

Deficiency of Vitamin D: Influence on Diabetic Retinopathy and Hearing Loss Among Patients with Diabetes Mellitus Type 2

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ABSTRACT

Objective: To find a relationship between serum level of vitamin D with diabetic retinopathy and hearing loss in patients with diabetes mellitus type2.

Study design and setting: This cross-sectional study was carried out at Ophthalmology, ENT and family physician Outpatient clinic of Mohsin Consultant Clinic Federal B Area, Karachi from study was April 2019 to December 2019.

Methodology: Total 181 eligible type 2 diabetes mellitus patients. Complete ophthalmological, ENT and physical evaluation was carried out. Retinopathy and hearing status were recorded and were compared to serum 25-OH Vitamin D levels to find any association. SPSS version 23.0 was used to analyze the data.

Results: Mean age of participants were found to be 60.56 ± 7.3 (SD). When diabetic retinopathy status and hearing status was compared, non-proliferative diabetic retinopathy patients with normal hearing were 24(42.1%), with mild hearing 32(56.1%) and only 1(1.8%) with moderate-severe hearing loss was observed with P-value of <0.0001 . Retinopathy status was compared with vitamin D levels. Insufficiency was seen in 14(38.9%) non-proliferative diabetic retinopathy, 2(5.6%) proliferative diabetic retinopathy patients and deficiency level was found in 33(32.7%) non-proliferative diabetic retinopathy and 15(14.9%) proliferative diabetic retinopathy patients. Level of vitamin D was compared to DR and HL status. Significantly low level of vitamin D was found with increasing severity of DR and HL with P-value <0.0001 .

Conclusions: Low level of vitamin D was associated with the severity of diabetic retinopathy and hearing loss in patients suffering from diabetes mellitus type2.

Key words: Diabetic retinopathy, Diabetes mellitus type 2, Hearing Loss, Vitamin D.

How to cite this Article:

Farooq MUZ, Inamullah Syed, Mashhood S, Rana MA, Fahim MF. Deficiency of Vitamin D: Influence on Diabetic Retinopathy and Hearing Loss Among Patients with Diabetes Mellitus Type 2. J Bahria Uni Med Dental Coll. 2020; 10(4): 282-286 DOI: <https://doi.org/10.51985/JBUMDC2020068>

INTRODUCTION:

Vitamin D deficiency (VDD) has emerged as a global health issue.¹The deficiency involves almost all regions and all age groups. VDD is found to be more prevalent in Pakistan.² The classical effect of vitamin D is regulation of bone remodelling and mineral homeostasis. Additionally, effects of vitamin D on immune modulation, glucose regulation

and in developing diabetes mellitus type 2 (DMT2) have also been found.³ Study results of Palomer X et al and Joergensen C et al. have demonstrated effects of VDD in developing diabetes mellitus (DM) and its microvascular complications.⁴⁻⁵ The mortality and morbidity secondary to DM has become worldwide public health issue affecting over 300 million people.⁶

In Pakistan, an estimated 7 million of population is having DM and it has been estimated that by the year 2030 this figure will rise to nearly 13.8 million.⁷ Diabetic retinopathy (DR) is an important complication in patients suffering from DMT2. Diabetic retinopathy is found to be a leading cause of visual loss and blindness. DR accounts for 12% of all new cases of blindness each year. Different risk factors have been identified for the occurrence of DR in patients of DMT2 including long duration of diabetes, systemic hypertension, hyperlipidemia, obesity and positive family history of diabetes with elevated blood glucose level being the important one.⁸⁻⁹ Hearing loss (HL) is one more health problem having devastating effect on the social, functional, and psychological well-being of the person thereby reducing the quality of life. Beside causing DR, diabetes also affects auditory function. HL is a frequent finding in DMT2 patients with hyperglycaemia as a cause.¹⁰ Insulin is regulator of glucose metabolism and lack of insulin in DM results in poor glucose

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Received: 17-Aug-2020
Accepted: 18-Sep-2020

metabolism leading to elevated blood glucose level. Adequate levels of vitamin D are required for effective insulin secretion as demonstrated in studies of Danescu L.G et al., Cavalier E. et al.¹¹

Lack of insulin function in diabetes is linked to VDD as shown in animal model of Mathieu C et al.¹² Studies have identified low levels of Vitamin D as an important risk factor in DMT2 for developing DR and HL.¹³⁻¹⁵ In view of the important association of low level of vitamin D this study was aimed to find a relationship between serum level of vitamin D with diabetic retinopathy and hearing loss in patients with diabetes mellitus type2.

