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Proliferative diabetic retinopathy in type 2 diabetic patients with stage 5 chronic kidney disease.

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Abstract

Introduction: The microvascular similarities of the retina and the kidney cause the manifestations of diabetic microangiopathy to occur in both systems. There are few epidemiological data on this group of patients with stage 5 chronic kidney disease (CKD), so this study aimed to determine the prevalence of proliferative and non-proliferative diabetic retinopathy (PDR) in patients undergoing hemodialysis.

Methods: In this cross-sectional study, 205 type two diabetic patients with stage 5 CKD undergoing hemodialysis at the "Eugenio Espejo" Hospital in June 2013-May 2014 were evaluated. In all patients (n=205), comorbidity was determined. Associated abilities, glycosylated hemoglobin, time of evolution of DM2, time of diagnosis of diabetic retinopathy. In all eyes (n=410), visual acuity, degree of diabetic retinopathy, and complications of diabetic retinopathy were determined.

Results: Of 205 patients, 62.9% were women, 53.7% were aged between 70-79 years, the time of evolution of DM 2 was more significant than 20 years in 65.9%, and 83.4% were treated with insulin. 92.2% had DR, 58% were cases of non-proliferative DR, and 34.2% had PDR.

Conclusions: There is a high prevalence of DR in this group of a non-symmetrical type. The severity of the involvement concerning kidney damage, since more than half of the patients present RDNP while the kidney is in end-stage renal failure.

Keywords:

MESH: Kidney Failure, Chronic; Renal Insufficiency, Chronic; Diabetes Mellitus, Type 2; Diabetic Retinopathy; Renal Dialysis.

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Microangiopathy is one of the essential late complications of diabetes mellitus (DM) and is the leading cause of disabling injuries; this nosological entity is among the leading causes of blindness and end-stage renal disease in the Western Hemisphere [1]. Diabetic retinopathy is one of the leading causes of blindness in the US and the world in individuals between 20 and 74 years of age [2]. The prevalence of retinopathy increases with the duration of diabetes; almost all people with type 1 DM and more than 60% of those with type 2 DM have some type of retinopathy after 20 years of evolution. In the study " Wisconsin Epidemiologic Study of Diabetes Retinopathy" (WESDR), 3.6% of younger patients with type 1 DM and 1.6% of older patients with type 2 DM were completely blind [3] [4]. In an Ecuadorian study conducted in 2010, it was found that the global prevalence of diabetic retinopathy (DR) was 32.9%, nonproliferative diabetic retinopathy (NPDR) was 25.2%, and proliferative diabetic retinopathy (PDR) was 7.7% [5].

Diabetic nephropathy is associated with poor metabolic control, the presence of arterial hypertension, and, fundamentally, the previous presence of microalbuminuria [6]. To detect the onset and progression of diabetic nephropathy, an annual evaluation of urinary albumin excretion (UAE) is mandatory from the onset of type 2 DM, and calculation of the glomerular filtration rate (GFR) from serum creatinine by using currently validated formulas [7]. The similarities that exist in the vascular systems of the retina and the kidney [8] mean that the manifestation of DM appears in both organs in the small vessels since these organs are very susceptible to ischemia, the early signs being secondary to damage to the basement membranes and cells of the small vessels. In both cases, the lesions appear due to chronic hyperglycemia and the accumulation of products of the polyol pathway and nonenzymatic glycosylation. [9].

Experimental studies show a high correlation between pathological changes in the retinal vasculature and those in the renal vasculature. The concordance of microalbuminuria and diabetic retinopathy has been well reported in people with type 1 DM [10]; however, for type 2 diabetes, there is a paucity of data, and the association seems minor [11]. The presence of advanced retinal disease indicates a greater probability of advanced nephropathy, so the objective of the present study was to determine the presence of proliferative and nonproliferative retinopathy in a group of diabetic patients undergoing hemodialysis in a national reference public center in Quito, Ecuador.

Materials and methods

Study design
This study is observational and cross-sectional.

Scenery
The study was carried out in the hemodialysis service of the Eugenio Espejo Specialties Hospital of the Ministry of Public Health in Quito-Ecuador. The study period was from June 01, 2013, to May 31, 2014. The study was completed in June 2015.

