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Use of ophthalmic B-scan ultrasonography in determining the causes of low vision in patients with diabetic retinopathy

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ABSTRACT

Purpose: To determine the causes of low vision among Sudanese patients with diabetic retinopathy (DR) by using ophthalmic B-scan ultrasonography.

Materials and methods: A total of 100 patients with DR at different grades, were recruited prospectively between September 2016 and January 2018. Nidek (Echoscan US-4000) ultrasound unit was used to determine the causes of low vision in diabetic patients according to their glycated haemoglobin (HbA1c) and early treatment of diabetic retinopathy scale (ETDRS) severity levels.

Results: Vitreous hemorrhage (VH) 42(66.6%), asteroid hyalosis (AH) 12(14.3%), and partial retinal detachment (PRD) 9(19%) were the main cause of low vision in patients presenting with moderately regulated HbA1c and graded with either minimal or mild nonproliferative retinopathy (NPDR). While VH 15(40.5%), total retinal detachment (TRD) 12(32.4%), posterior vitreous detachment (PVD) 7(19%), and choroidal detachment (CD) 3(8.1%), were dominant in patients with poorly regulated HbA1c and graded either as moderate NPDR; severe NPDR; and proliferative retinopathy (PR).

Conclusions: Ophthalmic B-mode ultrasound is a rapid, noninvasive imaging technique that can be used with minimum discomfort in ophthalmological practice for the detection and evaluation of DR complications that predict the visual outcome.

1. Introduction

The term low vision describes vision disorders that cannot be corrected with medical treatment, surgical interference, or conventional eyeglasses or contact lenses. Hence, low vision refers to a wide range of vision reduction between normal vision and no light perception [1]. Low vision is visual acuity less than 6/18 and equal to or better than 3/60 in the better eye with best correction. A person with low vision is one who has an impairment of visual functioning even after treatment and/or standard refractive correction, and has a visual acuity of less than 6/18 to light perception, or a visual field less than 10 degrees from the point of fixation, but who uses, or is potentially able to use, vision for the planning and/or execution of a task for which vision is essential [2].

The prevalence of visual impairment and blindness due to diabetic retinopathy (DR) and diabetic eye complications is on the rise worldwide and more specifically in North Africa and the Middle East region. While in developing countries, it's a major public health problem in diabetics, mainly due to an increase in the number of older diabetics and the insufficiency of early tracing routines of diabetics at risk of blinding complications [3]. The prevalence of DR in Sudan was estimated to be around (17.2%) in 1991 [4]. Another study carried in out patient of 3 general hospitals in Khartoum, Sudan in 1995 for insulin-treated diabetic patients revealed that the prevalence of DR was (43%), nephropathy was (22%) and neuropathy was (37%) [5].

Low vision due to DR occurs through a variety of mechanisms, including retinal detachment (RD), preretinal or vitreous hemorrhage (VH), associated neovascular glaucoma, and macular edema or capillary nonperfusion. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany with

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Table 1
Abbreviated summary of the final version of the early treatment diabetes retinopathy study scale of DR severity for individual eyes [12].

Level	Severity	Definition
10	No retinopathy	DR absent
20	Very mild NPDR	Microaneurysms only
35	Mild NPDR	Microaneurysms plus hard exudates, soft exudates (cotton-wool spots) and/or mild retinal hemorrhages
43	Moderate NPDR	Microaneurysms plus mild IRMA* or moderate retinal hemorrhages
47	Moderate NPDR	More extensive IRMA. Severe retinal hemorrhages, or venous beading in one quadrant only
53	Severe NPDR	Severe retinal hemorrhages in 4 quadrants, or venous beading in at least 2 quadrants, or moderately severe IRMA in at least 1 quadrant
61	Mild PDR	NVE* < 1/2 disc area In 1 or more quadrants
65	Moderate PDR	NVE* ≥1/2 disc area In 1 or more quadrants, or NVD* < 1/4–1/3 disc area
71–75	High-risk PDR	NVD* ≥1/4–1/3 disc area and/or VH
81–85	Advanced PDR	Fundus partially obscured

* IRMA: Intraretinal Microvascular Abnormalities; NVE: New Vessels Elsewhere; NVD: New Vessels on or within 1 Disc Diameter of Optic Disc.

chronic hyperglycemia [6].

DR status was graded using the early treatment of diabetic retinopathy scale (ETDRS) on the basis of the ETDRS severity level as: minimal nonproliferative retinopathy (minimal NPDR), mild nonproliferative retinopathy (mild NPDR), moderate nonproliferative retinopathy (moderate NPDR), severe nonproliferative retinopathy (severe NPDR), and proliferative retinopathy (PR). The modified Airlie House classification of DR has been extended for use in the ETDRS on the basis of stereoscopic fundus examination with a 90 diopter lens [7–9]. Also, the glycated haemoglobin (HbA1c) levels of the diabetic eyes were separated into three distinct groups: well regulated (6.1–8%), moderately regulated (8.1-10%) and (≥10.1%) as poorly regulated [10,11]. Abbreviated summary of the ETDRS final scale of DR severity for individual eyes is presented in Table 1 [12].

