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CLINICAL & BASIC RESEARCH

Epidemiology of Common Ocular Manifestations among Patients on Haemodialysis in West Bank, Palestine

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abstract: ***Objectives:*** This study aimed to assess the prevalence of ocular manifestations and associated factors in patients on haemodialysis. ***Methods:*** A cross-sectional study of patients on haemodialysis from a haemodialysis unit in Nablus, Palestine, was conducted. Medical examination for ocular manifestations (intraocular pressure, cataract, retinal changes and optic neuropathy) was performed using Tono-Pen, portable slit-lamp and indirect ophthalmoscope. Predictor variables were age, gender, smoking, medical comorbidities (diabetes, hypertension, ischaemic heart disease [IHD], peripheral arterial disease [PAD]) and use of antiplatelet or anti-coagulation medications. ***Results:*** A total of 191 patients were included in this study. The prevalence of any ocular manifestation in at least one eye was 68%. The most common ocular manifestations were retinal changes (58%) and cataract (41%). The prevalence of non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and NPDR or PDR was 51%, 16% and 65%. Two patients had PDR in one eye and NPDR in the other, and therefore, they were counted only once making the total for this category 71 rather than 73 patients. An increase in age by one year increased the odds of having cataract by 1.10 (95% confidence interval [CI] = 1.06–1.14). Patients with diabetes had higher odds of having cataract (odds ratio [OR] = 7.43, 95% CI: 3.26–16.95) and any retinal changes (OR = 109.48, 95% CI: 33.85–354.05) than patients without diabetes. Patients with diabetes and IHD or PAD had higher odds of having NPDR than those with diabetes without IHD or PAD (OR = 7.62, 95% CI: 2.07–28.03). ***Conclusion:*** Retinal changes and cataract are common ocular manifestations among patients on haemodialysis. The findings emphasise the importance of periodic screening for ocular problems in this vulnerable population, especially older patients and those with diabetes, to prevent visual impartment and associated disability.

Keywords: Kidney Failure, Chronic; Renal Dialysis; Eye Diseases; Eye Manifestations; Cross-Sectional Studies; Palestine.

Advances in Knowledge

- *The present study showed that 68% of patients on haemodialysis in West Bank, Palestine, have at least one ocular manifestation in at least one eye.*
- *The most common ocular manifestations were retinal changes, cataract and non-proliferative as well as proliferative diabetic retinopathy.*
- *Age and diabetes were associated with presence of cataract and diabetes was associated with retinal changes, especially among patients with ischaemic heart disease and peripheral arterial disease.*

Application to Patient Care

- *Periodic screening and early detection and management of ocular manifestations among haemodialysis patients, especially older patients and those with diabetes, will help in prevention of visual impartment and associated disability in this vulnerable population.*

Visual impairment and blindness represent a significant cause of disability. Worldwide, approximately 2.2 billion people suffer from visual impairment and 50% of these visual impairments are preventable and treatable.[1] Chronic kidney disease (CKD) is very common, with a global prevalence rate of 11–13%.[2] CKD is often gradual and may lead to irreversible loss of kidney function, known as end-stage renal disease (ESRD). Dialysis—either haemodialysis or peritoneal dialysis—and kidney transplantation are the only treatment options for patients with ESRD.[3,4] Patients with ESRD are at an increased risk of ocular problems due to uraemia, effects of haemodialysis and other co-morbid conditions such as diabetes, hypertension and cardiovascular disease.[5] Common ocular problems among patients on haemodialysis include cataract, retinal changes (retinopathy, retinal haemorrhage, vitreous haemorrhage and retinal detachment) and other conjunctival and corneal changes.[5,6]

The prevalence of ESRD in Palestine reached 240.3 per million population in 2010, which is

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relatively lower than in other countries in the Middle East and other regions in the world.[7,8] However, the total number of patients with ESRD on haemodialysis increased from 666 cases in 2011 to 1,014 cases in 2015.[8,9] Therefore, early detection of ocular problems through screening of patients with ESRD may help in preventing visual impairment and associated disability. Research on epidemiology of ocular manifestations and associated factors among ESRD patients in Palestine has been given little attention until now. Therefore, this study aimed to estimate the prevalence of ocular manifestations and associated factors in a sample of Palestinian patients on haemodialysis.

