

Comprehensive Analysis of Diabetes Mellitus-Associated Visual Impairment: Insights from Ophthalmological Screening Program in Libya

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Abstract

Purpose: Diabetes Mellitus (DM) is a prevalent metabolic disorder associated with significant complications, including visual impairment. This study aimed to assess the prevalence and severity of visual impairment and its associated factors in diabetic patients in Libya. **Methods:** This cross-sectional study included 2365 DM patients (4730 eyes). Most participants were aged 30 - 49 (38.3%) and 50 - 69 (50.8%) with a nearly equal gender distribution (47.8% males, 52.2% females). Type 2 diabetes was predominant (92.6%), and 62.9% had HbA1c levels of 7.5% or higher. **Results:** Diabetic retinopathy (DR) was present in 2068 eyes (43.8%), with mild non-proliferative diabetic retinopathy (NPDR) affecting 1178 eyes (25%), moderate NPDR 476 eyes (10.1%), severe NPDR 228 eyes (4.8%), and proliferative diabetic retinopathy (PDR) 186 eyes (3.9%). Diabetic maculopathy was observed in 621 eyes (13.1%), with CSME in 287 eyes (6.07%) and non-CSME in 334 eyes (7.06%). Non-retinal conditions included cataracts in 1938 eyes (41%) and glaucoma in 252 eyes (5.3%). Visual impairment was observed in 1159 patients (49%), with 534 (23%) experiencing mild impairment, 382 (18%) moderate impairment, and 243 (12%) severe impairment; 142 patients (6%) were classified as legally blind. DR showed a strong association with visual impairment severity ($p < 0.001$). Cataracts, diabetic maculopathy, and glaucoma also correlated significantly with visual impairment severity ($p < 0.001$). The duration of diabetes and systemic comorbidities demonstrated significant associations with visual impairment ($p < 0.001$). **Conclusions:** These findings underscore the urgency for targeted

public health interventions to mitigate visual impairment in Libyan individuals with DM.

Keywords

Diabetes Mellitus, Visual Impairment, Diabetic Retinopathy, Cataracts, Glaucoma, Ophthalmological Screening Program, Libya, Public Health Strategies

1. Introduction

Diabetes Mellitus (DM) represents a spectrum of metabolic disorders characterized by elevated blood glucose levels due to defects in insulin secretion, action, or both. Type 1 diabetes is caused by the autoimmune destruction of pancreatic beta cells, resulting in absolute insulin deficiency, while Type 2 diabetes involves insulin resistance and a relative deficiency of insulin often associated with obesity and factors related to lifestyle [1] [2].

This metabolic disorder impacts millions worldwide and encompasses various age groups and socio-economic backgrounds. Its prevalence is reaching epidemic levels, with both developed and developing countries grappling with escalating rates [3].

In addition to its significant prevalence, DM shows a multifaceted challenge due to its complications, which extend far beyond glucose dysregulation. Acute complications like diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome, while chronic complications include neuropathy, nephropathy, and retinopathy [4]-[6]. Furthermore, the economic burden of diabetes is astounding stressing healthcare systems and economies globally [7].

Several previous studies demonstrate that visual impairment in diabetes is an essential complication that significantly impacts the quality of life and functional abilities of individuals with diabetes. It comprises a spectrum of visual impairment, ranging from mild blurriness to severe vision loss, and can result from several diabetic eye diseases, such as diabetic retinopathy, diabetic macular edema, cataracts, and glaucoma. Comprehending the mechanisms underlying this complication and their relationship to diabetes is crucial for effective management and prevention strategies [8]-[12].

The main objective of this study is to conduct an extensive assessment of visual impairment associated with Diabetes Mellitus. By investigating this multifaceted issue, we aim to gain deeper insights into the prevalence, risk factors, and patterns of visual impairment among individuals affected with diabetes. Through rigorous analysis, our research seeks to contribute substantially to the comprehension of diabetic complications, especially in the field of visual health. The study draws upon data collected through the Ophthalmological Screening Program established at the National Center for Diabetes Diagnosis and Treatment in Benghazi, Libya.

This program stands as an essential initiative aimed at early detection and management of diabetic eye diseases. Our study seeks to illuminate the landscape of diabetes-associated visual impairment within the Libyan context and improve visual health outcomes.

