Clinical Evaluation of Ophthalmological Manifestations in Uremic Patients

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Summary:

Uremic patients due to chronic kidney diseases may have chronic complications that alter their quality of life, such as ophthalmological complications, produced by comorbidities of the chronic kidney diseases, or due to its own effects. This study aimed to assess the ocular findings and manifestations in a conventional uremic patients with chronic kidney disease. The study was conducted at Gazi Al-Harere Teaching Hospital for Surgical specialization, department of ophthalmology, during the period from January to August -2017 included 46 uremic patients who were clients of the nephrology department. Bilateral and comparative ophthalmic examination was performed in all patients by one ophthalmologist and eth findings were documented. According to ophthalmic examination, abnormal findings were documented in 38/92 eyes, giving a proportion of abnormal findings of (41.3%), cataracts was the more common findings reported in 38 eyes (41.3%) cases, non-proliferative diabetic retinopathy was the more frequent ophthalmological finding with a definite diagnosis found in (31.5%). In conclusion Abnormal ophthalmological findings are frequent in our uremic CKD cases , with few patients with normal visual acuity. There is a high frequency of hyperopia and astigmatism as well as non-proliferative diabetic retinopathy and macular degeneration

Keywords: *Uremia, chronic kidney disease, ocular manifestations, epidemiology, pathogenesis*

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1. Introduction

There is a large number of systemic diseases that may cause ocular manifestations at some point in their evolution. These alterations can cause symptoms by themselves, can help diagnose the systemic disease that originated them or can serve to monitor the evolutionary course (1). Chronic kidney disease (CKD) is common and is currently considered a global public health problem, with estimates that report a prevalence of about 12% in the general population and with a tendency to be increasing (2–4). Due to advances in renal diseases management , such as transplantation, dialysis and other therapy, the life expectancy of these patients has increased. This has allowed to observe a series of alterations that occur in this type of patients, such as ophthalmological ones, which have different etiologies and include changes in the conjunctiva, cornea, retina and macula that could compromise the quality of life of our patients (1,5).

Uremia refers to the complex and multi-organ clinical manifestations caused by accumulation of nitrogenous waste products due to renal failure (6). Chronic renal failure, dialysis and kidney transplantation have been associated with various ocular complications (6–8) . These ocular complications are important indicators of the severity and duration of renal disease. Some are pathognomonic of this, while others such as hypertensive retinopathy are secondary to hypertension resulting from renal impairment (9). The accumulation of nitrogenous waste products have the potential ability to irritate the ocular surface and ultimately cause various ocular manifestations, especially the “red eye” (6). The other reason could be the chronic inflammatory response to calcium accumulation in the conjunctiva.

Many uremic patients suffer from chronic ocular irritation that may be due to decreased lacrimation, alterations in blink reflex, and chronic systemic inflammation (1,10)

Conjunctival pallor is due to the anemia and malnutrition that accompany Chronic Kidney Disease, degenerative changes in conjunctiva could found in patients with Chronic Kidney Disease. These changes on biopsy appear to be of elastotic type of degeneration. They are at times accompanied by deposits of calcium. Pingecula4 along with a reduction in goblet cell density is a common finding (11).

Subconjunctival hemorrhage is found in many patients with renal failure due to the propensity for bleeding spontaneously. The degree of subconjunctival hemorrhage may vary from small innocuous spots to severe hemorrhage which involves all quadrants of the conjunctiva along with chemosis. The secondary conjunctival vessels sclerosis, due to hypertension may lead to ruptured vessels due to fluctuation in blood pressure which lead to subconjuctival hemorrhage (12).

Dry eye is not uncommon in patients with renal failure due to variety of factors in these patients and the main factors are the reduction in the density of Goblet cells and the changes in the ocular surfaces which lead to instability of the tear film. Severe dryness of the eye may lead to secondary ocular infection (13).