Ophthalmic B-scan ultrasonography is an imaging modality that can be useful in proliferative diabetic retinopathy (PDR). B-scan ultrasonography creates an image of the eye by using sound waves transmitted at a high frequency from a transducer to the target tissue, which then return to the transducer at varying times and amplitudes. These signals are then interpreted and summed to construct a two-dimensional (2D) image of the eye [13]. While it is most useful in patients with VH or other media opacity. It can demonstrate if a RD is present and can show other retinal pathology such as a VH or posterior vitreous detachment (PVD) [14].

In Sudan, it was noticed that most hospitals, private clinics and specialists are concentrated in Khartoum State, where approximately (70%) of eye care is found [1]. Unfortunately, limited information is available about the risk factors and frequency of DR in Sudanese population. Therefore, this study was designed with an aim to determine the causes of low vision among Sudanese patients with DR by using ophthalmic B-scan ultrasonography.

2. Materials and methods

2.1. Selection and description of patients

After receiving approval from the local ethics committee, a group of 100 patients with DR at different grades, presenting at the ultrasound clinic, Makkah Eye Hospital, Khartoum, Sudan, were recruited between September 2016 and January 2018 in this prospective study. A waiver of informed consent was granted in accordance with institutional guidelines.

Before starting the ophthalmic ultrasound scanning, all patients underwent standard physical and ophthalmologic examinations. Were a detailed history and complete preoperative eye examination protocol, including slit lamp examination, visual acuity tests, intra-ocular pressure, pupillary reaction, biomicroscopy, fundoscopy, and tonometry were done. The diagnostic of DR was based on the clinical and retinography examinations performed. In addition, to ensure the credibility of the obtained results, a very strict inclusion criteria were followed, which were the existence of one of the following conditions in patients: Sudanese nationality, area of location in Sudan, gender difference either male or females, ages and ethnicities, patients with any type of diabetes mellitus (DM) (fasting serum glucose > 126 mg/dL on two independent determinations), with no hypertension or ocular hypertension (> 20 mm Hg), no previous history of ocular trauma or ocular surgery at any time or afferent pupillary conduction defect, and not undergoing insulin treatment. Also, patients with type 2 DM with no proliferative DR or hypertension and not undergoing insulin treatment were included in the study.

2.2. Ophthalmic B-scan ultrasonography examination

All sonographic examinations were performed in a supine position in a thermally controlled room of (26 °C; 78 °F) by the same sonographer. The diagnostic B-mode was performed using a Nidek (Echoscan US-4000) ultrasonic unit, equipped with a high frequency direct contact 10 MHz transducer. It allows high-resolution images from 400 lines of sampling over 60°, displayed on the 1024 × 768 extended graphics array/adaptor (XGA) touch screen monitor with built-in thermal printer. Initial examination was performed under high gain (80 dB to 90 dB) and low gain (60 dB to 70 dB) sensitivity for more detailed inspection during ultrasonography.

For efficient and accurate diagnosis of ultrasound images, the appropriate time gain compensation and dynamic range control of ultrasound echo signals were automatically set by the system and/or manually adjusted by the sonographer to obtain the desired image quality on the screen. Time gain compensation was used for compensating the attenuation of ultrasound echo signals along the depth, and the dynamic range adjusted was for controlling the image contrast resolution, i.e., To increase the ability to distinguish between different echo amplitudes of adjacent structures.

Minims Tetracaine Hydrochloride (0.5%) w/v, eye drops solution was used for local anesthesia and Aquasonic 100 Ultrasound Gel was applied as the coupling material. B-scans were performed with the patient lies in the supine position. The transverse probe position (Fig. 1) was used to demonstrate the lateral extent of the pathology. With the eye anesthetized, the patient was instructed to look in the direction of the area of interest. The probe face is coated in ultrasound gel and positioned on the opposite conjunctival surface parallel to the limbus, regardless of probe location around the globe, with the marker aimed either superiorly or nasally. Consequently, the marker is oriented superiorly when examining the nasal or temporal globe (3 O'clock or 9 O'clock positions) and toward the nose when examining the superior or inferior globe (12 O'clock or 6 O'clock positions).

B-scans with longitudinal probe positions (Fig. 2) were also used to represent the radial extent. As with transverse scans, the patient is instructed to look in the direction of the area of interest, and the probe face is placed on the opposite conjunctival surface. However, in longitudinal scanning, the probe face is rotated so that it is perpendicular to the limbus, with the marker directed toward the limbus, or to the area of interest, regardless of the clock hour being examined. This results in the optic nerve shadow being represented at the bottom on the right side of each longitudinal echogram, and the posterior pole just above the nerve shadow.