Participants
Patients aged over 30 years with stage 5-D chronic renal failure who started the hemodialysis program in the study period with a diagnosis of diabetic nephropathy were included. Patients who did not have an ophthalmological assessment at admission to the renal function replacement program were excluded.

Variables
It is described whether the patients had proliferative or nonproliferative diabetic retinopathy. Population variables such as sex and age were measured. The value of hemoglobin HbA1c, time of evolution of type 2 diabetes, time of the start of hemodialysis, type of diabetes treatment, and presence of comorbidities such as hypertension or dyslipidemia were determined.

Data sources/measurements
The variables were taken from the institutional clinical file. The institution's ophthalmologists performed ocular fundus consultations. The laboratory studies were performed in the institutional laboratory within the usual protocol for assessing a patient with stage 5 chronic kidney disease at the start of the hemodialysis program. Visual acuity measurements used the Wecker scale from <0.05 (worst vision) to 1 (best vision).

Biases
To avoid possible interviewer, information, and memory biases, the foremost researchers guarded the data at all times with appropriate guidelines and records. Observation and selection bias was avoided by applying the participant selection criteria.

Studio size
The sample was a nonprobabilistic census type, in which all possible cases of the institution that entered a hemodialysis program were included. All analyzable cases were entered.

Quantitative variables
Categorical variables are presented as frequencies and percentages. The age variable was categorized by ranges and is presented as frequency and percentage.

Statistical analysis

A descriptive analysis of prevalence is presented. A 95% confidence interval is presented for a proportion of the most critical categorical variables.

Results

Participants

A total of 205 patients entered the study. The participant diagram is presented in Figure 1.

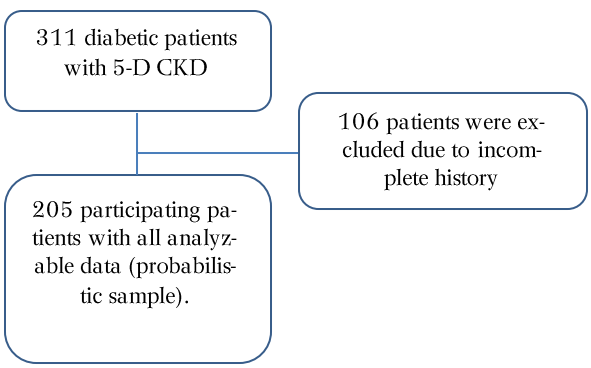

Figure 1. Diagram of study participants.

Characteristics of the study population

There were 205 patients, 129 women (62.9%) and 76 men (37.1%). From 30 to 49 years old, there were 8 cases (3.9%), and from 50 to 69 years old, there were 65 cases (31.7%). From 70 to 79, 110 cases (53.7%), and from 80 years old or older, 22 cases (10.7%). The participants' evolution time of type 2 DM was 65.9%, which was more than 20 years (Figure 2).

The diagnosis of retinopathy is presented in Figure 2. The diagnosis of some degree of diabetic retinopathy was made in 51.7% of the patients after 20 years of evolution of DM2. Stage V CKD was diagnosed in 58.5% of the patients after 20 years of evolution of DM2.

Comorbidities

The clinical management of people with diabetes was mostly with insulin, corresponding to 171 cases (83.4%). Oral antidiabetics was used in 8 cases (3.9%), and no treatment was used in 2 cases (1%). It was observed that 89.8% of the cases presented hypertension and dyslipidemia in 21 cases (10.2%). Glycosylated hemoglobin was 6 to 7% in 51 cases (15.6%), 8 to 10% in 117 cases (65.9%), and more than 10% in 37 cases (18.5%).

Ophthalmological characteristics

The findings of the 410 eyes (n=205) evaluated, such as visual acuity, degree of diabetic retinopathy, and complications of diabetic retinopathy, are described. Visual acuity A total of 41.2% of the included patients presented a significant decrease in vision worse than 0.1 (Table 2). The overall prevalence of DR was 92.2%, 58% corresponding to nonproliferative diabetic retinopathy and 34.2% to proliferative diabetic retinopathy (Table 2).

The distribution of the patients included in the study according to the complications of diabetic retinopathy. The most frequent DR complication was hemoviterous (20%), followed by diabetic macular edema (16.1%) (Table 3).