Corneal deposits are chalk like materials found to be deposited on the cornea. There is a clear deposit free zone between the deposit and limbal margin. They are predominantly near the area of conjunctival degeneration. It has been found that in patients who undergo hemodialysis or those who have underwent renal transplant the deposits regress with the correction of uremia state (7,14–16)

Cataract is possibly complicated uremic cases with ESRD, however, in patients with renal failure cataracts occurs mostly due to the inciting factor and also due to the treatment modalities. Renal failure per se does not cause cataract with increased frequency. Cataracts in renal failure is due to hypocalcemia, however, it still unclear if cataract are more common in those patients. From other point of view, previous case reports of early cataract in younger age ESRD patients with higher uremia contributed the higher incidence of cataract in uremic patients to other comorbidities associated with uremia and ESRD such as type II, use of corticosteroids, and hypertension which might act as risk factors to develop cataract (1,5,7) .

Glaucoma Secondary glaucoma in the form of neovascular glaucoma may occur in patients with diabetes and also in hypertensive who have retinal vessel occlusion (5,17).

Vitreous hemorrhage in uremic patients it may occur due to advanced proliferative diabetic retinopathy, untreated or accelerated hypertension , bleeding tendency, and the anemia along with the capillary changes. When uremic status and renal function improved, there is partial reversal of hypertensive retinopathy and improvement of visual acuity but arteriolar

vasoconstriction persists. Hemorrhage has a significant concern in uremic patients particularly those undergoing hemodialysis, as those patients heparinized and some of them have proliferative diabetic retinopathy and would be at high risk of vitreous hemorrhage. Some case reports and studies documented that in patients with renal insufficiency and high uremic levels, retinal detachment (RD) may occurred. As reported in previous studies describing bullous exudative RD, uremic status may be the causative factor where it is believed that uremic patients have focal alteration of choriocapillary permeability which result in the exit of larger molecules like fibrinogen into the subretinal space causing subretinal edema and RD (18–22). Numerous hypothesis have been suggested for retinal detachments; dilutional hyponatremia, severe hypertension, ischemic infarction of choroids and choroidal spasm. This type of retinal detachment is reversible when various causes or the complications are managed adequately such as renal transplantation or dialysis, on the other hand, previous studies have reported that RD in renal failure patients is an indication for early dialysis (18,19).

Optic neuropathy Anterior and posterior ischemic optic neuropathy can occur in these. Systemic and metabolic manifestations of advanced renal disease can produce optic disc edema and diffuse retinal edema. A toxic form of optic neuropathy was documented in uremic patients as uremic optic neuropathy (23–26).

Secondary ocular infection as the patients with renal failure are in a state of immune suppression due to defective immunity or due to chronic steroid therapy. Hence they are more liable to secondary infections which can affect the ocular coats or at times may be blood borne and get seeded in the vitreous. Vision threatening infections may be uncommon but do occur and needed timely and appropriate intervention(13).

Other manifestations as secondary to occlusion of choroidal capillaries, seen as atrophic areas, yellow, rounded, multiple, isolated and pigment accumulation; decreased visual acuity, reflex spasm of the cerebral vessels and result in an ischemia of the occipital lobes parietotemporales and with apparently normal retina (1).

Other studies mentioned that uremia could be associated with *increased intraocular pressure (IOP)* due to ultrafiltration and solute clearance. The chronic elevation in IOP may

lead to damage to the optic nerve, some studies documented that IOP increase in hemodialysis patients (7,27–29) .

On the other hand , due to the inflammatory process, those patients may have *superior limbic keratoconjunctivitis* which is usually bilateral and affects the superior palpebral conjunctiva (1,13,27).

Lid edema is a common accompaniment in patients with Chronic Kidney Disease . It may be the result of the systemic tendency to accumulate fluid in all parts of the body. This kind of edema is associated with facial puffiness. Lid edema can also occur due to the chronic irritation of the ocular surface and lids by the contents in exhaled air (6,7).