Methods

This was a cross-sectional study of patients with ESRD on haemodialysis from the haemodialysis unit of An-Najah National University Hospital, Nablus, West Bank, Palestine. All patients were on four hours of haemodialysis three times per week. The number of haemodialysis patients in this unit represents approximately 20% of the entire haemodialysis patient population in West Bank.[9] During the study period (August to December 2016), there were 214 patients receiving haemodialysis in the unit. All patients who agreed to participate in the study were included. Demographic and clinical information, previously associated with ESRD and ocular problems were extracted from medical records (age, gender, duration on haemodialysis in years, diabetic status, hypertension status, use of anti-platelet or anticoagulation medication and diagnosis of ischaemic heart disease [IHD] or peripheral arterial disease [PAD]).[10] Patients were asked about their smoking history. All patients underwent the clinical ophthalmic examination in the haemodialysis unit after completing their dialysis sessions by two registered ophthalmologists from An-Najah National University Hospital. For each patient, the clinical ophthalmic examination started with intraocular pressure (IOP) measurement using a Tono-Pen XL Tonometer (Reichert, Inc., New York, USA) after applying local anaesthetic drops (lidocaine 4%) in both eyes.

Generally, normal IOP ranges between 10–21 mmHg.[11] IOP >21 mmHg was classified as raised IOP. Two IOP measurements were taken on each eye and were then averaged. After that, both pupils were dilated with tropicamide 1% (one drop per eye every 10 minutes for half an hour). Presence of cataract was evaluated using a portable slit-lamp (Keeler Ltd. Berkshire, UK) and presence of any vitreous or retinal changes was evaluated using indirect ophthalmoscope (Welch Allyn, New York, USA). Any vitreous or retinal changes, such as arteriovenous nipping or tortuous and vitreous haemorrhage, in non-diabetic patients were classified as retinal changes. The International Clinical Diabetic Retinopathy Disease Severity Scale was used to classify diabetic retinopathy among diabetic patients into non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR).[12] According to this classification, any microaneurysm or intraretinal macrovascular abnormalities were classified as NPDR and neovascularisation or vitreous/preretinal haemorrhage were classified as PDR. Presence of optic disc pallor or cupping were used as a relative measure of optic neuropathy.[13,14]

Descriptive statistics were used to summarise the data. Categorical variables were summarised with frequency and percentage. Continuous variables were summarised with mean and standard deviation. Multivariable logistic regression analyses were performed in order to obtain adjusted associations between predictor variables (demographic and medical characteristics of patients) and presence of ocular manifestations of interest in at least one eye (raised IOP, cataract, retinal changes, optic neuropathy) for all patients as well as NPDR, PDR, or either NPDR or PDR for patients with diabetes (patients could have NPDR in one eye and PDR in the other eye). In the analysis, all ocular manifestations were categorised as binary variables. Associations between the predictor variables and the ocular manifestations were summarised using odds ratios (OR) with 95% confidence intervals (CI). Any association with a P value of <0.05 was considered statistically significant. Data analysis was performed using the Statistical Package for Social Sciences (SPSS) Version 27.0 (IBM Corporation, Armonk, New York, USA).

Full verbal and written consent was obtained from all participants. The study was approved by the Institutional Review Board of An-Najah National University (ethical approval archive number 03/AUG/2016).

Results

A total of 191 patients were included in this study. The mean age was 57.5 ± 13.8 years and 46.6% were females. The mean duration on haemodialysis was 3.3 ± 2.9 years. A total of 80.6% and 57.1% of participants had hypertension and diabetes, respectively. One-fifth of the patients (19.4%) had IHD or PAD and 52.4% were on antiplatelet or anticoagulant medications. The prevalence of smoking among participants was 24.6% [Table 1].