If any posterior pathology is detected during basic screening, it should be centered on the right side of the echogram to achieve greater resolution. This is accomplished by determining the clock hour represented in the center, top, and bottom of the right side on the

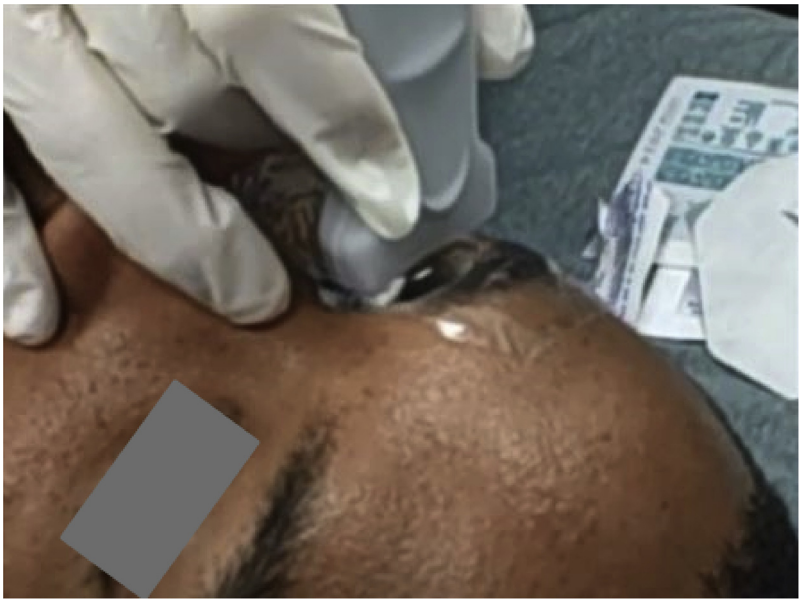

Fig. 1. Ocular B-scan with a transverse probe position. The probe face is coated in ultrasound gel and positioned on the opposite conjunctival surface parallel to the limbus.

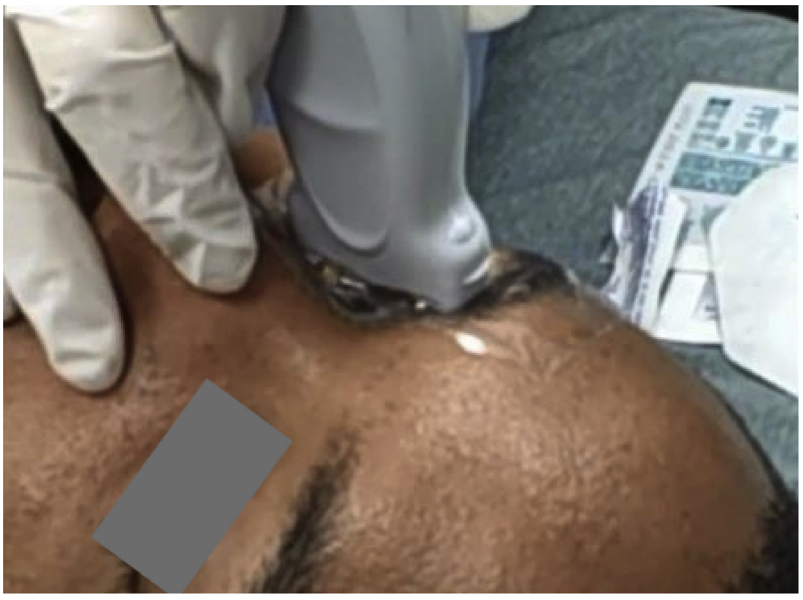

Fig. 2. Ocular B-scan with a longitudinal probe position. The probe face is rotated so that it is perpendicular to the limbus, or to the area of interest.

transverse scan where it was discovered, and then determining where this pathology lies in relation to those clock hours. Once determined, the patient should be instructed to redirect his or her gaze to that meridian, with the probe then placed on the opposite scleral surface. Perpendicularity to the pathology is achieved when it is centered and when the vertex of the pathology is a brighter white. The gain is now reduced until the greatest resolution is achieved, and photographic documentation is produced with proper labeling.

2.3. Especial considerations for performing ophthalmic B-scan ultrasonography examination

To confirm safety procedures with regard to eye imaging in the current study, the guidelines for probe and ultrasound scanner used were concentrated on several variables as, initial power setting, exposure time, stationary probe. The initial power setting for the ultrasound scanners used during eye ultrasonography was set up so that the default setting of the acoustic output power control is low. The output power was only increased during the investigation if this was necessary to produce a satisfactory result. Also, the overall examination exposure time for each case was kept as short as was necessary to produce a useful diagnostic result. The used ultrasound transducer for eye ultrasonography was not held in a fixed position for any longer than was necessary, and was removed from the patient whenever there was no need for a real time image. For example, the authors used the freeze frame or cine loop facilities to allow images to be reviewed and discussed without continuing the exposure. Particular care should be taken to reduce the risk of thermal and non-thermal effects during investigations of the eye.