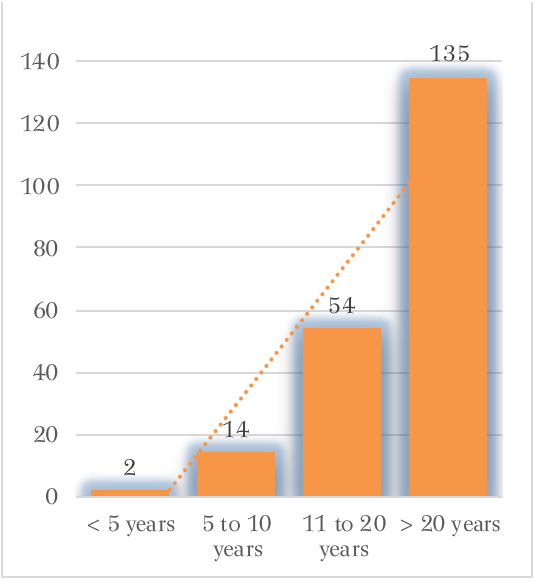

Figure 2. Time of evolution of type 2 diabetes in the study participants.

Discussion

This study investigates the prevalence of DR and its different degrees, associated factors, and general characteristics of the population in patients with DM2 with end-stage renal damage on dialysis. Regarding the gender and age characteristics of the study population, it was mainly composed of women (62.9%); similar results to a recent study carried out in the Ecuadorian diabetic population where the female sex corresponded to 67.9% [12] and lower than that reported by Rosales 76.9% in the Ecuadorian population [13]. While Mur, in his study in a European population, on chronic kidney disease in type 2 diabetics, men were slightly more affected (53.7%) [14]. Regarding age, half of the patients were in the range of 70-79 years (53.7%), mainly affecting the older adult population,

which is susceptible to advanced complications of chronic diseases such as DM2 [15]. The time of evolution of DM2 in more than half of the patients (65.9%) was greater than 20 years, one of the most critical factors being the time of evolution for the development of nephropathy and retinopathy [16]. The time stage V CKD was diagnosed in the study was 58.5% after 20 years of evolution of DM2, and 51.7% were diagnosed with some degree of DR after this same period of evolution. Similar results to those reported by Retnakaran, who indicated that 60% of type 2 diabetic patients have some degree of DR after 20 years of disease [16].

In the present study, it was observed that 89.9% of the population presented hypertension, of which 64.3% was accompanied by dyslipidemia; close to the 87.7% reported in a Chilean study in diabetic patients on hemodialysis [17]. Poor control of blood pressure favors the development and progression of diabetic retinopathy; according to a study carried out in Australia, the presence of hypertension over more than four years of evolution is significant [18]; the presence of diastolic hypertension is considered a risk factor for the appearance of proliferative retinopathy [6]. The other morbidity investigated was dyslipidemia, which occurred in 74.5% of the patients; higher than that reported in type 2 diabetic patients without advanced renal involvement of 20.54%, taking into account that the severity of retinopathy is positively associated with the concentration of triglycerides and closely associated with the progression of albuminuria [19].

Table 1. Visual acuity of the study group, with Wecker scale.

Visual acuity	n=410	Percentage
From 1 to 0.4	143	35%
From 0.3 to 0.2	98	23.8%
From 0.1 to 0.05	78	19%
From 0.04 to 0.02	64	15.7%
HM-LP	21	5%
NLP	6	1.5%

MM-PL: Hand movement/light perception. NPL: No Light Perception

Table 2. Degrees of diabetic retinopathy in the study group.

Degree of diabetic retinopathy	n=410	Percentage
Mild NPDR	36	8.8%
Moderate NPDR	76	18.5%
Severe NPDR	126	30.7%
Mild-moderate PDR	86	21.0%
RDP high risk	54	13.2%
None	32	7.8%

NPDR: nonproliferative diabetic retinopathy. PDR: Proliferative diabetic retinopathy.

Table 3. Complications of diabetic retinopathy.

Complications of diabetic retinopathy	n=410	Percentage
None	238	58.0%
Hemovitreous	82	20.0%
Macular edema	66	16.1%
RD	12	2.9%
Neovascular glaucoma	12	2.9%

RD: retinal detachment.

