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

A cross-sectional study

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Abstract

Objectives: To assess the prevalence of ocular manifestations and associated factors in patients on haemodialysis. ***Methods:*** A cross-sectional study of 191 patients on haemodialysis from a haemodialysis unit in Nablus, Palestine. 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, ischemic heart disease (IHD), and peripheral arterial disease (PAD)), and use of antiplatelet or anti-coagulation medications. ***Results:*** 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), preoperative diabetic retinopathy (PDR), and either NPDR or PDR was 51%,16%, and 65%, respectively. Increase in age by one year was

associated with increase in 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 patients with diabetes and free from IHD or PAD (OR 7.62; 95% CI, 2.07, 28.03). ***Conclusion:*** Retinal changes and cataract are very common ocular manifestations among patients on haemodialysis. The findings emphasize the importance of periodic screening for ocular problems 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.

Advances in knowledge

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

Application to patient care

- Ocular problems are highly prevalent among patients on haemodialysis.
- 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.

Introduction

Visual impairment and blindness represent a significant cause of disability. Worldwide, about 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 of 11% to 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 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,[7] which is relatively lower than that in other countries in the Middle East and other regions in the world.[8] However, the total number of patients with ESRD on haemodialysis has increased from 666 cases in 2011 to 1014 cases in 2015.[8, 9] Therefore, early detection of ocular problems through screening of patients with ESRD may help in prevention of visual impairment and associated disability in this population. Research on epidemiology of ocular manifestations and associated factors among ESRD patients in Palestine has been given little attention until now. The aim of this study was to estimate the prevalence of ocular manifestations and associated factors in sample of Palestinian patients on haemodialysis.

Methods

Study design, population, and setting

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 haemodialysis three times per week. The number of haemodialysis patients in this unit represents about 20% of all haemodialysis patients' population in West Bank.[9] During the study period (August and December 2016), there were 214 patients receiving haemodialysis in the unit. All patients who agreed to participate in the study were included (n= 191). The study was approved by the Institutional Review Board of An-Najah National University (ethical approval archive number 03/AUG/2016). Full verbal and written consent have been obtained from all participants.

Data collection

Demographic and clinical information, previously associated with ESRD and ocular problems[10] were extracted from medical records (age, gender, duration on haemodialysis in years, diabetic status (yes, no), hypertension status (yes, no), use of anti-platelet or anticoagulation medication (yes, no), and diagnosis of ischemic heart disease (IHD) or peripheral arterial disease (PAD) (yes, no). Patients were asked about their smoking history (yes, no). 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[11] after applying local anaesthetic drops (lidocaine 4%) in both eyes. Generally, normal IOP ranges between 10 and 21 mmHg.[12] IOP more than 21 mmHg was classified as raised IOP. Two IOP measurements were taken on each eye and then were 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,[13] and presence of any vitreous or retinal changes was evaluated using indirect ophthalmoscope.[14] Any vitreous or retinal changes in non-diabetic patients such as arteriovenous nipping or tortuous and vitreous haemorrhage were classified as retinal changes. We used the International Clinical Diabetic Retinopathy Disease Severity Scale to classify diabetic retinopathy among diabetic patients into non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR).[15] According to this classification, any microaneurysm or intraretinal macrovascular abnormalities were classified as NPDR, and neovascularization or vitreous/preretinal haemorrhage were classified as PDR. Presence of optic disc pallor or cupping were used as a relative measure of optic neuropathy.[16, 17]

Data analysis

Descriptive statistics were used to summarize the data. Categorical variables were summarized with numbers and percentages. Continuous variables were summarized with mean and standard deviation (SD). We performed multivariable logistic regression analyses to obtain adjusted associations between predictor variables (demographic and medical characteristics of patients) and presence of ocular manifestations of interest (raised IOP, cataract, retinal changes, optic

neuropathy) for all patients, and NPDR, PDR, or either NPDR or PDR for patients with diabetes. In analysis, all ocular manifestations were categorized as binary variables (yes, no). 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 Statistical Package for Social Sciences (SPSS) version 27.0.

Results

Table 1 presents the characteristics of participants. The mean age was 57.5 years, and 46.6% were females. The mean duration on haemodialysis was 3.3 years. About 80.6% and 57.1% of participants had hypertension and diabetes, respectively. Around 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 2 presents the prevalence of ocular manifestations in at least one eye among participants. The overall prevalence of any ocular problem was 68.0%. About 40.8% of patients had cataract 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%. About 9.9% of patients had optic neuropathy at least in one eye. Only 3 patients (1.6%) had raised IOP at least in one eye.

Around 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 DRP was 65.1% (Table 2).