METHODOLOGY:

This cross-sectional study was carried out at Ophthalmology, ENT and family physician Outpatient clinic of Mohsin Consultant Clinic Federal B Area, Karachi. Duration of study was April 2019 to December 2019. A prior approval was taken from the ethical review committee of the institute. ERC approval letter with reference number CO/RA/14/2019 was issued by the ethical review committee of the institute. Study was conducted in accordance with principles of the Helsinki Declaration of 1975, as revised in 2000. Non-probability convenience sampling technique was used sample size was calculated from online software openepi.com by taking 5% margin of error and 95% confidence interval. Prevalence of diabetes was 26.3% as of second National Diabetes Survey of Pakistan¹⁶, 2016–2017. The sample size was derived to be 181 patients. Patients suffering from DMT2 of either gender attending eye, ENT and family physician outpatient clinic were included. Inclusion criteria were patient having age between 40-70 years, diagnosed to be suffering from DMT2 for the last three years. Exclusion criteria were patients suffering from Type 1 diabetes mellitus, suffering from any other ocular disorder or surgery, limited outdoor activities, suffering from any disorders other than DMT2 that could affect the retinal microvascular structure like renal failure, liver disorders, cancer, tuberculosis, hyper or hypothyroidism, cardiovascular diseases, epilepsy, and behavioural disorders, patients taking medicines that could affect the vitamin D metabolism like antioxidants, calcium, and vitamin D supplements and those suffering from middle and external ear pathology or surgery.

After considering the inclusion and exclusion criteria, a total of 181 patients were enrolled. Visual acuity with Snellen's chart and detailed ocular examination was performed. Fundus examination was done with slit lamp biomicroscope using 90 D lens and indirect ophthalmoscope. Retinopathy status was recorded. Severity of DR was classified by Early Treatment Diabetic Retinopathy Study (EDTRS) and patients were categorized as having No Retinopathy, Non-proliferative diabetic retinopathy (NPDR) and Proliferative diabetic retinopathy (PDR).¹⁷

Detailed ENT examination was performed. Pure tone audiometry was used to test hearing threshold in a sound isolated room. Hearing was described according to WHO guidelines as normal with ≤ 25 dB and from 26-40 dB as mild, 41-60 moderate, 61-80 dB severe and >81 dB as profound loss.¹⁸ Mean value of the two ears was used. In final analysis, severe and profound hearing loss is grouped as severe visual loss. Detailed physical examination was performed. Blood sample was taken using all aseptic precautions for measuring serum 25(OH)D level. Vitamin D concentration was considered normal with value of 25-OHD = or > 30 ng/ml, insufficiency with level 20.1-29.9 ng/ml and deficiency with value < 20 ng/ml.¹

Data was entered and analyzed on SPSS version 23.0. Mean age was reported in mean and standard deviation. Categorical parameters were considered as frequency and percentages. To know the association between Vitamin D, DR and Hearing status Chi-square test or Fischer Exact test was applied. P-value = 0.05 considered to be statistically significant.

RESULTS:

A total of 181 patients were included in this study. Mean age of participants were found to be 60.56 ± 7.3 (SD) with minimum of 40 and maximum of 70 years. Gender distribution showed 16% (n=29) female and 84% (n=152) male patients.