2. Methodology

This cross-sectional study enrolled 2365 individuals diagnosed with diabetes mellitus, representing a total of 4730 eyes. Data were collected from a comprehensive ophthalmological screening program conducted at the National Center for Diabetes Diagnosis and Treatment, Benghazi, Libya from November 2022 to April 2024.

2.1. Patient Recruitment and Data Collection

Patients were recruited from the outpatient department of the National Center for Diabetes Diagnosis and Treatment over a designated period inclusion criteria were broad, encompassing individuals with either type 1 or type 2 diabetes mellitus, with ages ranging from 14 to 73 years. Through meticulous scrutiny of medical records, essential demographic and clinical data were obtained, including age, gender, duration of diabetes diagnosis, type of diabetes mellitus, and glycated hemoglobin (HbA1c) levels. Patients were excluded if they had non-diabetic ocular diseases (e.g. keratopathy, uveitis), hereditary retinal diseases, ocular trauma, incomplete medical records, or were pregnant.

2.2. Systemic Involvement Data Collection

In addition to demographic and clinical data, Systemic involvement data were obtained by carefully reviewing the patient's medical records. These records are gathered by physicians and endocrinologists at the center, including but not limited to systolic and diastolic blood pressure readings, lipid profiles, renal function tests, and records of any cardiac diseases. In addition to demographic and clinical data, this meticulous documentation enabled us to conduct a comprehensive assessment of systemic conditions commonly associated with diabetes mellitus.

2.3. Ophthalmological Examination

Visual acuity assessment was conducted using the Snellen chart, following WHO standards to categorize participants into different levels of visual function. Those achieving visual acuity of 6/12 or better were classified as having Normal Vision. In contrast, participants with visual acuity below the threshold for normal vision but better than 6/18 were classified as having Low Vision. Additionally, participants were further categorized based on the severity of impairment: 1—Mild Impairment (6/12 - 6/18), 2—Moderate Impairment (6/18 - 6/60), and 3—Severe Impairment (<6/60). Those with visual acuity less than 3/60 were classified as Legally Blind [13]. Intraocular pressure measurement was conducted using an applanation tonometer (Keeler KAT-T type), and a detailed anterior segment

examination was performed using a Keeler 25z slit lamp. Cataract severity was assessed using The Lens Opacities Classification System III (LOCS III), categorizing cataracts into three main levels: Mild, Moderate, and Severe. This system provides a standardized method for evaluating the severity of lens opacities, aiding in the assessment of cataract-related visual impairment [14].

A dilated fundus examination was performed to assess the posterior segment using a +90 D Volk lens, encompassing the retina, optic nerve, and macula. The severity of diabetic retinopathy was classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria [15]. Optical coherence tomography (OCT) imaging by Topcon Triton provided high-resolution cross-sectional images of the macula, facilitating the categorization of macular edema into clinically significant macular edema (CSME) and non-CSME according to ETDRS criteria. Fluorescein angiography (FFA) was also performed in selected cases to confirm the diagnosis.

2.4. Data Analysis

The data were analyzed using SPSS version 23 for Windows software. The results were expressed as mean \pm Standard deviation, Numbers, and percentages.

Descriptive statistics were used to summarize demographic and clinical characteristics, while inferential statistics, including chi-square tests and logistic regression analysis, were employed to assess associations between variables and visual impairment severity. Statistical significance was set at a p-value of <0.05 .

2.5. Ethical Considerations

The study adhered to ethical principles by the Declaration of Helsinki. Before enrollment, informed consent was obtained from all participants. The investigator explained to each patient the study's nature, objectives, procedures, expected duration, and any discomfort that may arise. Participants were assured of the voluntary nature of their participation and their right to withdraw at any time without explanation. It was emphasized that withdrawal would not affect their medical care or relationship with their healthcare provider. The study ensured confidentiality and voluntary participation. Approval for the research protocol was granted by the Ethics Committee at the National Center for Diabetes Diagnosis and Treatment.