As shown in table 3, age and diabetes status were the only two variables associated with 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.

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

As shown in Table 5, 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).

Among patients with diabetes, there were no statistically significant associations between the characteristics of participants and diabetic retinopathy (either NPDR or PDR); see Table 6. 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)

Discussion

The aim of current study was to estimate the prevalence of ocular manifestations among a sample of Palestinian patients on haemodialysis and identify associated factors. The study showed that common ocular manifestations are highly prevalent among patients on haemodialysis. About two thirds of 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 patients with diabetes had either NPDR or PDR in at least on eye. About 10% of patients had optic neuropathy at least in one eye. Age was positively associated with cataract, and diabetes was associated with presence of cataract and any retinal changes. Among patients with diabetes, the presence of IHD or PAD was associated with NPDR.

The study showed that 40.8% haemodialysis have cataract, and 21.5% of patients had cataract surgery. This finding is consistent with prior studies that cataract is common among patients on haemodialysis.[18-20] For example, one study found that 61% of patients on haemodialysis have cataract.[20] In the current study, the prevalence of NPDR (51%) and PDR (16%) are very similar

to those found in a previous study, which reported a prevalence of 57% and 14% for NPDR and PDR among patients on haemodialysis, respectively.[20] Similarly, the prevalence of optic neuropathy (10%) in our study is consistent with the prevalence of optic neuropathy (7%) reported in a previous study.[21] This finding also agrees with previous reports on occurrence of optic neuropathy among patients on haemodialysis.[22] In the current study, the prevalence of raised IOP was very low (2%), which is identical to the findings of a prior study.[20] Our 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.[23] We found that diabetic patients had significantly higher odds of having any retinal changes, which is also consistent with the literature.[5, 6, 24] Among patients with diabetes, we found no association 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 microvascular abnormalities.[25-27] 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.[28] 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 hypothesized 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, 23, 29]

Strengths and limitations

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. 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 to differ from those in other

units in West Bank because haemodialysis service and related costs is 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 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 our findings significantly. Additionally, our 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 generalizable 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 for other ocular manifestations among patients on haemodialysis, such as dry eyes and corneal abnormalities. However, our study covered most prevalent ocular manifestations among this population (e.g. cataract, retinal changes, and optic neuropathy) which are associated with visual impairment and disability globally.[30] Also, 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. So, we were not able to establish whether the observed ophthalmic manifestations were new or old in majority of patients. However, our aim was to estimate the prevalence of ocular manifestations rather than incidence of ophthalmic manifestations which requires a different study design with long follow-up period. Additionally, although Goldman applanation tonometer is considered the gold standard instrument for measuring IOP, we measured IOP using a Tono-Pen instrument. Prior research suggests that Tono-Pen underestimates IOP in persons with elevated IOP.[31] However, one study found no statistically significant differences in IOP values between Goldman applanation tonometer and Tono-Pen in non-glaucoma patients with systemic illness.[32, 33] Another limitation is that retinal changes were examined using 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, interpreting data, and drafting of manuscript. OY, AAS, ZH, OH, and HH were involved in study concept and design and data collection. All authors reviewed the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript.

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Conflict of Interest

The authors declare no conflicts of interest.

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Table 1 Characteristics of participants

Variable	**Mean (SD) or number (%)**
Age (years)	57.5 (13.8)
Gender	
Female	89 (46.6)
Male	102 (53.4)
Duration on Haemodialysis (years)	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*, Ischemic Heart Disease; *PDA*, Peripheral Arterial Disease

343 **Table 2** Prevalence of ocular manifestations in at least one eye among participants

Ocular manifestation	Number (%)
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)

344 *NPDR,* Non-proliferative diabetic retinopathy; *PDR,* Proliferative diabetic retinopathy

345 **Table 3** Association between characteristics of participants and cataract

Variable	Patient has no cataract (n=87)	Patient has cataract (N=104)	Adjusted OR (95 % CI)	P- value
Age (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	
Male	46 (52.9)	56 (53.8)	0.80 (0.36, 1.81)	0.597
Duration on Haemodialysis (years)	3.4 (3.3)	3.2 (2.5)	1.13 (0.98, 1.30)	0.102
Diabetes Mellitus				
No				
yes	59 (67.8)	23 (22.1)	Ref	
	28 (32.2)	81 (77.9)	7.43 (3.26, 16.95)	<0.001
Hypertension				
No	22 (25.3)	15 (14.4)	Ref	
Yes	65 (74.7)	89 (85.6)	0.65 (0.23, 1.85)	0.413
IHD or PAD				
No	74 (85.1)	80 (76.9)	Ref	
Yes	13 (14.9)	24 (23.1)	0.52 (0.20, 1.32)	0.165
Anti-platelet or anticoagulation				
No	50 (57.5)	41 (39.4)	Ref	
Yes	37 (42.5)	63 (60.6)	1.72 (0.78, 3.78)	0.178
Smoking				
No	66 (75.9)	78 (75.0)	Ref	
yes	21 (24.1)	26 (25.0)	1.05 (0.39, 2.77)	0.930

