally in the macula, (the central area at 1mm was the thickest area, followed by area at 3mm, and lastly at 6mm), and this could be explained by understanding the anatomy and histology of macula, and the pathophysiology of CME, the macular region is predisposed to the collection of transudated fluids by virtue of its anatomic structure, the horizontal course of the outer plexiform layer extend transversally from cone nuclei to bipolar cells, and the resultant laxity of this layer predisposes to the formation of reservoir for the accumulation of transudate (Yamada [26]). Furthermore, the avascularity of the foveolar area restricts absorption of fluid (Jaffe [27]). As a result of this predilection for the accumulation of fluid, the macula has been said by some investigators to "act as a sponge" (Cogan et al [28]). In addition to these anatomic considerations, the foveal region has large concentrations of cells with a high metabolic activity, inflammatory, metabolic, or vascular disturbance can lead to increased concentrations of tissue metabolites with loss of biochemical activity (Ffyche and Blach [29]).

5. Conclusions:

1. Diabetic retinopathy is the most common causative factor of CME, (54.66%) of cases, followed by cataract surgery (13.34%)
2. The macular edema is more sever in diabetic retinopathy, CRVO and after cataract surgery.
3. Cystoid Macular Edema is more sever at the fovea centralis and the edema is reduced as peripheral as from the fovea.
6. REFERENCES:


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