Most of the respondents had duration of diabetes < 5 years (n=85-46.96%), between 5-10 years (n=75-41.43%) and > 10 years (n=21-11.6%) only. Vitamin D insufficiency was seen in 14(38.9%) NPDR patients and 2(5.6%) PDR patients. Deficiency level was found in 33(32.7%) NPDR patients while 15(14.9%) PDR patients. While Vitamin D insufficiency was seen in 12(33.3%) patients with mild HL and 1(2.8%) with moderate & severe HL. Deficiency level was found in 85(84.2%) with mild HL while 4(4.0%) with moderate & severe HL patients. (Table 2). Level of vitamin D was compared to DR and HL status. Significantly low level of vitamin D was found with increasing severity of DR and HL with P-value < 0.0001 . (Table 3)

Table 1: Comparison of DR and Hearing status

Hearing	DR status			P-value
	No DR (n=106)	NPDR (n=57)	PDR (n=18)	
Normal	49	24	3	0.001
	46.2%	42.1%	16.7%	
Mild	56	32	12	
	52.8%	56.1%	66.7%	
Moderate & Severe	1	1	3	
	0.9%	1.8%	16.7%	

Table 2: Comparison of DR (Diabetes Retinopathy) & Hearing with Vitamins D levels

	Normal > 30ng/ml (n=44)	Insufficiency 20.1-29.9 ng/ml (n=36)	Deficiency < 20ng/ml (n=101)	P-value
Diabetic Retinopathy status				
No DR	33	20	53	0.037
	75.0%	55.6%	52.5%	
NPDR	10	14	33	
	22.7%	38.9%	32.7%	
PDR	1	2	15	
	2.3%	5.6%	14.9%	
Hearing				
Normal	41	23	12	0.000
	93.2%	63.9%	11.9%	
Mild	3	12	85	
	6.8%	33.3%	84.2%	
Moderate & Severe	0	1	4	
	0.0%	2.8%	4.0%	

Table 3: Correlation analysis of DR, Hearing and Vitamin D level

Diabetic Retinopathy status	Hearing Status	Normal > 30ng/ml (n=44)	Insufficiency 20.1-29.9 ng/ml (n=36)	Deficiency < 20ng/ml (n=101)	P-value
No DR	Normal	31	11	7	0.000
		93.9%	55.0%	13.2%	
	Mild	2	8	46	
		6.1%	40.0%	86.8%	
	Moderate & Severe	0	1	0	
		0.0%	5.0%	0.0%	
NPDR	Normal	10	12	2	0.000
		100.0%	85.7%	6.1%	
	Mild	0	2	30	
		0.0%	14.3%	90.9%	
	Moderate & Severe	0	0	1	
		0.0%	0.0%	3.0%	
PDR	Normal	0	0	3	0.000
		0.0%	0.0%	20.0%	
	Mild	1	2	9	
		100.0%	100.0%	60.0%	
	Moderate & Severe	0	0	3	
		0.0%	0.0%	20.0%	

DISCUSSION:

The results of this study demonstrated a strong correlation between serum vitamin D levels, the degree of DR, and the severity of sensorineural HL with similar results as in study of Bener et al.¹⁵ In our study, there was a relationship of vitamin D level with DR and HL with P value of 0.000. In the study of Bener et al, this relationship had a significance value of <0.001.

When DR status and Hearing status was compared, NPDR

with normal hearing patients were 24(42.1%), NPDR with mild HL were observed in 32(56.1%) patients whereas only 1(1.8%) patient was observed with Moderate and severe HL with significant P-value of <0.001. When compared with PDR, 66.7% had mild and 16.7% had moderate-severe HL with P value 0.001 whereas normal hearing was found in only 16.7%.

Vitamin D level was compared to DR and hearing status separately. In patients having normal level of vitamin D,

75% showed no DR while 22.7% had NPDR and 2.3% had PDR. Similarly, in patients with normal serum vitamin D level, 93.2% had normal hearing and 6.8% had NPDR and none was found to have PDR. Low level of vitamin D with insufficiency and deficiency had significance association with worsening DR ($P=0.037$) and HL ranging from mild-moderate and severe showed P value 0.000.