346 *IHD*, Ischemic heart disease; *PAD*, Peripheral arterial disease; *OR*, Odds ratio; *CI*, Confidence
347 interval. Note: percentages may not add up to 100 due to rounding

348 **Table 4** Association between characteristics of participants and retinal changes

Variable	Patient has no retinal changes (n=80)	Patient has retinal changes (n=111)	Adjusted OR (95 % CI)	P- value
Age (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	
Male	41 (51.2)	61 (55.0)	0.84 (0.25, 2.81)	0.771
Duration on Haemodialysis (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	
yes	7 (8.8)	102 (91.9)	109.48 (33.85, 354.05)	<0.001
Hypertension				
No	27 (33.8)	10 (9.0)	Ref	
Yes	53 (66.3)	101 (91.0)	1.98 (0.51, 7.78)	0.326
IHD or PAD				
No	75 (93.8)	79 (71.2)	Ref	
Yes	5 (6.3)	32 (28.8)	2.44 (0.46, 13.02)	0.298
Anti-platelet or anticoagulation				
No	47 (58.8)	44 (39.6)	Ref	
Yes	33 (41.3)	67 (60.4)	1.33 (0.44, 4.03)	0.616
Smoking				
No	61 (76.3)	83 (74.8)	Ref	
yes	19 (23.8)	28 (25.2)	0.42 (0.10, 1.74)	0.231

349 *IHD*, Ischemic heart disease; *PAD*, Peripheral arterial disease; *OR* Odds ratio; *CI*, Confidence
350 interval. Note: percentages may not add up to 100 due to rounding

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

Variable	Patient has no optic disc pallor (n=172)	Patient has optic disc pallor (n=19)	Adjusted OR (95 % CI)	P- value
Age (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	
Male	90 (52.3)	12 (63.2)	2.04 (0.71, 5.86)	0.188
Duration on Haemodialysis (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	
yes	99 (57.6)	10 (52.6)	0.83 (0.28, 2.49)	0.740
Hypertension				
No	33 (18.6)	5 (26.3)	Ref	
Yes	140 (81.4)	14 (73.7)	0.98 (0.17, 5.21)	0.984
IHD or PAD				
No	138 (80.2)	16 (84.2)	Ref	
Yes	34 (19.8)	3 (15.8)	0.63 (0.16, 2.50)	0.512
Anti-platelet or anticoagulation				
No	84 (48.8)	7 (36.8)	Ref	
Yes	88 (51.2)	12 (63.2)	1.98 (0.70, 5.63)	0.201
Smoking				
No	128 (74.4)	16 (84.2)	Ref	
yes	44 (25.6)	3 (15.8)	0.41 (0.10, 1.63)	0.204

IHD, Ischemic heart disease; *PAD*, Peripheral arterial disease; *OR* Odds ratio; *CI*, Confidence interval. Note: percentages may not add up to 100 due to rounding

354 **Table 6** Association between characteristics of participants and diabetic retinopathy

Variable	Patient has no NPDR or PDR (n=38)	Patient has NPDR or PDR (n=71)	Adjusted OR (95 % CI)	P- value
Age (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	
Male	24 (63.2)	38 (53.5)	0.99 (0.39, 2.50)	0.981
Duration on Haemodialysis (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	
Yes	34 (89.5)	66 (93.0)	1.88 (0.43, 8.24)	0.405
IHD or PAD				
No	30 (78.9)	47 (66.2)	Ref	
Yes	8 (21.1)	24 (33.8)	2.09 (0.78, 5.61)	0.142
Anti-platelet or anticoagulation				
No	14 (36.8)	29 (40.8)	Ref	
Yes	24 (63.2)	42 (59.2)	0.82 (0.32, 2.10)	0.667
Smoking				
No	23 (60.5)	56 (78.9)	Ref	
yes	15 (39.5)	15 (21.1)	0.42 (0.15, 1.15)	0.091

355 *NPDR,* Non-proliferative diabetic retinopathy; *PDR,* Proliferative diabetic retinopathy; *IHD,*

356 Ischemic heart disease; *PAD,* Peripheral arterial disease; *OR* Odds ratio; *CI,* Confidence interval.

357 Note: percentages may not add up to 100 due to rounding