The early detection of ocular changes and abnormalities in uremic patients may interfere with the physician decision about the mode of treatment , follow up and monitoring of these patients to improve the patients' quality of life and prevent complications that threaten vision and require frequent ophthalmological assessment. However, despite the frequent nature of renal disease and uremic status, further studies still required to be done to describe the ocular findings in these patients, hence the present study aimed to describe the ocular manifestations accompanied the uremic status of a group of Iraqi patients in the aspects of visual acuity (VA), intraocular pressure (IOP) , fundoscopy and to assess the common ocular lesions that detected in these patients.

2. Patients and Methods:

This was an observational prospective study conducted at the Department of Ophthalmology and Department of nephrology in Gazi Al Harere Hospital for Surgical Specialization during the period from January to August -2017 included 46 patients with chronic kidney disease who were enrolled from the clients of the Nephrology department and were examined by the ophthalmologist (The researcher), the total examined eyes were 92. Full medical and surgical history of the patients were reported in addition to the history of their renal disease regarding the stage of the disease, duration , mode of treatment and any associated complication with their renal insufficiency. The patient was considered eligible in the study if he/she was adult aged 18 years or above and of both genders . Patients with acute renal failure, history of traumatic eye injuries or other known ocular disorder before the onset of their renal disease were excluded from the study. Patients who

refused to participate or of non-Arabic nationality were also been excluded. Verbal informed consent were obtained from all patients before they were included. Hematological and biochemical investigations were asked for and all patients performed these investigations in the teaching laboratory department and their findings were reported.

Data were collected using a pre-constructed data collection sheet (questionnaire) for the purpose of this study including the demographic , clinical and laboratory findings. Bilateral and comparative ophthalmic examination was performed in all patients by one ophthalmologist , the researcher, and their findings were documented.

Visual acuity measured using the Snellen chart, an ocular physical examination was performed with slit lamp and direct ophthalmoscopy after pupil dilation. Tear function tests and Tear film break up time was considered altered when the film broke before ten seconds. Ophthalmic examination performed looking for keratopathy, conjunctival disorders, , presence of cataract , vitreitis , presence of diabetic retinopathy, hypertensive retinopathy, retinal vascular occlusion, retinal detachment and chorioretinitis. According to the findings additional tests were requested.

Statistical analysis: was performed using the statistical package for social sciences (SPSS) 22, appropriate statistical tests were applied accordingly , percentages, means and standard deviations, as well as descriptive tables are used to summarize the general and demographic data.

3. Results:

A total of 46 patients were enrolled in this study and the total examined eyes were 92. The age and gender distribution of the studied group, revealed that the mean age of the uremic cases was 48.7 ± 11.3 years, and majority of the cases aged more than 40 years. Males were the dominant contributed for 63% of the studied group, (**Table 1**).

Regarding the causes of renal impairment that lead to uremia, hypertension alone was the more frequent, (41.3%), in 16 patients (34.8%) both hypertension and diabetes, in 7 patients the cause was diabetes mellitus alone cause (34.8%) of renal impairment, diabetes mellitus was the cause in (15.2%) and other causes were reported in only 4 patient (8.7%), (**Table 2**).

The most frequent ocular symptoms that the patients presented with were blurred vision in 26 patients (56.5%), tearing in 15 (32.6%), itching in 11(23.9%), ocular burning and pain in 5 patients (10.9%) and redness of the eye in 2 patients (4.3%), **(Table 3).**

Among the 92 examined eyes, majority, (72.8%) with a visual acuity (VA) of 6/18 or better, 21 (22.8%), with VA of 6/24 – 6/48 and only four eyes (4.3%) with VA of 6/60. Fortunately, none of the patients was had blindness , **(Table 4)**.

According to ophthalmic examination, abnormal findings were documented in 38/92 eyes, giving a proportion of abnormal findings of (41.3%), **(Figure 1).**

More details for the documented abnormal findings on ophthalmological examination of the 92 examined eyes revealed cataracts in 38 eyes (41.3%), alteration of tear film in 26 (28.3%), Corneo-conjunctival deposits 24 (26.1%), Conjunctival hyperpigmentation 23 (25%), Conjunctival Pallor 15 (16.3%), Lid edema 14 (15.2%), Pterygium 9 (9.8%), and Band shaped Keratopathy detected in only 2 eyes (2.2%), **(Table 5)**. On the other hand the mean intraocular pressure was 14.5 ± 5.3 mmHg .

