

# Relationship between Diabetic Retinopathy and HbA1c in Type 2 Diabetics, Kingdom of Saudi Arabia

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## ABSTRACT

**Introduction:** Diabetic Retinopathy (DR) is emerging fastly as one of the commonest causes of blindness. Globally in developed countries over 2.5 million people are blind due to diabetes. The relationship between DR and HbA1c level have been studied by many authors, and almost all the studies were in accord that elevated HbA1c level is significantly associated with the development of DR. However, this relationship has not been studied among type 2 diabetics residing outside the main cities in the Kingdom of Saudi Arabia (KSA).

**Material and Methods:** This cross-sectional study was conducted among 327 type 2 diabetics attending the primary healthcare centers in Al-Majmaah City, KSA. The data was collected using systematic random sampling technique using direct investigation method.

**Results:** The mean age of the patients was  $54.95 \pm 11.65$  years. Majority of the patients were males ( $n=201$ ; 61.4%) as compared to females ( $n=126$ ; 38.6%). A significant difference was observed in the mean HbA1c level and DR, showing that HbA1c was significantly raised in patients having DR ( $p<0.001$ ). Result of logistic regression analysis further showed that patients who have uncontrolled diabetes (high HbA1c levels) have 66.61% chance of developing the DR.

**Conclusion:** There is a strong relationship between HbA1c level and DR. The healthcare provider should empower the patients with knowledge regarding diabetes, its complications and make lifestyle changes (diet, exercise, and weight loss, etc.). The retinal screening should be carried out routinely under the supervision of ophthalmologist.

**Key words:** Type 2 Diabetes, Diabetic retinopathy, Kingdom of Saudi Arabia, HbA1c

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## INTRODUCTION

Diabetic Retinopathy (DR) is emerging fastly as one of the commonest causes of blindness. Globally in developed countries over 2.5 million people are blind due to diabetes. A study reported that globally there are approximately 93 million diabetics with DR of which 17 million diabetics have Proliferative Diabetic Retinopathy (PDR), Diabetic Macular Edema (DME) is present in 21 million diabetics, whereas Vision Threatening Diabetic Retinopathy (VTDR) is present in 28 million diabetic patients [1].

A DR prevalence of (19%) was reported in the UAE [2]. In Kuwait [3], it was (23.5%), India [4] (17.6%), Pakistan [5] (15.7%), Egypt [6] (43%), Jordan [7] (34.1%) and in Malaysia [8] it was (14.3%). The first study to report the prevalence of DR in Kingdom of Saudi Arabia (KSA) [9] was a hospital-based study conducted in the Asser region that revealed a prevalence of 11.3%. The study further concluded that the prevalence of DR was significantly greater among subjects residing in urban areas as compared to their rural counterparts ( $p<0.001$ ). The

prevalence of DR was also studied in Almajmaah city in 2016, result showed that it affected 35.8% of the diabetics [10].

The United Kingdom Prospective Diabetes Study [11] found that good blood sugar control reduces the risk and progression of DR. The Diabetes Control and Complications Trial [12], Diabetic Retinopathy Study [13], and Early Treatment of Diabetic Retinopathy Study [14] also supported that good glycogenic control is important especially in the early stage of the diabetes as it helps in delaying the onset of DR and halting the rate of progression. Hence, most studies indicated that the control of blood sugar level is an important factor in preventing DR.

A study was done by Yun [15] in 2010 on the association between DR and HbA1c concluded that DR was significantly more in patients having higher levels of HbA1c (odds ratio=3.46). Elevated HbA1c have been seen to be associated with increased severity of DR, i.e., from Non-Proliferative Diabetic Retinopathy (NPDR) to PDR [16]. Complication of diabetes such as DR can be detected at the time of the first diagnosis of diabetes [17]. The relationship between DR and HbA1c values have been studied by many authors, and almost all the studies were

in accord and pointed out that elevated HbA1c level is significantly associated with the development of DR [18-20].