In the present study, glycosylated hemoglobin (HbA1C) was found in 84.4% of patients outside normal limits, of which 65.9% were in the range of 8 to 10% and 18.5% were greater than 10%. Recent studies show that glycosylated hemoglobin levels are determinant for the incidence of DR; in fact, glycemic control was a risk factor for PDR in studies such as DCCT and UKPDS, in which they have shown that the benefit of reasonable metabolic control decreases the microvascular risk and progression to severe lesions [20] [21]; furthermore, elevated HbA1C levels are considered a risk factor for the development of diabetic nephropathy [6].

The clinical treatment in this study mainly was insulin in 83.4% of the cases, an expected result based on the time of evolution of DM2 and according to the management protocol for patients on hemodialysis in whom the use of OAD should be restricted due to the high risk of hypoglycemia, with pharmacological treatment being almost exclusively insulin [22]; in an Ecuadorian study carried out in patients with short evolution of DM2 (1 to 5 years), the treatment was oral antidiabetics in 57.2% [12].

Regarding visual acuity, 41.2% of the patients included presented a significant decrease in vision worse than 0.1, higher than the 17.1% reported by González in patients with DM2 without advanced kidney disease [19], taking into account that the study group is highly selective, there are no comparable data for this variable. The present study found, in this specific group of patients, an overall prevalence of DR of 92.2%, of which more than half (58%) had nonproliferative DR and 34.2% PDR. More significant than what was found by Padmaja in his study on the relationship between albuminuria and DR, he found that patients with macroalbuminuria (CKD Stage IV and V) had a prevalence of DR of 60.5% [10], considering that our population belongs exclusively to stage V CKD. Yoshimoto, for his part, reported that almost all patients with DM1 and 2/3 of patients with DM2 on dialysis have diabetic retinopathy [23]. In an Ecuadorian study in a type 2 diabetic population without advanced CKD, it was determined that the prevalence of RDNP was 25.2% and RDP 7.7% [13].

Regarding DR complications in this study, the most frequent was hemoviterous (20%), which coincides with that described by Jansen, who indicates that vitreous hemorrhage is the most common complication when starting hemodialysis due to the persistence of new vessels, a product of incomplete laser treatment or even despite having been treated with complete panphotocoagulation. This situation may be aggravated by hemostatic alterations associated with renal failure [24]. Followed by diabetic macular edema with 16.1%, complications were responsible for the worst vision in the studied group.

Conclusions

The overall prevalence of DR is high; however, more than half of these had nonproliferative DR, suggesting that end-stage renal damage is not symmetrical to the severity of retinal damage. More than half of the patients were diagnosed with diabetic retinopathy and stage V nephropathy after 20 years of evolution of DM2, which suggests that the time of evolution has an essential relationship with the appearance of microvascular complications. Within the comorbidities, hypertension was observed in the vast majority of the population, and more than half was accompanied by dyslipidemia, with a high prevalence in this specific group of patients, considered associated factors in the development and progression of diabetic retinopathy, mainly proliferative. The level of glycosylated hemoglobin (HbA1C) of the study population had poor metabolic control. Hemoviterous and diabetic macular edema were the most frequent complications, mainly responsible for the worse vision in the study population.

Abbreviations

OAD: Oral antidiabetics.
DM: diabetes mellitus.
CKD: Chronic kidney disease.
DR: diabetic retinopathy.
NPDR: nonproliferative diabetic retinopathy.
PDR: proliferative diabetic retinopathy.

Supplementary information

Supplementary materials have not been declared.

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Author contributions

Maricela Suleidy Rojas Canchala: Conceptualization, Data Curation, Formal Analysis, Fundraising, Research, Methodology, Project Management, Resources, Software, Writing – original draft.
Paola Cristina Troya Ronquillo: Conceptualization, Data Curation, Formal Analysis, Fundraising, Research, Methodology, Project Management, Resources, Software, Writing – original draft.
Patricio Almagro Guerrero: Conceptualization, supervision, validation, visualization, and writing: review and editing.
José Rivera Buse: conceptualization, supervision, validation, visualization, and writing: review and editing.
All authors read and approved the final version of the manuscript.