Table 1: Characteristics of patients with ESRD on haemodialysis included in this study (N = 191)

Characteristic	n (%)
Mean age in years ± SD	57.5 ± 13.8
Gender	
Female	89 (46.6)
Male	102 (53.4)
Mean duration on haemodialysis in years ± SD	3.3 ± 2.9
Diabetes mellitus	
No	82 (42.9)
Yes	109 (57.1)
Hypertension	
No	37 (19.4)
Yes	154 (80.6)
IHD or PAD	
No	154 (80.6)
Yes	37 (19.4)
Anti-platelet or anticoagulation	
No	91(47.6)
Yes	100 (52.4)
Smoking	
No	144 (75.4)
Yes	74 (24.6)

SD = standard deviation; IHD = ischaemic heart disease; PAD = peripheral arterial disease.

The overall prevalence of any ocular problem was 68.0%. Cataract was present in 40.8% of patients in at least one eye and 21.5% of patients had a history of cataract surgery. The prevalence of retinal changes in at least one eye was 58.1%. Optic neuropathy was present in 9.9% of patients in at least one eye. Only three patients (1.6%) had raised IOP in at least one eye. A total of 51.4% and 15.6% of patients with diabetes had NPDR and PDR in at least one eye, respectively. The prevalence of either NPDR or PDR was 65.1% (two patients had PDR in one eye and NPDR in the other eye) [Table 2].

Age and diabetes status were the only two variables associated with the presence of cataract. Increase in age by one year was associated with higher odds of having cataract in at least one eye by 1.10 (95% CI: 1.06–1.14). Similarly, patients with diabetes had higher odds of having cataract in at least one eye by 7.43 times (95% CI: 3.26–16.95) than patients without diabetes [Table 3].

Table 2: Prevalence of ocular manifestations in at least one eye among the participants included in this study (N = 191)

Ocular manifestation	n (%)
Cataract	
No	87 (45.5)
Yes	78 (40.8)
Previous cataract surgery	41 (21.5)
Retinal changes	
No	80 (41.9)
Yes	111 (58.1)
Optic neuropathy	
No	172 (90.1)
Yes	19 (9.9)
Intraocular pressure	
Normal	188 (98.4)
Raised	3 (1.6)
NPDR*	
No	53 (48.6)
Yes	56 (51.4)
PDR*	
No	92 (84.4)
Yes	17 (15.6)
NPDR or PDR*	
No	38 (34.9)
Yes	71 (65.1)

NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy.

**Number of patients with diabetes was 109 patients.*

Patients with diabetes had significantly higher odds of having any retinal changes by 109.48 times (95% CI: 33.85–354.05) compared to patients without diabetes; diabetes was the only variable significantly associated with any retinal changes among participants [Table 4].

No statistically significant associations were found between characteristics of participants and optic neuropathy including age (OR = 1.02, 95% CI: 0.98–1.05), gender (OR = 2.04, 95% CI: 0.71–5.86), duration on haemodialysis (OR = 1.04, 95% CI: 0.87–1.23), diabetes (OR = 0.83, 95% CI: 0.28–2.49), hypertension (OR = 0.98, 95% CI: 0.17–5.21), IHD or PAD (OR = 0.63, 95% CI: 0.16–2.50), anti-platelet or anticoagulation therapy (OR = 1.98, 95% CI: 0.70–5.63) and smoking (OR = 0.41, 95% CI: 0.10–1.63) [Table 5].