**MATERIALS AND METHODS**

This was a cross-sectional study that was conducted among the type 2 DM patients in Al-Majmaah City, Kingdom of Saudi Arabia. Diabetic patients in the city are registered at eight primary health centers (PHCs) and referred to one hospital, King Khalid Hospital. The study population was all Saudi adults, males and females, registered in the diabetic registry in all PHCs in Al Majmaah City (total number is 1546). The sample was selected from all PHCs proportional to the number of diabetic’s registered using systematic random sampling technique. The selected patients were called by phone and were directed to the eye clinic at the referral hospital for data collection. A minimum required sample size of 300 was calculated from the level of precision formula:  $n = Z^2 * pq / d^2$ . (Where,  $z = 1.96$ ,  $p = 0.265$ ,  $1 - p = 0.735$ ,  $d = 0.05$ ).

The data was collected through a pre-defined questionnaire asking information about the demographic variables, getting blood sample for the level of HbA1c and followed by detailed ophthalmic examination by an expert ophthalmology consultant for the detection of DR. This study was approved by the Ethical Review

Committee of Majmaah University. A written informed consent from the patients was taken before conducting the interview and examination. The data was entered and analyzed using IBM SPSS Statistics 25.0. Normality of the data was checked by one-sample Kolmogorov-Smirnov Test. As the data was normally distributed, therefore, Mean  $\pm$  S.D has been reported for quantitative variables. Frequencies and percentages are given for qualitative variables. Two-independent sample t test was applied to compare the mean HbA1c with presence and absence of DR. Logistic regression analysis with backward conditional approach was also applied to observe the log odds between DR and HbA1c. The results are reported in adjusted odds ratio. A p-value of  $<0.05$  was considered as statistically significant.

**RESULTS**

The mean age of the patients was  $54.95 \pm 11.65$  years. Majority of the patients were males ( $n=201$ ; 61.4%) as compared to females ( $n=126$ ; 38.6%). The overall prevalence of any stage of DR in at least one eye among the study group was found to be 35.8% ( $n=117$ ). The mean HbA1c of patients with DR was  $9.32 \pm 1.07\%$ , and without DR it was  $7.29 \pm 1.86\%$ . A significant difference was observed in the mean HbA1c level, showing that HbA1c was significantly raised in patients having DR ( $p < 0.001$ ). Results are presented in Table 1.

**Table 1: Comparison of HbA1c with the absence and presence of DR.**

Scores	Presence of DR Mean $\pm$ S.D n=117	Absence of DR Mean $\pm$ S.D n=210	p-value
HbA1c%	9.32 $\pm$ 1.07	7.29 $\pm$ 1.86	<0.001*

\*statistically significant at 5% level of significance

To confirm the association between HbA1c and DR binary logistic regression was used. The categorical dependent variable was DR which had values (0=no, 1=yes), it was used to predict HbA1c. The goodness-of-fit test proposed by Lemeshow and Hosmer, classification table (Table 2), beta ( $\beta$ ), odds ratio and its confidence

interval were calculated before proceeding for interpretation. Value of model chi-square was 93.98 and for Hosmer-Lemeshow the value was 109.75. Both the chi-square values were significant at 5% level of significance. Therefore, we are 95% confident that the fitted model is appropriate.

**Table 2: Classification table.**

DR (observed)	DR (predicted)		Percentage correct
	No	Yes	
No	165	45	78.60%
Yes	82	35	29.90%
	Overall percentage		61.20%

From the above classification Table 2, we can see that 165 patients who do not have DR were correctly specified as not having DR. Thirty Five patients who had DR were correctly specified as having DR. Whereas, a total of 127 patients (82+45) were miss-classified. Overall, the model correctly classified 61.2% patients.

The odds ratio for HbA1c was 1.995. Therefore, patients who have high HbA1c levels have 1.995 times more chances to develop DR. The confidence limits are 1.69–2.353 which does not include 1. Therefore, HbA1c variable is playing a significant role in predicting the development of DR ( $p < 0.001$ ). By converting the odds ratio into probability (odds/1+odds) we observed that

patients who have uncontrolled diabetes (high HbA1c levels) have 66.61% chance of developing DR (Table 3).