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The authors provided research expenses. The laboratory studies and analyses were part of the regular institutional activity and were not expenses added to the institution or the patients.

Availability of data or materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality but are available from the corresponding author upon reasonable academic request.

Statements

Ethics committee approval and consent to participate

The ethics committee of Hospital Eugenio Espejo approved the protocol of this investigation prior to conducting the study.

Consent to publication

This does not apply when images or photographs of the physical examination or radiography/tomography/MRI of patients are not published.

Conflicts of interest

The authors report having no conflicts of interest.

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References

1. León-Regal M, González-Otero L, González-Otero Z, de-Armas-García J, Urquiza-Hurtado A, Rodríguez-Caña G. Etiopatogenia de la microangiopatía diabética. Consideraciones bioquímicas y moleculares. Revista Finlay 2013;3(4):1-13. SU: revfinlay.cu/242.

2. Olmos P, Araya-Del-Pino A, González C, Laso P, Irribarra V, Rubio L. Fisiopatología de la retinopatía y nefropatía diabéticas. Rev. méd. Chile 2009;137(10):1375-1384. SU: scielo.cl/S0034. DOI: 10.4067/S0034-98872009001000015.

3. Guduru A, Martz TG, Waters A, Kshirsagar AV, Garg S. Oxygen Saturation of Retinal Vessels in All Stages of Diabetic Retinopathy and Correlation to Ultra-Wide Field Fluorescein Angiography. Invest Ophthalmol Vis Sci. 2016 Oct 1;57(13):5278-5284. DOI: 10.1167/iovs.16-20190. PMID: 27723894.

4. El-Asrar AM, Al-Mezaine HS, Ola MS. Changing paradigms in the treatment of diabetic retinopathy. Curr Opin Ophthalmol. 2009 Nov;20(6):532-8. DOI: 10.1097/ICU.0b013e328330b533. PMID: 19644368.

5. Yépez E, Rosales W, Yansaguano M, Benítez R. Retinopatía en pacientes diabéticos tipo 2 que se atienden en el Hospital Pablo Arturo Suarez periodo Marzo 2010 a Febrero 2011. [Tesis en Medicina Interna]. Universidad Central del Ecuador 2012; **SU**:: dspace.uce/T-UCE-0006-3

6. Romero P, Espeso O, Castillo D. Estudio prospectivo de correlación entre retinopatía diabética y microalbuminuria en pacientes diabéticos tipo 1. Arch. Soc. Esp. Oftalmol 2000;75(5):307-314. **SU**: ibecs.isciii.es/6484

7. Lopez-Jaramillo P, Lahera V, Lopez-Lopez J. Epidemic of cardiometabolic diseases: a Latin American point of view. Ther Adv Cardiovasc Dis. 2011;5(2):119-31. **DOI**: 10.1177/1753944711403189. Epub 2011 Mar 15. **PMID**: 21406494.

8. Chavers BM, Mauer SM, Ramsay RC, Steffes MW. Relationship between retinal and glomerular lesions in IDDM patients. Diabetes. 1994;43(3):441-6. **DOI**: 10.2337/diab.43.3.441. **PMID**: 8314018.

9. Bain SC, Chowdhury TA. Genetics of diabetic nephropathy and microalbuminuria. J R Soc Med. 2000;93(2):62-6. **DOI**: 10.1177/014107680009300204. **PMID:** 10740571.

10. Rani PK, Raman R, Gupta A, Pal SS, Kulothungan V, Sharma T. Albuminuria and Diabetic Retinopathy in Type 2 Diabetes Mellitus Sankara Nethralaya Diabetic Retinopathy Epidemiology And Molecular Genetic Study (SN-DREAMS, report 12). Diabetol Metab Syndr. 2011;3(1):9. **DOI**: 10.1186/1758-5996-3-9. **PMID:** 21612596.

11. Penno G, Solini A, Zoppini G, Orsi E, Zerbini G, Trevisan R, et al., Renal Insufficiency And Cardiovascular Events (RIACE) Study Group. Rate and determinants of association between advanced retinopathy and chronic kidney disease in patients with type 2 diabetes: the Renal Insufficiency And Cardiovascular Events (RIACE) Italian multicenter study. Diabetes Care. 2012;35(11):2317-23. **DOI**: 10.2337/dc12-0628. **PMID:** 23093684; **PMCID**: PMC3476898.