Table 3: Association between characteristics of participants and cataract (N = 191)

Variable	n (%)		Adjusted OR (95% CI)	*P* value
	Patients without cataract (n = 87)	Patients with cataract (n = 104)		
Age in years	50.1 ± 14.7	63.6 ± 9.4	1.10 (1.06–1.14)	<0.001
Gender				
Female	41 (47.1)	48 (46.2)	Ref: 0.80 (0.36–1.81)	0.597
Male	46 (52.9)	56 (53.8)		
Duration on haemodialysis in years	3.4 ± 3.3	3.2 ± 2.5	1.13 (0.98–1.30)	0.102
Diabetes mellitus				
No	59 (67.8)	23 (22.1)	Ref: 7.43 (3.26–16.95)	<0.001
Yes	28 (32.2)	81 (77.9)		
Hypertension				
No	22 (25.3)	15 (14.4)	Ref: 0.65 (0.23–1.85)	0.413
Yes	65 (74.7)	89 (85.6)		
Anti-platelet or anticoagulation				
No	50 (57.5)	41 (39.4)	Ref: 1.72 (0.78–3.78)	0.178
Yes	37 (42.5)	63 (60.6)		
Smoking				
No	66 (75.9)	78 (75.0)	Ref: 1.05 (0.39–2.77)	0.930
Yes	21 (24.1)	26 (25.0)		

OR = odds ratio; CI = confidence interval; IHD = ischaemic heart disease; PAD = peripheral arterial disease.

Patients with diabetes and IHD or PAD had higher odds of having NPDR than patients with diabetes and without IHD or PAD, but this was not statistically significant (OR = 2.09, 95% CI: 0.78–5.61). Among patients with diabetes, there were no statistically significant associations between the characteristics of participants and diabetic retinopathy (either NPDR or PDR) [Table 6].

Discussion

This study showed that common ocular manifestations are highly prevalent among patients on haemodialysis. Approximately two-thirds of the patients had at least one ocular manifestation in at least one eye. Retinal changes and cataract were the most common ocular manifestations. About two-thirds of the patients with diabetes had either NPDR or PDR in at least on eye. Optic neuropathy was present in 10% of patients at least in one eye. Age was positively associated with

Table 4: Association between characteristics of participants and retinal changes (N = 191)

Variable	n (%)		Adjusted OR (95% CI)	*P* value
	Patients without retinal changes (n = 80)	Patients with retinal changes (n = 111)		
Age in years	52.2 ± 16.4	61.2 ± 10.1	1.01 (0.97–1.06)	0.561
Gender				
Female	39 (48.8)	50 (45.0)	Ref: 0.84 (0.25–2.81)	0.771
Male	41 (51.2)	61 (55.0)		
Duration on haemodialysis in years	3.8 ± 3.5	2.9 ± 2.2	1.06 (0.88–1.27)	0.558
Diabetes mellitus				
No	73 (91.3)	9 (8.1)	Ref: 109.48 (33.85–354.05)	<0.001
Yes	7 (8.8)	102 (91.9)		
Hypertension				
No	27 (33.8)	10 (9.0)	Ref: 1.98 (0.51–7.78)	0.326
Yes	53 (66.3)	101 (91.0)		
IHD or PAD				
No	75 (93.8)	79 (71.2)	Ref: 2.44 (0.46–13.02)	0.298
Yes	5 (6.3)	32 (28.8)		
Anti-platelet or anticoagulation				
No	47 (58.8)	44 (39.6)	Ref: 1.33 (0.44–4.03)	0.616
Yes	33 (41.3)	67 (60.4)		
Smoking				
No	61 (76.3)	83 (74.8)	Ref: 0.42 (0.10–1.74)	0.231
Yes	19 (23.8)	28 (25.2)		

OR = odds ratio; CI = confidence interval; IHD = ischaemic heart disease; PAD = peripheral arterial disease.

cataract and diabetes was associated with the presence of cataract and any retinal changes. Among patients with diabetes, the presence of IHD or PAD was associated with NPDR.