The ophthalmological findings with a definite diagnosis were non-proliferative diabetic retinopathy (31.5%), Proliferative diabetic retinopathy 5 (5.4%), age-related macular degeneration 11 (12%), hypertensive retinopathy 6 (6.5%), and glaucoma (2.2%). Clinically significant macular edema was found in 10 eyes (10.9%), moreover, Alterations of refractions was reported in 24 eyes (26.1%), (**Table 6**).

Table 1. Age and gender distribution of 46 uremic cases

Variable		No.	%
Age (year)	≤ 40	8	17.4%
	41 - 50	20	43.5%
	> 50	18	39.1%
	Mean +SD	48.7 ± 11.3	-
Gender	Male	29	63.0%
	Female	17	37.0%

Table 2. Causes of renal disease of the studied group (N = 46)

	No.	%
Hypertension	19	41.3
Hypertension and diabetes	16	34.8
Diabetes Mellitus	7	15.2
Others	4	8.7
Total	46	100.0

Table 3. Ocular complaints of uremic patients (N=46)

Complaint	No. of eyes	%
Blurred vision	26	56.5
Tearing	15	32.6
Itching	11	23.9
Ocular burning and Pain	5	10.9
Redness	2	4.3

Table 4. Evaluation of visual acuity of 92 examined eyes

Visual acuity	**No. of eyes**	**%**
≥ 6/18	67	72.8
6/24 - 6/48	21	22.8
6/60	4	4.3
Total	92	100.0

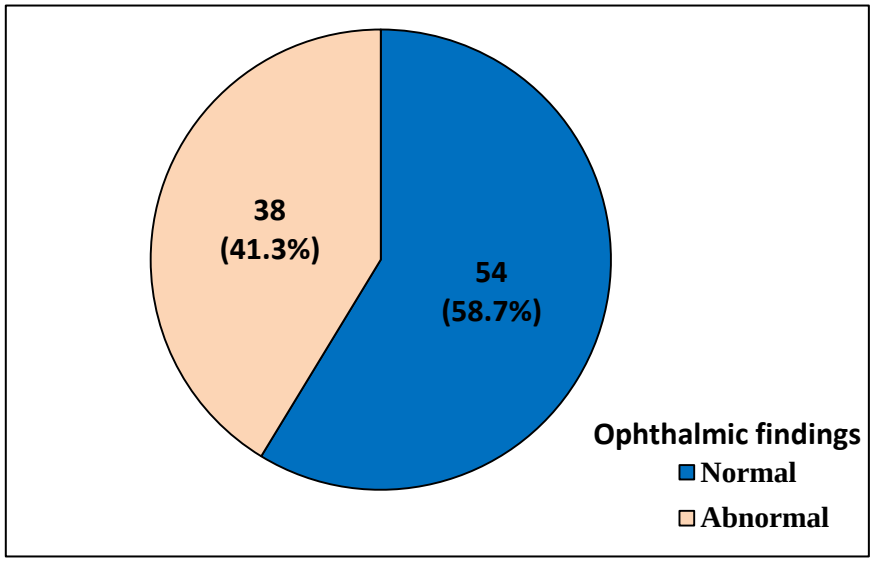

Figure 1. Distribution of findings of ophthalmic examination of 92 eyes of uremic patients

Table 5. Findings of Ophthalmological examination of 92 examined eyes

Finding	Total eyes	%
Cataract	38	41.3
Alteration of the tear film	26	28.3
Corneo-conjunctival deposits	24	26.1
Conjunctival hyperpigmentation	23	25.0
Conjunctival Pallor	15	16.3
Lid edema	14	15.2
Pterygium	9	9.8
Band shaped Keratopathy	2	2.2