**Table 3: Association between DR and HbA1c using binary logistic regression with backward conditional approach.**

	$\beta$	Wald	p-value	Odds Ratio	95% CI for Odds	
					Lower	Upper
HbA1c	0.691	66.98	0	1.995	1.691	2.353

## DISCUSSION

In our study, the prevalence of DR was 35.8%. This prevalence of DR was compared with global, neighbouring GCC countries and local estimates. DR prevalence in this study was higher than two studies conducted in United States of America (USA) which reported a prevalence of 28.2% and 28.5% [21,22]. Study conducted in the United Kingdom (UK) [23] reported a DR prevalence of 30.1%, which is also close to the prevalence reported from our study. A study conducted in Shandong Peninsula of China [24] over a period of 5 years among type 2 diabetics showed that the prevalence of DR was 25.08% which is quite less to the findings of our study.

Yun et al. [15] studied the association between DR and HbA1c, results concluded that DR was significantly more in patients having higher levels of HbA1c (odds ratio=3.46). Our study results also support this finding, patients who have high HbA1c levels have 1.995 times more chances to develop DR. Furthermore, HbA1c is a good indicator of glycemic control as it can help diabetic individuals in deterrence of microvascular complications especially DR. Our study results showed that majority of the patients had poorly controlled diabetes as reflected by high HbA1c levels. A study conducted by Hou et al. [25] reported that less than 50% of the participants had heard of HbA1c and only 17% had understood its true meaning. It shows that knowledge of diabetics regarding DM is also an important factor to consider.

In our study, the mean HbA1c level of patients who had DR was 9.32% which showed that patients had poorly controlled diabetes. Moreover, this result was statistically significant among patients having DR ( $p < 0.001$ ). In addition, a population-based study in Chennai conducted in 2008 [26] concluded that type 2 diabetics having HbA1c more than 8% gave maximum capitulate to vision-loss-retinopathies. The study further reported that average HbA1c level in patients with DR was 8.2%. Our study result is again consistent with this as the mean HbA1c level of type 2 diabetics was 9.32% which shows that these patients can develop vision-loss-retinopathies. Complications of DR with respect to HbA1c values have been studied by many authors, and almost all the studies were in accord and pointed out that elevated HbA1c level resulted in worsening of DR [18-20]. Our study results also confirm this finding.

Based on our findings, urgent interventions are required by the authorities to deal with the issue of managing glycemic control of type 2 diabetics. The healthcare

provider should empower the patients with knowledge regarding diabetes, its complications and make lifestyle changes (diet, exercise, and weight loss, etc.). It has been proved that unhealthy lifestyle significantly influences HbA1c. Most important factor in lifestyle modification is dietary practices as it has a direct link with HbA1c. Therefore, apart from describing benefits of exercise and weight loss, the treating doctor must emphasize upon the benefits of healthy eating according to the recommended intake. In addition, patients should be empowered with knowledge regarding diabetic diet, especially the foods that affect HbA1c level. It is also important that primary care physicians or general practitioners should be made well equipped with the knowledge of diet control of diabetic patients through Continuing Medical Education (CME) and other programs.

Now diabetic patients are being referred to ophthalmologists according to the type, onset and duration of diabetes. As evidence of strong link between DR and HbA1c is rising, it is time to consider HbA1c level as one of the proposed factors that may influence the referral. The treating doctor should persuade the patients to undergo screening for retinopathy whether needed or not. This humane attitude between the family physicians or general practitioners and ophthalmologists bears cardinal position in diabetes education programs. Positive results can be achieved using patient empowerment approach and regularly conducting diabetes self-management educational programs using state-of-the-art methods emphasizing upon lifestyle modification.

## CONCLUSION

There is a strong relationship between HbA1c and DR. The healthcare provider should empower the patients with knowledge regarding diabetes, its complications and make lifestyle changes (diet, exercise, and weight loss, etc.). In DR screening programs, HbA1c level should be considered in addition to the onset and duration of diabetes as a determinant of referring patients to ophthalmologist. Further studies should be conducted to set the roles of that as this can help additionally in early detection of DR.

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