3. Results

This study included 2365 patients with diabetes mellitus, representing 4730 eyes. The demographic and clinical characteristics of the patients are summarized in **Table 1**. The majority of patients were between the ages of 30 - 49 (38.3%) and 50 - 69 (50.8%), with a nearly equal distribution of males (47.8%) and females (52.2%). The duration of diabetes diagnosis varied, with 43.1% diagnosed for 10 - 20 years, 26.1% for less than 10 years, and 7.8% for over 30 years. The majority of patients had type 2 diabetes mellitus (92.6%), while 7.4% had type 1 DM. Most

patients (62.9%) had HbA1c levels of 7.5% or higher, indicating suboptimal glycemic control.

The distribution of diabetic retinopathy (DR) within the study cohort is illustrated in **Table 2**. Of the total sample, 2068 eyes (43.8%) were diagnosed with diabetic retinopathy. Mild non-proliferative diabetic retinopathy (NPDR) was the most prevalent subtype, affecting 1178 eyes (25.0%), followed by moderate NPDR in 476 eyes (10.1%), severe NPDR in 228 eyes (4.8%), and proliferative diabetic retinopathy (PDR) in 186 eyes (3.9%). Additionally, diabetic maculopathy was observed in 621 eyes (13.1%), with clinically significant macular edema (CSME) in 287 eyes (6.07%) and non-CSME diabetic maculopathy in 334 eyes (7.06%).

The distribution of non-retinal ocular conditions observed within the study cohort is summarized in **Table 3**. Cataracts emerged as the most prevalent ocular condition, affecting 1938 eyes (41%), with mild cases accounting for 834 eyes (17.6%), moderate cases for 601 eyes (12.7%), and severe cases for 503 eyes (10.6%). Glaucoma was identified as another significant ocular comorbidity, affecting 252 eyes (5.3%), with open-angle glaucoma being the predominant subtype (210 eyes, 4.4%).

The distribution of visual impairment categories among the study participants is outlined in **Table 4**. The majority of patients (1159, 49%) presented with some degree of visual impairment, with 534 patients (23%) classified as experiencing mild impairment, 382 patients (18%) classified as having moderate impairment, and 243 patients (12%) classified as having severe impairment. Additionally, 142 patients (6%) were categorized as legally blind.

An in-depth analysis of factors influencing visual impairment among diabetic patients is detailed in **Table 5**. Diabetic retinopathy emerges as a cornerstone, exhibiting a profound association across all severity categories of visual impairment, with prevalence rates of 78% for low vision, 86% for mild impairment, 87% for moderate impairment, 81% for severe impairment, and a statistically significant p-value of <0.001 . Cataracts and diabetic maculopathy also demonstrate significant correlations with increasing severity of visual impairment, with highly significant p-values of <0.001 . The prevalence of glaucoma among individuals with visual impairment was 3.5% in the low vision group, 8.9% in the mild impairment group, 17.6% in the moderate impairment group, and 33% in the severe impairment group. The association between glaucoma and visual impairment was statistically significant ($p < 0.001$). The duration of diabetes mellitus (DM) unveils a significant association with visual impairment severity among diabetic individuals, with patients with longer disease duration demonstrating higher prevalence rates of visual impairment across all severity categories, with statistically significant p-values of <0.001 . Vitreous hemorrhage and tractional retinal detachment represent advanced ocular complications associated with visual impairment among diabetic patients, with highly significant p-values of <0.001 . Similarly, tractional retinal detachment exhibits a notable association with visual impairment severity, with increasing prevalence rates observed across severity categories, and

Table 1. The demographic and clinical characteristics of the patients.

Variable	NUMBER OF PATIENTS	Percentage (%) (Total Sample)
Sex		
Males	1130	47.8%
Females	1235	52.2%
Age group		
14 - 29	89	3.7%
30 - 49	908	38.3%
50 - 69	1203	50.8%
70 - 73	165	7.0%
Duration of DM		
< 10 years	616	26.1%
10 - 20 years	1019	43.1%
20 - 30 years	546	23.1%
> 30 years	184	7.8%
Type of DM		
Type 1 DM	175	7.4%
Type 2 DM	2190	92.6%
HbA1c		
< 7.5	876	37.1%
≥ 7.5	1489	62.9%
Systemic involvement		
Hypertension	994	42%
Dyslipidemia	344	14.5%
Heart Disease	237	10%
Diabetic Nephropathy	101	4.3%

Table 2. Diabetic Retinopathy Distribution.