This study showed that 40.8% patients on haemodialysis had cataract and 21.5% of patients have had cataract surgery. This finding is consistent with prior studies, which revealed that cataract is common among patients on haemodialysis.[15–17] For example, one study found that 61% of patients on haemodialysis had cataract.[17]

In the current study, the prevalence of NPDR (51.4%) and PDR (15.6%) are very similar to those found in a previous study, which reported a prevalence

Table 5: Association between characteristics of participants and optic disc pallor/cupping

Variable	n (%)		Adjusted OR (95% CI)	*P* value
	Patients without optic disc pallor (n = 172)	Patients with optic disc pallor (n = 19)		
Age in years	57.2 ± 14.0	59.4 ± 12.3	1.02 (0.98–1.05)	0.411
Gender				
Female	82 (47.7)	7 (36.8)	Ref: 2.04 (0.71–5.86)	0.188
Male	90 (52.3)	12 (63.2)		
Duration on haemodialysis in years	3.3 ± 2.8	3.6 ± 3.6	1.04 (0.87–1.23)	0.678
Diabetes mellitus				
No	73 (42.4)	9 (47.4)	Ref: 0.83 (0.28–2.49)	0.740
Yes	99 (57.6)	10 (52.6)		
Hypertension				
No	33 (18.6)	5 (26.3)	Ref: 0.98 (0.17–5.21)	0.984
Yes	140 (81.4)	14 (73.7)		
IHD or PAD				
No	138 (80.2)	16 (84.2)	Ref: 0.63 (0.16–2.50)	0.512
Yes	34 (19.8)	3 (15.8)		
Anti-platelet or anticoagulation				
No	84 (48.8)	7 (36.8)	Ref: 1.98 (0.70–5.63)	0.201
Yes	88 (51.2)	12 (63.2)		
Smoking				
No	128 (74.4)	16 (84.2)	Ref: 0.41 (0.10–1.63)	0.204
Yes	44 (25.6)	3 (15.8)		

OR = odds ratio; CI = confidence interval; IHD = ischaemic heart disease; PAD = peripheral arterial disease.

Table 6: Association between characteristics of participants and diabetic retinopathy (N = 191)

Variable	n (%)		Adjusted OR (95% CI)	*P* value
	Patients without NPDR or PDR (n = 38)	Patients with NPDR or PDR (n = 71)		
Age in years	62.1 ± 7.2	61.3 ± 10.7	0.99 (0.95–1.04)	0.710
Gender				
Female	14 (36.8)	33 (46.5)	Ref: 0.99 (0.39–2.50)	0.981
Male	24 (63.2)	38 (53.5)		
Duration on haemodialysis in years	2.4 ± 2.4	2.9 ± 2.0	1.09 (0.89–1.34)	0.423
Hypertension				
No	4 (10.5)	5 (7.0)	Ref: 1.88 (0.43–8.24)	0.405
Yes	34 (89.5)	66 (93.0)		
IHD or PAD				
No	30 (78.9)	47 (66.2)	Ref: 2.09 (0.78–5.61)	0.142
Yes	8 (21.1)	24 (33.8)		
Anti-platelet or anticoagulation				
No	14 (36.8)	29 (40.8)	Ref: 0.82 (0.32–2.10)	0.667
Yes	24 (63.2)	42 (59.2)		
Smoking				
No	23 (60.5)	56 (78.9)	Ref: 0.42 (0.15–1.15)	0.091
Yes	15 (39.5)	15 (21.1)		

OR = odds ratio; CI = confidence interval; NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; IHD = ischaemic heart disease; PAD = peripheral arterial disease.

of 57% and 14% for NPDR and PDR among patients on haemodialysis, respectively.[17] Similarly, the prevalence of optic neuropathy (10%) in the present study is consistent with the prevalence of optic neuropathy (7%) reported in a previous study.[18] This finding also agrees with previous reports on occurrence of optic neuropathy among patients on haemodialysis.[19]

In the current study, the prevalence of raised IOP was very low (1.6%), which is similar to the findings of a prior study.[17] The researchers' finding of an independent positive associations between age and diabetes with cataract is consistent with the findings of a 12-year prospective cohort study of patients on haemodialysis.[20] The present study found that diabetic patients had significantly higher odds of having any retinal changes, which is also consistent with the literature.[5,6,21] Among patients with diabetes, no association was found between any of the included patients' characteristics and the prevalence of diabetic retinopathy. This finding underscores the important independent associations between diabetes and retinal changes, including NPDR and PDR. Diabetic retinopathy is the most common microvascular complication of diabetes due to hyperglycaemia and related macro- and micro-vascular abnormalities.[22–24] The independent association between IHD or PAD and NPDR observed in the current study also agrees with the literature. Prior studies have shown associations between retinal microvascular abnormalities and coronary heart disease among patients with diabetes.[25] The mechanisms underlying ocular manifestations and observed associations are likely explained by