2.4. Statistical analysis

The all measurable data were initially summarized as a mean ± standard deviation (SD) in a form of comparison tables and graphs.

Table 2
Age distribution among DM patients in the study sample.

Age ranges (years)	Frequency (n); percentage (%) of age ranges in male patients	Frequency (n); percentage (%) of age ranges in female patients	Mean age ± SD (years) in male patients	Mean age ± SD (years) in female patients	Mean age ± SD (years) in the sample
14–24	6(8%)	1(4%)	16 ± 1.2	22 ± 2.2	19 ± 1.7
25–35	8(10.7%)	2(8%)	26 ± 1.1	28 ± 1.2	27 ± 1.2
36–46	12(16%)	2(8%)	39 ± 1.7	45 ± 1.9	42 ± 1.8
47–57	25(33.3%)	10(40%)	55 ± 2.1	52 ± 0.8	53.5 ± 1.5
58–68	10(13.3%)	4(16%)	63 ± 1.1	65 ± 1.7	64 ± 1.4
69–79	14(18.7%)	6(24%)	71 ± 0.8	75 ± 1.1	73 ± 1.0
Total	75(100%)	25(100%)	45 ± 1.3	47.8 ± 1.5	46.4 ± 1.4

Table 3
Comparison between mean DM duration among different ethnics.

Ethnics	Male patients frequency (n); percentage (%)	Female patients frequency (n); percentage (%)	Mean duration of DM in male patients (years ± SD)	Mean duration of DM in female patients (years ± SD)	Mean duration of DM in the sample (years ± SD)
Patients from Center of Sudan	44(58.7%)	14(56%)	20 ± 2.1	29 ± 1.9	24.5 ± 2.0
Patients from North of Sudan	18(24%)	5(20%)	12 ± 1.7	26 ± 2.1	19 ± 1.9
Patients from East of Sudan	6(8%)	3(12%)	27 ± 0.8	17 ± 1.7	22 ± 1.3
Patients from West of Sudan	4(5.3%)	2(8%)	15 ± 1.1	11 ± 1.8	13 ± 1.5
Patients from South of Sudan	3(4%)	1(4%)	13 ± 1.9	19 ± 1.3	16 ± 1.6
Total	75(100%)	25(100%)	17.4 ± 1.5	20.4 ± 1.8	18.9 ± 1.7

Range, mean, and SD across minimal NPDR, mild NPDR, moderate NPDR, severe NPDR, and PR patients, were calculated for age, duration of DM, HbA1c levels. The statistical diagnostic test was used to detect sensitivity and specificity of ophthalmic B-scan ultrasonography in diagnosing the causes of low vision in diabetic patients. Statistical analysis was performed using the standard Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 20 for windows.

3. Results

In this prospective study, a total of 100 known diabetic patients (200 eyes) completed standard physical, ophthalmology examinations, and ophthalmic B-scan ultrasonography examination. A total of 75(75%) patients were males and the rest 25(25%) were females (ratio of 3:1). The mean age ± SD was was 46.4 ± 1.4 years (45 ± 1.3 years for males and 47.8 ± 1.5 years for females) with age ranges from 14 up to 79 years (Table 2). In male population, 25 patients were in the age group 47–57 years, representing (33.3%) of the population. The age group 14–24 years was the smallest (8%) of the population (Table 2). In the population of the females, 10 patients were in the age group 47–57 years, representing (40%) of the population. The age groups 14-24 years was the smallest (4%) of the population (Table 2).

The highest mean duration of DM was (29 ± 1.9 years) and found in males from Center of Sudan, while the lowest mean duration of diabetes (11 ± 1.8 years) was detected in patients from West of Sudan. Female patients from Center of Sudan (20 ± 2.1 years) presents with the highest mean of diabetes duration in comparing to (12 ± 1.7 years) found in female patients from North of Sudan, whom present with the lowest mean duration of the disease. The mean duration of diabetes in the sample was (18.9 ± 1.7 years) with a disease duration range from 11 years to 29 years (Table 3).

According to the grading of the status of retinopathy by using the ETDRS severity level, results demonstrate that majority of patients (34%) present with mild NPDR. In addition, HbA1c levels of the diabetic eyes were found to be ranged from (9.55 ± 1.7 to 11.9 ± 1.1) as moderately regulated to poorly regulated (Table 4). Furthermore, the distribution of NPDR among patients regarding to patients age, gender, duration of DM, and ethnicity was also presented in Table 4.

Ophthalmic ultrasound revealed that VH 57(57%), RD 21(21%) either partial 9(9%) or total 12(12%), PVD 7(7%), asteroid hyalosis (AH) 12(12%), and choroidal detachment (CD) 3(3%), were the main causes of low vision among Sudanese patients with DR in the current study (Figs. 3–8).