Retinopathy	Frequency (Eyes)	Percentage (%) (Total Sample)
Total (Non-Diabetic Retinopathy)	2662	56.2%
Total (Diabetic Retinopathy)	2068	43.8%
Mild NPDR	1178	25.0%
Moderate NPDR	476	10.1%
Severe NPDR	228	4.8%
PDR	186	3.9%
Total (Diabetic Maculopathy)	621	13.1%
CSME (Diabetic Maculopathy)	287	6.07%
Non-CSME (Diabetic Maculopathy)	334	7.06%
Vitreous Hemorrhage	27	0.5%
Tractional Retinal Detachment	19	0.4%

Table 3. Non-retinal ocular involvement.

Ocular condition	Frequency (Eyes)	Percentage (%) (Total Sample)
Cataract N = 1938, 41%		
Mild	834	17.6%
Moderate	601	12.7%
Severe	503	10.6%
Glaucoma N = 252, 5.3%		
Open-angle glaucoma	210	4.4%
Neovascular glaucoma	42	0.8%

Table 4. Visual impairment.

Visual Acuity Category	Number of Patients	Percentage (%) (Total Sample)
A-Normal Vision (6/12 or better)	1064	45%
B-Low vision	1159	49%
1-Mild Impairment (6/12 - 6/18).	534	23%
2-Moderate Impairment (6/18 - 6/60).	382	18%
3-Severe Impairment (<6/60).	243	12%
C-Legally Blind (<3/60).	142	6%

Table 5. Factors influencing visual impairment among diabetic patients.

	Low vision N = 1159				p value
	Mild IMPAIRMENT N = 534	Moderate IMPAIRMENT N = 382	Severe IMPAIRMENT N = 243	Legally Blind N = 142	
Diabetic Retinopathy	N = 416, 78%	N = 328, 86%	N = 211, 87%	N = 115, 81%	<0.001
Cataract	N = 378, 70.7%	N = 267, 69.8%	N = 123, 50.6%	N = 17, 11.9%	<0.001
Diabetic Maculopathy	N = 79, 14.7%	N = 176, 46%	N = 107, 44%	N = 19, 13.3%	<0.001
Glaucoma	N = 19, 3.5%	N = 34, 8.9%	N = 43, 17.6%	N = 47, 33%	<0.001
Duration of DM < 10 years	N = 258, 48.3%	N = 38, 9.9%	N = 27, 11.1%	N = 9, 6.3%	<0.001
Duration of DM 10 - 20 years	N = 123, 23%	N = 171, 44.7%	N = 98, 40.3%	N = 23, 16.15%	<0.001
Duration of DM 20 - 30 years	N = 89, 16.6%	N = 76, 19.8%	N = 55, 22.6%	N = 43, 30%	<0.001
Duration of DM > 30 years	N = 64, 11.9%	N = 97, 25.3%	N = 63, 25.9%	N = 67, 47.1%	<0.001
HbA1c > 7.5	N = 243, 45.5%	N = 269, 70.4%	N = 154, 63.3%	N = 78, 54.9%	<0.001
Vitreous Hemorrhage	N = 3, 0.56%	N = 7, 1.8%	N = 19, 7.8%	N = 13, 9.15%	<0.001
Tractional Detachment	N = 0	N = 9, 2.3%	N = 11, 4.5%	N = 9, 6.3%	<0.001
Hypertension	N = 247, 46.2 %	N = 143, 37.4%	N = 123, 50.6%	N = 61, 42.9%	<0.001
Dyslipidemia	N = 44, 8.2%	N = 32, 8.3%	N = 59, 24.2%	N = 19, 13.3%	<0.001
Heart Disease	N = 6, 1.1%	N = 17, 4.4%	N = 29, 11.9%	N = 42, 29.5%	<0.001
Diabetic Nephropathy	N = 8, 1.4%	N = 13, 3.4%	N = 24, 9.8%	N = 37, 26%	<0.001

a highly significant p-value of <0.001. Moreover, systemic comorbidities including hypertension, dyslipidemia, heart disease, and diabetic nephropathy, demonstrate varying degrees of association with visual impairment, with highly significant p-values of <0.001, emphasizing the systemic nature of diabetic ocular complications.