Table 6. Ophthalmological findings with a definite diagnosis

Finding	Total eyes	%
non-proliferative diabetic retinopathy	29	31.5
Proliferative diabetic retinopathy	5	5.4
age-related macular degeneration	11	12.0
hypertensive retinopathy	1	1.1
glaucoma	2	2.2
macular edema	10	10.9
Alterations of refractions*	24	26.1
* hypermetropic astigmatism , myopic astigmatism , isolated astigmatism		

4. Discussion

Since it is known that ophthalmological complications are more frequent in patients with chronic kidney diseases and uremic pathology than in the general population (30, 31) many studies have not been done describing the ocular findings specifically in the uremic patients, however, it is important to study them since ophthalmological diseases can alter the quality of life of patients who suffer from it (32, 33). In this regard, the low prevalence of normal visual acuity in our population is the same as in dialysis has been related to the presence of cataracts, refractive alterations, (34) maculopathy and proliferative diabetic retinopathy (7) . We have not found many cases of proliferative diabetic retinopathy, but of cataracts, as other authors have reported (35,36) 12-15, as well as a high prevalence of refractive alteration . In the same way as in other reports, the visual deficit was generally bilateral (7,35). A significant finding in the external examination is the presence of deposits or corneo conjunctival calcifications, in previous studies prevalence ranges from 14 to 60% (34-36). Calcifications of the conjunctiva and the cornea that even some authors have reported as the first metastatic calcification at one year of follow-up on uremic cases managed with dialysis (37). The alteration in the tear film have been a frequent pathology in the present study, which is attributed to the hyperosmolarity of bodily fluids due to the high levels of urea; therefore, the tear is also hyperosmolar, an initial point to trigger the dry eye syndrome16 with symptoms such as itching and burning eyes as reported by our patients. Given the high prevalence of hypertension in our population, it is striking that there is no greater prevalence of hypertensive retinopathy. However, it is known that unlike the relationship between diabetic retinopathy and diabetic nephropathy, especially in type 2 diabetes the association between hypertensive retinopathy and nephroangiosclerosis due to hypertension is not so clear, except for some reports that relate retinopathy severe hypertension with renoparenquimal hypertension (38) . The findings vary according to the population studied; thus, some authors have hypertensive retinopathy as their most frequent finding (39) , while for other authors it is diabetic retinopathy (7,35,36) . Our findings of IOP are interesting, because they are in normal ranges, although this may be affected in patients on hemodialysis. In that sense, the conclusions of the different works in this regard differ significantly. Thus, there are studies that conclude that uremic patients on

hemodialysis does not have significant changes in intraocular pressure in non-glaucomatous and non-occludable eyes (40) while others conclude that IOP may decrease to some extent after HD23. The timing of the evaluation (after dialysis) may have influenced these findings. Goldstein (41) describes progression of diabetic retinopathy and blindness in a uremic patients on dialysis. However, Yashimoto (42) found a stable visual activity in 26 of 28 patients on dialysis after a 6-month follow-up on dialysis. On the other hand, Watanabe (49) found visual disturbances in 73.1% of the patients and at 60 months of follow-up the findings were stable in 87.1%, having improved in 4.8% and worsened in 8.1% .

Evidently, due to the number of patients, we cannot evaluate associations or generalize the findings to other centers.

5. Conclusion

Abnormal ophthalmological findings are frequent in our uremic CKD cases , with few patients with normal visual acuity. There is a high frequency of hyperopia and astigmatism as well as non-proliferative diabetic retinopathy and macular degeneration.

Conflict of interest : None

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Ethical clearance: All the official agreement were obtained prior to initiation of the study and selection of patients. Verbal Informed consent of all participants was approved before participation in the study and examination . Patients data were collected in accordance with the World Medical Association (WMA) Declaration of Helsinki – Ethical principles for medical research involving human subjects, 2013. [www.wma.net]

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