The ophthalmic ultrasound findings in patients presenting with

Table 4
Grading of DR status in the eyes of the diabetic patients.

Variables	Minimal NPDR	Mild NPDR	Moderate NPDR	Severe NPDR	PR
Numbers in the sample	29	34	21	11	5
Mean age ± SD (years)	23 ± 0.8	41 ± 1.7	55 ± 2.3	59 ± 1.5	67 ± 2.1
Duration of DM	14 ± 1.9	17 ± 2.1	20 ± 1.8	23 ± 2.8	25 ± 3.1
HbA1c (%)	9.55 ± 1.7	9.92 ± 2.1	10.3 ± 0.1	10.9 ± 0.5	11.9 ± 1.1
Male-Female (in the sample)	22–7	24–10	16–5	9–2	4–1
Male-Female (Center of Sudan)	10–5	18–6	7–2	3–0	2–1
Male-Female (North of Sudan)	6–1	2–0	4–1	4–1	0–0
Male-Female (East of Sudan)	3–0	3–1	2–0	1–0	1–0
Male-Female (West of Sudan)	2–1	0–3	3–1	0–1	0–0
Male-Female (South of Sudan)	1–0	1–0	0–1	1–0	1–0

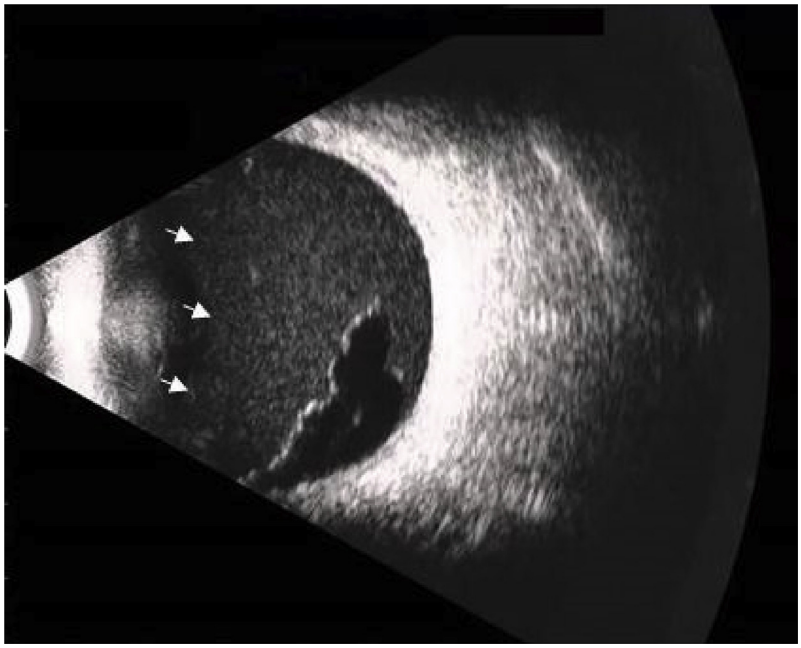

Fig. 3. B-mode ophthalmic ultrasound scan of a 20 year old male, demonstrates the features of a fresh VH (arrows).

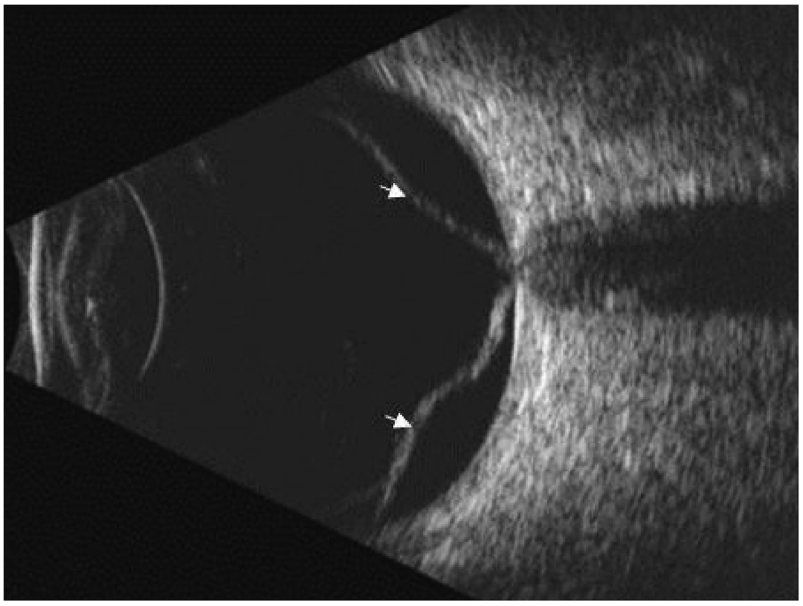

Fig. 4. An axial scan in a 39 year old female demonstrates features related to PRD (arrows).

moderately regulated HbA1c and graded with either minimal or mild NPDR, were VH 42(66.6%), AH 12(14.3%), and partial retinal detachment (PRD) 9(19%) were the main cause of low vision (Table 4 and Fig. 9). In contrast, the ultrasound findings of VH 15(40.5%), total retinal detachment (TRD) 12(32.4%), PVD 7(19%), and CD 3(8.1%), were dominant in patients classified with poorly regulated HbA1c and graded either as moderate NPDR; severe NPDR; and PR (Table 4 and Fig. 9).