4. Discussion

Diabetes is a substantial concern in the context of global public health. The urgent requirement for precise assessments of vision loss caused by diabetes highlights the necessity for efficient public health strategies focused on decreasing the risk of visual impairment and managing diabetic complications. To the best of our knowledge, our study represents the first investigation of its kind in Libya, undertaken within the context of the ophthalmic screening program at the National Center for Diabetes Diagnosis and Treatment in Benghazi. This center, located in the second largest city in Libya, covers the eastern region of the country and serves a population with significant ethnic diversity. By providing novel insights into diabetic eye disease within our region, we aim to lay the groundwork for informed interventions and strategic initiatives to address the challenges posed by visual impairment in diabetes within Libya.

The results of our study reveal an elevated incidence of diabetic retinopathy (DR) among individuals with diabetes in Libya, indicating a significant burden of this condition within our cohort. The prevalence rate we observed was 43.8%, significantly higher than the prevalence rate recorded in Libya between 1981 and 1991, which was 30.5%. This suggests a concerning increase in the prevalence of DR in the country in recent years. Several factors could potentially contribute to this increase. Within our group, the majority of patients (62.9%) had HbA1c levels of 7.5% or above, which indicates inadequate glycemic control. Moreover, a significant percentage of patients (50.8%) fell within the age range of 50 - 69, and a substantial majority (73.9%) had been diagnosed with diabetes for over a decade. Comorbid conditions such as hypertension were present in 42% of our cohort. Socioeconomic factors, including the impact of wars during the last decade, may also play a role in this rising incidence by affecting access to healthcare and the ability to control diabetes effectively [16].

In addition, our study revealed the distribution of DR grades among the patients. The prevalence rates for different stages of diabetic retinopathy are as follows: 25.0% for mild non-proliferative diabetic retinopathy (NPDR), 10.1% for moderate NPDR, 4.8% for severe NPDR, and 3.9% for proliferative diabetic retinopathy (PDR). In Egypt, a study revealed that the prevalence rates of mild non-proliferative diabetic retinopathy (NPDR) were 67.5%, moderate NPDR was 15.5%, severe NPDR was 6%, and proliferative diabetic retinopathy (PDR) was 6.2% [17].

Comparing our results with studies conducted in the Eastern Mediterranean region reveals comparable prevalence rates. For instance, research from the Eastern

Mediterranean region reported a prevalence of diabetic retinopathy at 31%, closely aligning with our findings. However, it is important to highlight that the prevalence rate seen in our study is higher than the prevalence rates reported in other regions [18].

Furthermore, the International Diabetes Federation (IDF) presented a global overview of diabetic retinopathy prevalence based on studies carried out between 2015 and 2019. The findings showed that the prevalence of diabetic retinopathy reached 27.0%. The prevalence of diabetic retinopathy (DR) was highest in Africa at 33.8%, followed by the MENA region (Middle East and North Africa) at 33.8%, and the Western Pacific region at 36.2%. This highlights the significant burden of DR in our country [19]. Furthermore, a study conducted in Latin America and the Caribbean revealed that the prevalence of diabetic retinopathy ranges from 37.3% to 40.6% among individuals diagnosed with diabetes mellitus [20].

The findings from our study provide an extensive perspective into the factors associated with visual impairment among individuals with diabetes in Libya, highlighting the multifactorial nature of this debilitating complication. Our study reveals a distribution of several factors throughout different categories of visual impairment, ranging from low vision to legally blind. Among the participants in our study cohort, a substantial percentage, which involved 1159 individuals (49%), demonstrated various degrees of visual impairment. Upon further analysis, we found that 23% of patients demonstrated mild impairment, 18% had moderate impairment, and 12% encountered severe impairment. Significantly, 6% of patients fulfilled the criteria for legal blindness. Comparing our findings with the findings from other studies, a study conducted in Tunisia reported that 22.2% of patients demonstrated visual impairment, with 4.4% categorized as legally blind, closely resembling our results of visual impairment and legal blindness [21]. Similarly, a study in Jordan demonstrated a prevalence of blindness among diabetic patients at 7.4%, while 10.1% were determined to be visually impaired [22].

Furthermore, a study carried out in India designed to determine the prevalence and risk factors of vision impairment and blindness among individuals with diabetes determined that out of 7910 people with diabetes included in the analysis, the estimated national prevalence of vision impairment was 21.1% and blindness was 2.4% [23].

