ASSOCIATION OF *GSTM1* AND *GSTT1* DELETION POLYMORPHISMS WITH RETINAL COMPLICATIONS IN DIABETIC PATIENTS

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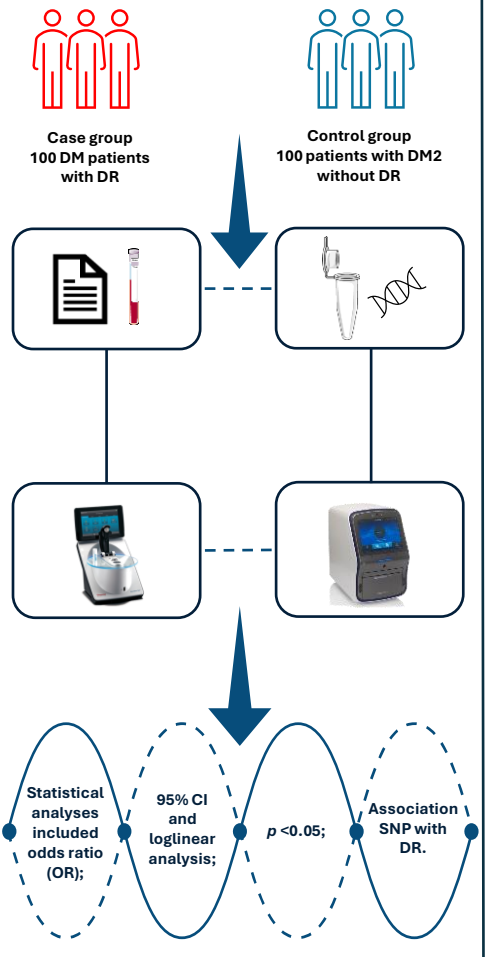
INTRODUCTION

Diabetic retinopathy (DR) is a major microvascular complication of diabetes and a leading cause of adult blindness, driven by hyperglycemia-induced oxidative stress and early retinal neurodegeneration. Genes from the *glutathione S-transferase* (*GST*) family, which regulate redox balance, may play a critical role in modulating susceptibility to DR through their antioxidant function. The objective of this study was to investigate the association between the deletion polymorphism of *glutathione S-transferase* genes (*GSTM1* and *GSTT1*) and type 2 diabetes *mellitus* (T2DM) patients with DR.

METHODOLOGY



SUPPORT

UFG CAPES CNPq

RESULTS

Table 1. Distribution of genotypic frequencies for *GSTM1* and *GSTT1* for risk analysis to diabetic retinopathy.

Gene	Genotype	Case, n (%)	Control, n (%)	OR (95% IC)	p
GSTT1	Present	73 (73,0)	129 (87,8)	Ref	-
	Null	27 (27,0)	18 (12,2)	2.65 (1.34 to 5.13)	0,0004*
GSTM1	Present	42 (42,0)	83 (56,5)	Ref	-
	Null	58 (58,0)	64 (43,5)	1.80 (1.07 to 3.00)	0,0262*
TOTAL		100 (100)	147 (100)		

Analysis by multiple logistic regression to obtain adjusted odds ratio values (OR) and confidence intervals (95% CI). *Significant difference between groups ($p < 0.05$).

Table 2. Distribution frequencies of genotypes combinations between *GSTM1* and *GSTT1* in case and control groups and a risk analysis to diabetic retinopathy.

Genotypes GSTM1/GSTT1	Case, n (%)	Controle, n (%)	OR (95% IC)	p
Present/Present	15 (15,0)	71 (48,3)	Ref	
Null/Present	53 (53,0)	58 (39,4)	4.33 (2,21 to 8,45)	<0.0001
Present/Null	24 (24,0)	12 (8,2)	9.47 (3,90 to 23,03)	<0,0001
Null/Null	8 (8,0)	6 (4,1)	6,32 (1,90 to 20,87)	0,0025

Analysis by multiple logistic regression to obtain adjusted odds ratio values (OR) and confidence intervals (95% CI). *Significant difference between groups ($p < 0.05$).

DISCUSSION

In individuals with *GSTT1* and *GSTM1* null genotypes, the reduced enzymatic activity impairs the detoxification of ROS generated during chronic hyperglycemia. This leads to the accumulation of oxidative stress in retinal cells, particularly within the microvascular endothelium. Excess oxidative stress can damage endothelial cells, disrupt the integrity of the blood-retinal barrier, and promote inflammation. Consequently, microvascular damage manifests as capillary basement membrane thickening, pericyte loss, microaneurysm formation, and increased vascular permeability, key pathological features of diabetic retinopathy. The inability to effectively neutralize oxidative insults due to *GSTT1* and *GSTM1* deletions exacerbates this microvascular injury, accelerating retinal ischemia and further contributing to disease progression.

CONCLUSION

This genetic association study highlights the critical role of *GSTM1* and *GSTT1* deletion polymorphisms in increasing DR risk. The significant associations found reinforce the hypothesis that deletion polymorphisms disrupt cellular defense mechanisms, impairing the detoxification of oxidative stress by products in retinal cells and contributing to disease progression. These results support further investigation of deletion polymorphisms as biomarkers for risk stratification and personalized therapeutic approaches in diabetic retinopathy.

REFERENCES

References

Lattes Curriculum