Diagnostic testing revealed a sensitivity of (98.95%) (95% confidence interval (CI) of 94.27%–99.97%), and specificity of (85.71%) (95% CI of 57.19% to 98.22%) for the performance of ophthalmic ultrasound in detection the causes of low vision in diabetic patients. Furthermore, results showed positive predictive value (PPV) of (97.92%) and negative predictive value (NPV) of (92.31%) for ultrasound performance too (Table 5).

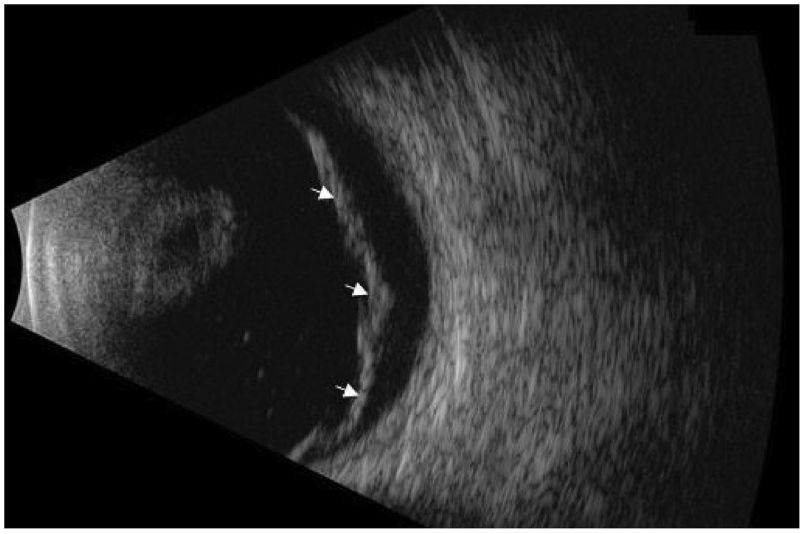

Fig. 5. A male patient of 32 years old presents with sonographic features that are compatible with TRD (arrows).

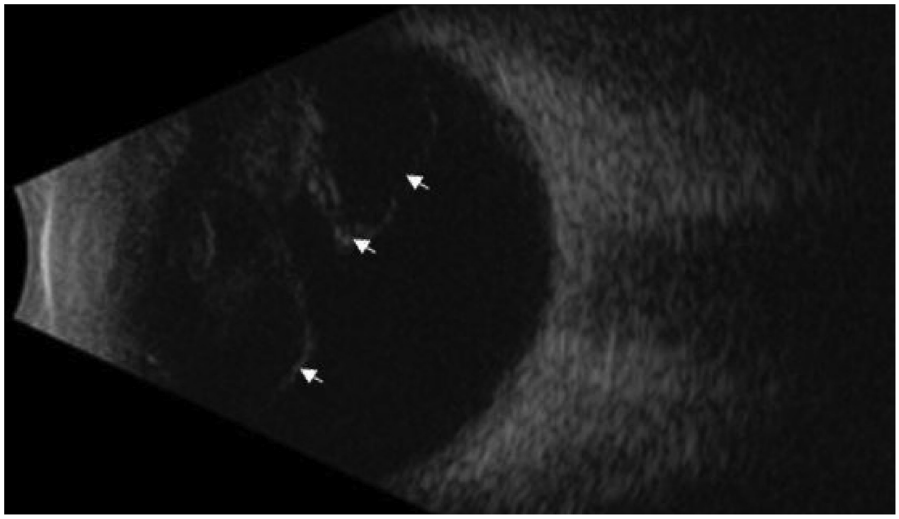

Fig. 6. Sonographic features of PVD (arrows), presented in a 30 year old male. Signs of an irregular shaped membrane with no posterior pole attachment were also noticed.