In our sample, 75.69% ($n=137$) patients were found to have low levels (insufficiency and deficiency) of vitamin D. While examining the association of vitamin D with status of DR and HL, it was found that 80% ($n=12$) patients having PDR and HL were having vitamin D level of $<20\text{ng/ml}$. While 93.9% ($n=31$) had NPDR and HL with deficiency of vitamin D. Similarly, insufficient level of vitamin D were found in all patients having PDR and HL and 14.3% ($n=2$) were having NPDR and HL. The 86.8% ($n=2$) patients who were having HL also showed deficiency of vitamin D and 45% ($n=9$) had vitamin D insufficiency without retinopathy with P value at 0.000.

Effects of diabetes in the form of retinopathy, neuropathy and nephropathy are well established. However, its effect on sensorineural hearing is examined recently and a relationship has been demonstrated between them by Ooley C et al.¹⁰ A relationship between retinopathy status and level of hearing loss has also been found in our study. Our study also examined the relationship of vitamin D with DR and a positive relationship is found as has been described widely in different studies.^{4,13} DR and HL appear to have hyperglycemia as an important common risk factor which occurs secondary to disturbances of insulin secretion which is found to be dependent on adequate levels of vitamin D. In animal model of Mathieu C *et al* and further demonstration in the meta-analysis of B-A et al., hyperglycaemia is linked to deficiency of vitamin D that is required for adequate insulin secretion and function.¹¹⁻¹² The results of our study have identified vitamin D as a factor for causing DR and HL amongst patients of DMT2. It is therefore necessary to treat VDD to preserve vision and hearing. Vitamin D is also identified to inhibit retinal neovascularization as identified by DM¹⁹, thereby opening avenues for further research. Other important variables like hypertension have also been identified to be causing HL and DR. However, some researchers have found no correlation of VDD and DR.²⁰⁻²¹ Therefore, further research with large sample size, is advised to confirm the association of low levels of vitamin D with DR and HL and to find valid strategies to control the menace of diabetes.

CONCLUSION:

Current study suggest that low level of vitamin D is associated with the severity of DR and HL in patients suffering from DMT2. Correction of VDD and effective glycaemic control are important in controlling the visual and hearing complications in patients suffering from DMT2.

Author Contribution:

Mashhood-uz-Zafar Farooq: Concept, synthesis, planning of research, manuscript writing.
 Syed Inamullah: Concept, design, data collection, Literature search.
 Shama Mashhood: Planning of research, review of study, manuscript writing.
 Mahmood Akhter Rana: Data collection, literature search.
 Faisal Fahim Siddiqui: Data handling, data analysis, result writeup

REFERENCES:

1. Van-der-Meer IM, Middelkoop BJ, Bo-eke AJ, Lips P. Prevalence of vitamin D deficiency among Turkish, Moroccan, Indian and sub-Sahara African populations in Europe and their countries of origin: an overview. *Osteoporos Int.* 2011; 22:1009–1021. doi:10.1007/s00198-010-1279-1.
2. Alam U, Fawwad A, Shaheen F, Tahir B, Basit A, Malik RA. Improvement in Neuropathy Specific Quality of Life in Patients with Diabetes after Vitamin D Supplementation. *J Diabetes Res.* 2017; 2017: 7928083. Published online 2017 Dec 28. doi:10.1155/2017/7928083
3. Alcubierre N, Valls J, Rubinat E, Cao G, Esquerda A, Traveset A, Granado-Casas M, Jurjo C and Mauricio D. Vitamin D Deficiency Is Associated with the Presence and Severity of Diabetic Retinopathy in Type 2 Diabetes Mellitus. *J Diabetes Res.* 2015; 2015: 374178. Published online 2015 May 20. doi: 10.1155/2015/374178
4. Palomer X., González-Clemente J. M., Blanco-Vaca F., Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. *Diabetes, Obesity and Metabolism.* 2008;10(3):185–197. doi: 10.1111/j.1463-1326.2007.00710.x.
5. Joergensen C., Hovind P., Schmedes A., Parving H.-H., Rossing P. Vitamin D levels, microvascular complications, and mortality in type 1 diabetes. *Diabetes Care.* 2011;34(5):1081–1085. doi: 10.2337/dc10-2459.
6. Sherwin R., Jastreboff A.M. Year in diabetes 2012: the diabetes tsunami. *J. Clin. Endocrinol. Metab.* 2012; 97:4293–4301. doi: 10.1210/jc.2012-3487.
7. Shaikh MZ. Controlling diabetes mellitus: struggle continued. *J Coll Physicians Surg Pak.* 2010;20(4):223–224.
8. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care.* 2012;35(3):556–564. DOI:10.2337/dc11-1909.
9. Anwar SB, Asif N, Naqvi SAH, and Malik S. Evaluation of multiple risk factors involved in the development of Diabetic Retinopathy. *Pak J Med Sci.* 2019 Jan-Feb; 35(1): 156–160.
10. Ooley C., Jun W., Le K., et al. Correlational study of diabetic retinopathy and hearing loss. *Optometry and Vision Science.* 2017;94(3):339–344. doi:10.1097/OPX.0000000000001025.
11. Luo BA, Gao F, Qin L-L. The Association between Vitamin D Deficiency and Diabetic Retinopathy in Type 2 Diabetes: A Meta-Analysis of Observational Studies. *Nutrients.* 2017 Mar; 9(3): 307. Published online 2017 March 20. doi: 10.3390/nu9030307
12. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. *Diabetologia.* 2005; 48:1247–1257. doi: 10.1007/s00125-005-1802-7.