multifactorial pathogenesis associated with aging, ESRD and comorbid conditions (diabetes and hypertension), uraemia and haemodialysis, chronic anaemia and 'polypharmacy'.[10] The main hypothesised multifactorial pathogenesis includes atherosclerosis, endothelial dysfunction, oxidative stress, chronic inflammation, renin-angiotensin system dysfunction, genetic polymorphisms, Klotho, hypocalcaemia, the accumulation of toxic metabolites and repeated osmotic shift during dialysis.[5,6,10,20,26]

The main strength of this study is that patients in the haemodialysis unit in An-Najah National University Hospital represent roughly 20% of patients on haemodialysis in West Bank, Palestine. Additionally, this study included the majority (89%) of patients undergoing haemodialysis in the unit and covered a wide range of age groups. It is unlikely that the sociodemographic and clinical characteristics of patients in An-Najah National University Hospital differ from those in other units in West Bank because the haemodialysis service and its related costs are free and completely covered by the Palestinian Ministry of Health. Additionally, ophthalmic examination of the participants was performed independently by two resident ophthalmologists. Very few disagreements in classification of ocular manifestations were present. These disagreements were resolved by discussion or by seeking the opinion of a third resident ophthalmologist. Therefore, the potential for diagnostic errors or misclassification of ocular manifestations is unlikely to have affected the researchers' findings significantly. Additionally, the study's findings were consistent with those of previous studies on ocular manifestations among patients on haemodialysis. Therefore, the findings from this study are highly likely to be generalisable to other patients on haemodialysis in West Bank.

The study has some limitations. This was a cross-sectional study design and, therefore, temporal associations remain unclear. Another limitation is that this study did not examine other ocular manifestations among patients on haemodialysis, such as dry eyes and corneal abnormalities. However, this study covered the most prevalent ocular manifestations among this population (e.g. cataract, retinal changes and optic neuropathy) which are associated with visual impairment and disability globally.[27] In addition, medical records had no clinical information on previous history of ocular problems among patients and many elderly patients said that they have a history of ophthalmic problems but did not know what they were. The researchers were, therefore, not able to establish whether the observed ophthalmic manifestations were new or old in the majority of patients. However, the researchers' aim was to estimate the prevalence of ocular manifestations rather their incidence, which requires a different study design with a long follow-up period. Additionally, although Goldmann applanation tonometer is considered the gold standard instrument for measuring IOP, the researchers measured IOP using a Tono-Pen instrument (Reichert, Inc.) because it was not feasible to transfer the non-portable slit-lamp from the ophthalmic unit to the haemodialysis unit. Prior research suggests that Tono-Pen (Reichert, Inc.) underestimates IOP in persons with elevated IOP.[28] However, one study found no statistically significant differences in IOP values between Goldmann applanation tonometer and Tono-Pen (Reichert, Inc.) in non-glaucoma patients with systemic illness.[29,30] Another limitation is that retinal changes were examined using an indirect ophthalmoscope. It would be more ideal to take fundus photographs for evaluation by retina specialists. However, this was not feasible in the present study.

Conclusion

Ocular problems are highly prevalent among patients on haemodialysis. Most common ocular manifestations were retinal changes and cataract. Without early detection and treatment, such conditions may lead to significant visual impairment and disability. The findings underscore the importance of regular ophthalmic screening for patients on haemodialysis, especially older patients and those with diabetes, to prevent visual impartment and associated disability in this population.

AUTHORS' CONTRIBUTION

YS and MS led study conception and design, supervision, data collection, statistical analysis, interpretation of data and drafting of manuscript. OY, AAS, ZH, OH and HH were involved in study concept and design and data collection. All authors critically reviewed the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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