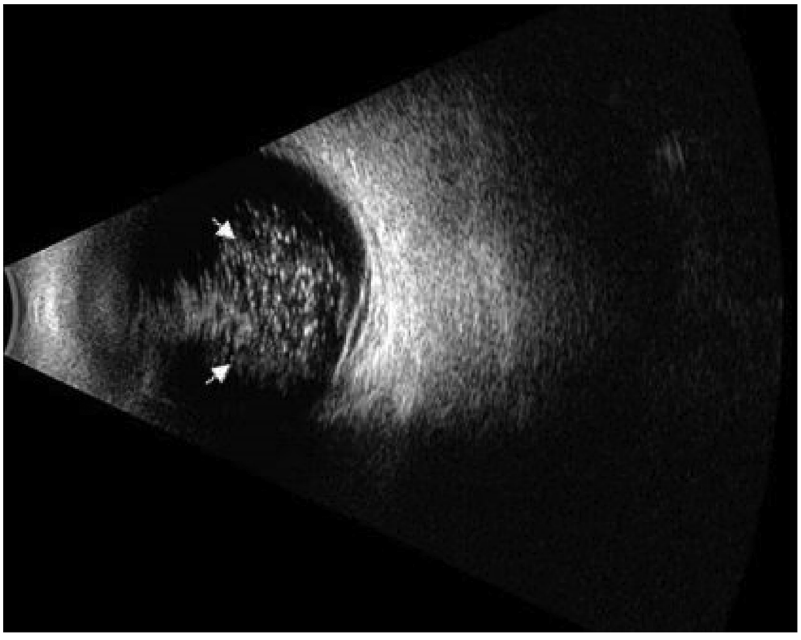

Fig. 7. Ophthalmic ultrasound scan of a 25 year old female demonstrates diffused hyper-echogenic foci (arrows) that involved all the vitreous area and associated with AH.

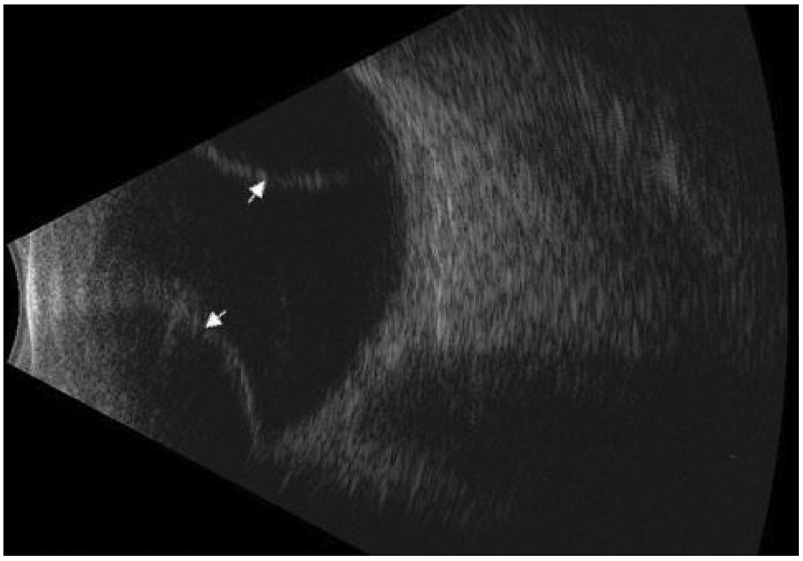

Fig. 8. An axial ultrasound scan of a 30 year old male, shows the features of CD (arrows).

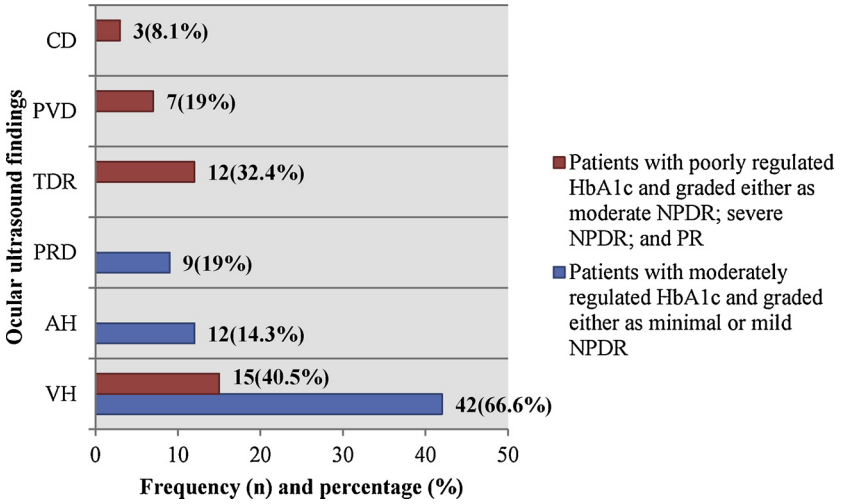

Fig. 9. Causes of low vision as classified sonographically in diabetic patients according to their HbA1c and ETDRS severity levels.

Table 5
Performance of ophthalmic ultrasound in detection the causes of low vision in diabetic patients.