The distribution of various factors related to visual impairment further illustrates the multifactorial nature of this complication among individuals with diabetes in Libya. Diabetic retinopathy comes as a prevalent contributor to visual impairment, with a significant percentage of patients diagnosed across all severity categories. Our study additionally demonstrated a significant association between diabetic retinopathy and visual impairment severity. Particularly, among individuals with low vision, 78% were diagnosed with diabetic retinopathy, while the prevalence rates increased to 86%, 87%, and 81% for those with mild, moderate, and severe visual impairment, respectively. This highlights the essential significance of diabetic retinopathy as a major determinant of visual impairment among

diabetic individuals in our region. In addition, the incidence of Diabetic Maculopathy, showed a comparable pattern, ranging from 14.7% in the low vision group to 13.3% in the legally blind group, indicating a significant association between diabetic maculopathy and low visual impairment.

Our findings corroborate previous studies that have identified diabetic retinopathy and maculopathy as significant factors contributing to visual impairment among diabetic individuals [24] [25].

The legally blind group, which consists of individuals with the most severe visual impairment, demonstrated distinct patterns and associations with various factors. The study revealed that glaucoma and diabetic retinopathy had the highest prevalence rates in this group among the factors examined.

Diabetic retinopathy was found in 81% of individuals in the legally blind group. This indicates a significant association between diabetic retinopathy and legal blindness. It is important to emphasize that diabetic retinopathy is a progressive condition, and its severity increases with the duration of diabetes. Therefore, early detection and effective diabetes management are essential in preventing or delaying the onset of legal blindness associated with diabetic retinopathy.

Glaucoma, a further contributor in the legally blind group, demonstrated a prevalence rate of 33%. This indicates a significant association between glaucoma and legal blindness. Glaucoma is a group of eye conditions characterized by damage to the optic nerve, if not treated, it can result in irreversible loss of vision. The high prevalence of glaucoma in the legally blind group highlights the importance of regular eye examinations, especially for individuals with diabetes, to detect and manage this illness promptly.

Additionally, cataracts were present in 11.9% of individuals in the legally blind group. While the prevalence rate for cataracts in this group was relatively lower than for diabetic retinopathy and glaucoma, it still contributed significantly to visual impairment.

In the context of diabetic maculopathy, a complication affecting the macula was observed in 13.3% of the legally blind group. This finding indicates a significant association between diabetic maculopathy and legal blindness.

In addition, several other factors reviewed in the study demonstrated significant correlations with legal blindness. These factors included longer duration of diabetes, higher levels of HbA1c, presence of vitreous hemorrhage, tractional detachment, hypertension, dyslipidemia, cardiovascular disease, and diabetic nephropathy. These findings emphasize the complex relationship between systemic health and visual impairment in individuals with diabetes.

The findings of this study can be instrumental in enhancing Libya's healthcare system by guiding targeted public health interventions to reduce the burden of visual impairment in diabetic patients. The high prevalence of diabetic retinopathy (DR) and associated visual impairment underscore the need for early detection programs, such as regular ophthalmic screenings, especially for high-risk groups. Improved glycemic control through diabetes management programs and

patient education on the importance of monitoring blood sugar levels can help prevent or delay the progression of DR.

Additionally, this data supports the implementation of multidisciplinary care approaches, integrating ophthalmologists, endocrinologists, and primary care providers to manage diabetes holistically. By addressing systemic factors like hypertension, cardiovascular disease, and dyslipidemia, the healthcare system can mitigate the complex risks contributing to visual impairment. These efforts will improve patient outcomes and alleviate the long-term socioeconomic impact of diabetes-related blindness on individuals and communities.

5. Conclusion

In conclusion, this study highlights the critical need for efficient public health strategies to address the rising burden of visual impairment in individuals with diabetes. By providing novel insights into the prevalence and factors associated with visual impairment among diabetic populations in Libya, this study contributes invaluable data to the global effort to address diabetic complications. The results highlight the essential significance of diabetic retinopathy as a major determinant of visual impairment and highlight the importance of early detection and management of this disease. Moreover, the study sheds light on the complex relationship between systemic health factors and visual impairment, demonstrating the multifactorial nature of this complication. To mitigate the impact of visual impairment on individuals with diabetes and improve their quality of life, it is crucial to implement targeted interventions and strategic initiatives according to these findings.

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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