12. Catellanos G. Tiempo transcurrido desde el diagnóstico de DM tipo 2 aprimer control oftalmológico y patologías oculares secundarias a la diabetes. UCE 2014. **SU:** dspace.uce.edu.ec

13. Rosales YM. Retinopatía En Pacientes Diabéticos Tipo 2 Que Se Atienden En El Hospital Pablo Arturo Suarez Periodo Marzo 2010 A Febrero 2011. Facultad de Ciencias Médicas, Universidad Central del Ecuador, 2011 **SU:** dspace.uce.edu.ec

14. Mur T, Villaró M, Porta N, Jaén A, Clanchet T, López C, et al. Enfermedad renal crónica en diabéticos tipo 2 en el área de Salud del Vallès occidental, enfermedad cardiovascular y factores asociados. hospital Mutua de Terrasa. Comunicados de XXV Congreso Nacional de la Sociedad Española de Diabetes Pamplona, 03-05 Abril 2014. Avances en Diabetología 2014;30:O-012. **SU**: elsevier.es/congres/855

15. Freire W, Ramirez MJ, Belmont P, Mendieta MJ, Silva MK, Romero N, et al. Resumen Ejecutivo. Tomo I. Encuesta Nacional de Salud y Nutrición del Ecuador. ENSANUT:ECU 2011-2013. Ministerio de Salud Pública/Instituto Nacional de Estadísticas y Censos. Quito Ecuador. **SU:** ecuadorencifras.gob.ec

16. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR; UKPDS Study Group. Risk factors for renal dysfunction in type 2 diabetes: U.K. Prospective Diabetes Study 74. Diabetes. 2006;55(6):1832-9. **DOI**: 10.2337/db05-1620. **PMID:** 16731850.

17. Sanhueza M, Cotera A, Elgueta L, López G, Loncon P, Macan F, et al. Diabetes y hemodiálisis. Caracterización de una cohorte y seguimiento a cuatro años. Rev. méd. Chile 2008;136(3):279-286.**SU**: scielo.cl **DOI:** 10.4067.

18. Carstensen B, Borch-Johnsen K. Register-based studies of diabetes. Scand J Public Health 2011;39(7S):175-9. **DOI**: 10.1177/1403494811404279. **PMID**: 21775379.

19. Gonzalez G. Caracteristicasclinicas de la retinopatiadiabetica en pacientes enviados al servicio de oftalomogia. Revista de medicina e investigación 2013;1(2):68-73 **SU:** r.diauaemex.com

20. Lawes CM, Parag V, Bennett DA, Suh I, Lam TH, Whitlock G, et al; Asia Pacific Cohort Studies Collaboration. Blood glucose and risk of cardiovascular disease in the Asia Pacific region. Diabetes Care. 2004;27(12):2836-42. **DOI**: 10.2337/diacare.27.12.2836. **PMID**: 15562194.

21. Acosta A, Acevedo A, Cabrera E, Delgado W, Piccardo R, Acosta C. Microalbuminuria en pacientes con diabetes tipo 2. 2005 Mem. Inst. Investig. Cienc. Salud, 2005;3(1):37-42. **SU:** scielo.iics.una.py

22. Snyder RW, Berns JS. Use of insulin and oral hypoglycemic medications in patients with diabetes mellitus and advanced kidney disease. Semin Dial. 2004;17(5):365-70. **DOI**: 10.1111/j.0894-0959.2004.17346.x. **PMID**: 15461745.

23. Yoshimoto M, Matsumoto S. [Changes in diabetic retinopathy and visual acuity in patients with end-stage diabetic nephropathy after the introduction of hemodialysis]. Nippon Ganka Gakkai Zasshi. 2006;110(4):271-5. Japanese. **PMID:** 16642943.

24. Janssen MJ, van der Meulen J. The bleeding risk in chronic haemodialysis: preventive strategies in high-risk patients. Neth J Med. 1996;48(5):198-207. **DOI**: 10.1016/0300-2977(96)00005-8. **PMID**: 8710039.

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