Causes of low vision in diabetic patients		Number of cases (n)
True positive		94
True negative		12
False positive		2
False negative		1
Performance of ophthalmic ultrasound	**Value**	**(95%) CI**
Sensitivity (%)	(98.95%)	(94.27% to 99.97%)
Specificity (%)	(85.71%)	(57.19% to 98.22%)
Positive likelihood ratio	6.93	1.92 to 24.99
Negative likelihood ratio	0.01	0.00 to 0.09
Disease prevalence (%)	(87.16%)	(79.39% to 92.80%)
PPV (%)	(97.92%)	(92.87% to 99.41%)
NPV (%)	(92.31%)	(62.80% to 98.84%)

4. Discussion

Ophthalmic B-scan ultrasonography is most useful in diabetic patients with VH or other media opacities, where the retina cannot be visualized directly on ophthalmic examination. B-scan ultrasonography can demonstrate if RD is present and can show other retinal pathology such as a VH or PVD [14]. This study established the causes of low vision in DM patients (age ranges from 14 up to 79 years) from different

ethnicities in Sudan (Tables 2–4), according to their ETDRS severity level and HbA1c (%) as presented in Table 4. The current study showed that eyes of diabetic patients are subjective to several pathologies in patients with poorly regulated HbA1c levels in comparing to moderately regulate HbA1c, as well as the increasing of the NPDR severity (Figs. 3–9). Therefore, an improvement in diagnostic accuracy of ophthalmic sonography might be obtained if the results of sonographic examination of diabetic patients were referenced to ETDRS and HbA1c (%) levels.

Tissue hypoxia in diabetic patients is the major cause that leads to decreased visual function. Also the increase in the level of vascular endothelial growth is probably one of the major angiogenic factors implicated in the pathogenesis of DR. The microangiopathy and capillary occlusion together lead to microvascular leakage and breakdown of the blood retinal barrier, resulting in retinal hemorrhage and edema, as well as the development of macular edema. These patients suffer from an irregular ocular vascular function with depressed autoregulatory responses to differing oxygen levels or medications [15,16]. Thus, ultrasound findings in our study demonstrate that the highest frequency of eye abnormalities in diabetic patients was VH, AH, RD, PVD, and CD (Figs. 3–9).

The causes of low vision in this study could be compared to the results of a study about sonographic ocular findings in DR, where ocular sonography is very useful diagnostic tool in detection and evaluation of DR complications, because it shows the nature and extent of lesions in eyes with vitreous opacification, which is usually not visualized on ophthalmoscopy, helping to determine the clinical treatment or timing of surgery, and to predict the visual outcome and it may serve as a useful extension of the initial investigation of the symptomatic or asymptomatic patients [17].

The effectiveness of any screening modality is assessed by its sensitivity and specificity. The sensitivity and specificity of ophthalmic ultrasound in this study were (98.95% and 85.71%) respectively. Furthermore, ophthalmic ultrasound showed a PPV of (97.92%) and NPV of (92.31%) (Table 5). Also findings regarding the sensitivity and specificity of ophthalmic ultrasonography were in agreement with several studies in the same field [18–20].

The prevalence of DR in Sudan was estimated to be around (17.2%) in 1991 [4]. In addition, our results revealed that the majority of diabetic patients were from Center of Sudan, therefore the distribution of low vision causes were dominant in this group compared to other ethnicities (Table 3). Such results could be compared to the findings of a study about the frequency of DR and associated risk factors in Khartoum, Sudan: population based study, where, among 316(100%) diabetic participants, the overall frequency of DR was 261(82.6%) [21].

This study is limited by the unevenness of the population (age groups, gender groups, and ethnic groups) as a result of the randomized selection process, which unfortunately might affect the accuracy of the DR influence on our measurement parameters, and in fact significantly reduce the power of our conclusions, because it makes other age groups have a lower statistical credibility if applied in future studies. The importance of the current study lies upon it is one of the recent studies that determine the causes of low vision among diabetic Sudanese patients with DR by the using of ophthalmic B-scan ultrasonography, which is more likely to be modest in magnitude in this case since the study was a population based in its nature.

5. Conclusion

In conclusion, the key to diabetic vision loss is to prevent it through early detection and treatment. Ophthalmic B-mode ultrasound is a rapid, noninvasive imaging technique that can be used with minimum discomfort in ophthalmological practice for the detection and evaluation of DR complications, because it shows the nature and extent of diabetic effects in eyes with vitreous opacification, which is usually not visualized on ophthalmoscopy, helping to determine the clinical treatment or timing of surgery, and to predict the visual outcome. In addition, measurements derived from ophthalmic B-scan include visualization of the lesion, including its anatomic location, shape, borders, and size. Also, it's particularly helpful in determining the density and extent of a VH, the presence of vitreoretinal detachment, and fibrovascular membranes. Thus, ophthalmic ultrasound may serve as a useful extension of the initial investigation of symptomatic and asymptomatic diabetic patients.

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Conflict of interest

The authors have declared no conflict of interest.

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