MOLECULAR GENETIC STUDY OF MACULAR CORNEAL DYSTROPHY IN EGYPTIAN PATIENTS

Mohamed Bahgat Goweida, Shahira Rashad Khodary, Asmaa Kenawy Amin,* Asmaa Eisa Ghazy Mohamed
Department of Ophthalmolog, Faculty of Medicine, Medical Research Institute,* Alexandria University

INTRODUCTION

Macular corneal dystrophy is an autosomal recessive disorder with irregularly shaped superficial opacities of stroma occurs in the first decade of life with early symptom of diminishing vision, photophobia and corneal abrasions rarely and progresses to severe bilateral visual impairment in adulthood characterized by an accumulation of glycosaminoglycans in keratocytes and the endothelium due to metabolic abnormality in keratan sulfate. MCD is classified as Category 1 in the IC3D system genetics of MCD explain that the defect is due to the absence of sulfate residues in the carbohydrate side chains from keratan sulfate proteoglycan and the oligosaccharide side chains are smaller than normal cornea this due to mutations within the CHST6 gene on chromosome 16 . Diagnosing of MCD can be by anterior segment optical coherence tomography (OCT), In vivo confocal microscopy,Scheimpflug imaging , and Ultrasound bio microscopy (UBM). Management is by Phototherapeutic keratectomy (PTK), Femtosecond assisted lamellar keratectomy and Keratoplasty.

AIM OF THE WORK

The aim of the work was to identify the *CHST6* gene mutations in a group of Egyptian macular corneal dystrophy patients. This would confirm the clinical diagnosis, allowing proper management and genetic counseling.

PATIENTS AND METHODS

The study was carried on 16 patients from 9 unrelated Egyptian families. They were clinically diagnosed with MCD and recruited and selected from the last 5 years-records of the Ophthalmology Outpatient Clinic of Alexandria Main University Hospital (AMUH), Faculty of Medicine, Alexandria University.

Inclusion Criteria:

Isolated macular corneal dystrophy

Exclusion Criteria:

Any other congenital malformations
Any systemic diseases
All participants / their guardians were asked to freely volunteer to the study and informed written consents were gathered prior to their inclusion in the study.

Methods:

All patients were Subjected to the Following: ***Detailed Genetic History Including:***

-Personal history - Past ophthalmic history. - Detailed genetic history
- Medical history - Surgical history

Full Ophthalmologic Examination Including:

- Visual acuity if possible - Slit lamp examination - Any other associated findings.

Molecular genetic study
Blood sampling and DNA extraction

RESULTS

Table1: Detected Variants among all studied families:

Family	Variant	Position on Chromsome 16 /Genomic coordinates	Protein	Variant type	Effect	zygosity	ACMG classification	Previously reported variants/ novel
1	NM_ 021615.5: c.65T>C	16: 75479764	p. (Leu22Pro)	SNV	missense	homozygous	Likely pathogenic	reported
2	NM_ 021615.5: c.631C>T	16: 75479198	p. (Arg211Trp)	SNV	missense	homozygous	pathogenic	reported
3	NM_ 021615.5: c.494_495 delins CT	16: 75479334 -75479335	p. (Cys165Ser)	Indel, 2 bp	substitution	homozygous	pathogenic	reported
4	NM_ 021615.5: c.173delA	16: 75479655	p. (Gln58 Hisfs*12)	deletion	frameshift	homozygous	Likely pathogenic	Novel
5	NM_ 021615.5: c.572_583del	16: 75479246	p. (Pro191_ Asn194del)	deletion	in-frame	homozygous	Likely pathogenic	Novel
6	NM_ 021615.5: c.455T>C	16: 75479374	p. (Leu152Pro)	SNV	missense	homozygous	Likely pathogenic	reported
7	NM_ 021615.5: c.894dup	16: 75478935	p. (Leu299 Alafs*7)	duplication	frameshift	homozygous	pathogenic	reported
8	NM_ 021615.5: c.143C>T	16: 75479686	p. (Ser48Leu)	SNV	missense	homozygous	Likely pathogenic	Novel
9	NM_ 021615.5: c.1089_ 1090del	16: 75512637 -75512638	p. (Glu364 Glyfs*9)	deletion	frameshift	homozygous	pathogenic	reported

Table2: Demographic characteristics, family history, known consanguinity, clinical findings, and previous therapeutic procedures

Family no.	Case no.	Gender	Age at time of sample collection / age of onset	Parental consanguinity	Similarly Affected individual/ other genetic conditions	Past ophthalmic history
1	C1	F	32/20 years	+	+/ -	
	C2	M	27/15 years	+	+/ -	RD/glaucoma/traumatic wound dehiscence,
2	C3	M	31/15 years	-	-/ -	
3	C4	M	21/12 years	+	-/ -	
4	C5	M	54/35 years	+	+/ -	
	C6	F	36/30 years	+	+/ -	LT Lower RD
5	C7	M	51/19 years	+	+/ -	
	C8	M	47/20 years	+	+/ -	
	C9	F	40/16 years	+	+/ -	LT Lower RD
6	C10	F	33/12 years	+	+/ -	
	C11	F	42/19 years	+	+/ -	
7	C12	M	55/30 years	+	+/ -	
8	C13	F	45/21 years	+	+/ -	
	C14	F	43/11 years	+	+/ -	
	C15	M	39/15 years	+	+/ -	
9	C16	M	31/16 years	+	-/-	

CONCLUSION

This is the second report of molecular genetic analysis of MCD patients in the Egyptian population. Consangui nity is high in Egypt and this results in more prevalence of autosomal recessive disorders. We have identified three novel and six previously reported disease-causing *CHST6* variants as the cause of MCD in Egyptian patients who were previously diagnosed clinically and this confirms the diagnosis, and expands the mutational spectrum of MCD and could contribute to understand the underlying mechanisms in MCD. This study contributes towards genetic counseling for MCD patients of Egyptian families and help for proper early mangment.

2024 ©Alexandria Faculty of Medicine
CC-BY-NC