13. Aksoy H., Akçay F., Kurtul N., Baykal O., Avci B. Serum 1,25 dihydroxy vitamin D (1,25(OH)2D3), 25 hydroxy vitamin D (25(OH)D) and parathormone levels in diabetic retinopathy. *Clinical Biochemistry*. 2000;33(1):47–51. doi:10.1016/s0009-9120(99)00085-5.
14. Bener A, Hamaç AO, Abdulhadi K, Salahaldin AH, Gansan L. The impact of metabolic syndrome and vitamin D on hearing loss in qatar. *Otolaryngology*. 2017;7(3):1–6. doi: 10.4172/2161-119X.1000306.
15. Bener A, Elicaçyık M, Cincik H, Ozturk M, DeFronzo RA, and Abdul-Ghani M. The Impact of Vitamin D Deficiency on Retinopathy and Hearing Loss among Type 2 Diabetic Patients. *Biomed Res Int*. 2018; 2018: 2714590. Published online 2018 Jul 9.
16. Basit A, Fawwad A, Qureshi H, NDSP Members, et al. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016–2017. *BMJ Open* 2018;8: e020961. doi: 10.1136/bmjopen-2017-020961.
17. Pidro A, Ahmedbegovic-Pjano M, Grisevic S, Sofic-Drino V, Gabric K and Biscevic A. Epidemiology of Diabetic Retinopathy at Eye Clinic Svjetlost Sarajevo: Two Years Retrospective Single Center Study. *Mater Sociomed*. 2019 Dec; 31(4): 290–293.
18. Mahmood K, Akhter ST, Talib A, Haider I, Vitamin D status in a population of healthy adults in Pakistan. *Pak J Med Sci* 2009;25(4):545-550
19. Albert DM, Scheef EA, Wang S, Mehraein F, Darjatmoko SR, Sorenson CM, Sheibani N. Calcitriol is a potent inhibitor of retinal neovascularization. *Invest Ophthalmol Vis Sci*. 2007 May;48(5):2327-34. doi: 10.1167/iovs.06-1210.
20. Alam U, Amjad Y, Chan AWS, Asghar O, Petropoulos IN, and Malik RA. Vitamin D Deficiency Is Not Associated with Diabetic Retinopathy or Maculopathy. *J Diabetes Res*. 2016; 2016: 6156217. Published online 2016 Jan 14. DOI: 10.1155/2016/6156217
21. Engelen L., Schalkwijk C. G., Eussen S. J., et al. Low 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3 levels are independently associated with macroalbuminuria, but not with retinopathy and macrovascular disease in type 1 diabetes: the EURODIAB prospective complications study. *Cardiovascular Diabetology*. 2015;14, article 67. DOI: 10.1186/s12933-015-0231-2.

