CYP1B1 Gene Mutation Impact on Prognosis of Primary Congenital Glaucoma

Thesis

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By

Noha Salah Mohammad

MB. Bch, M.Sc., Ophthalmology
Faculty of Medicine, Ain Shams University

Supervised by

Prof. Dr. Saad Mohamed Rashad

Professor of Ophthalmology
Faculty of medicine, Ain-Shams University

Prof. Dr. Tarek Ahmed el Maamoun

Professor of Ophthalmology
Faculty of medicine, Ain-Shams University

Prof. Dr. Osama Kamal Zaki

Consultant of genetics
Ain-Shams University hospitals

Prof. Dr. Thanaa Helmy Mohamed

Professor of Ophthalmology
Faculty of medicine, Ain-Shams University

Dr. Samah Mahmoud Fawzy

Lecturer of Ophthalmology
Faculty of medicine, Ain-Shams University

Ophthalmology department
Faculty of Medicine
Ain Shams University
Cairo - Egypt

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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Noha Salah Mohammad

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List of Abbreviations

Abbrev.		Full-term
AA	**:**	Arachidonic acid
AC	**:**	Anterior chamber
AH	**:**	Aqueous humor
A119S	**:**	Polymorphism of alanine amino acid changed to serine. (non disease causing)
A443G	**:**	Mutation of alanine amino acid changed to glycine. (non disease causing)
ASD	**:**	Anterior segment dysgenesis
CCS	**:**	Conserved core structure.
CDR	**:**	Cup/disc ratio
Cm	**:**	centiMorgan unit of recombinant frequency which is used to measure genetic distance.
CW-TSCPC	**:**	Continuous wave transscleral cyclophotocoagulation
CYP1B1	**:**	Cytochrome P450 family 1 subfamily b
D430Afs*2	**:**	The frameshift mutation where aspartate amino acid was changed to alanine as a first amino acid affected by the change.
D449D	**:**	Polymorphism with no amino acid change. (non disease causing)
DNA	**:**	Deoxy ribo nucleic acid
dNTPs	**:**	Deoxy nucleotide triphosphate
E173K	**:**	Mutation of Glutamate Amino acid changed to lysine
EETs	**:**	Epoxyeicosatrienoic acid regioisomers

ECM	**:**	Extra cellular matrix
EUA	**:**	Examination under anesthesia
FDA	**:**	Food and drug administration
G329A	**:**	Mutation of Glycine Amino acid changed to alanine
G61E	**:**	Mutation of Glycine Amino acid changed to Glutamate
GSH	**:**	glutathione
HETEs	**:**	hydroxyeicosatetraenoic acids
H2O2	**:**	Hydrogen peroxide
IOP	**:**	Intraocular pressure
KCL	**:**	Potassium chloride
LM	**:**	longitudinal muscle
LTBP2	**:**	Latent transforming growth factor beta binding protein 2
MgCl2	**:**	Magnesium chloride
MMC	**:**	Mitomycin C
MP-TSCPC	**:**	Micro pulse transscleral cyctophotocoagulation
NAC	**:**	N‑acetylcysteine
N453S	**:**	Polymorphism of aspargine amino acid changed to serine. (non disease causing)
NCBI	**:**	National center for biotechnology information USA
OD	**:**	Oculus dextrus = right eye
OMIM	**:**	Online Mendelian inheritance in man
OS	**:**	Oculus Sinistrus = left eye
OU	**:**	Oculus Uterque = both eyes.

PCG	**:**	Primary congenital glaucoma
PCR	**:**	Polymerase chain reaction
RA	**:**	Retinoic acid.
Postn	**:**	periostin gene
ROS	**:**	Reactive oxygen species
R368H	**:**	Mutation of arginine Amino acid changed to Histidine at position 368
R469W	**:**	Mutation of arginine Amino acid changed to tryptophan at position 469
R444Q	**:**	Mutation of arginine Amino acid changed to glutamine
R48G	**:**	Polymorphism of arginine amino acid changed to glycine. (non disease causing)
S476P	**:**	Mutation of Serine Amino acid changed to proline
SIFT	**:**	Sorting intolerant from tolerant
SNPs	**:**	Single nucleotide polymorphisms
SOD	**:**	superoxide dismutase
SST	**:**	Subscleral trabeculectomy
Taq	**:**	Thermos aquatiqus thermostable DNA polymerase.
TBE	**:**	Trisborate EDTA
TM	**:**	Trabecular meshwork
tris-HCL	**:**	Buffer
V243V	**:**	Polymorphism with no amino acid change. (non disease causing)
V432L	**:**	Polymorphism of valine amino acid changed to leucine. (non disease causing)

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Introduction

Glaucoma refers to a group of disorders characterized by the death of retinal ganglion cells, optic nerve cupping, and visual field loss. This highly complex and multifactorial disease has multiple genetic and environmental influences ***(Aboobakar and Allingham, 2014).***

In recent years, substantial progress has been made toward understanding the genetic basis of various forms of the disease. Gene-based screening tests are currently available for several early-onset forms of glaucoma ***(Aboobakar and Allingham, 2014).***

Primary congenital glaucoma (PCG) is a severe form of glaucoma that presents early in life. PCG is a clinical and genetic entity that is distinct from juvenile forms of glaucoma. Despite its rarity, PCG and other forms of childhood glaucoma were once the leading cause of admission to schools for the blind in the United States in the first part of the 20th Century ***(Abu-Amero et al., 2011).***

PCG results from developmental abnormalities (trabeculodysgenesis) that affect the aqueous humor outflow pathway. These changes cause elevated intraocular pressure (IOP) and secondary glaucomatous optic nerve damage. (***Abu-***

Amero et al., 2011), and if left untreated, leads to irreversible blindness ***(Chakrabarti et al., 2010).***

The incidence of PCG varies among geographic locations and ethnic communities, from 1:10,000– 20,000 in western countries, to 1:2,500 and 1:250 in inbred Slovakian Gypsy and Saudi Arabian populations, respectively ***(Hilal et al., 2010).***

The link between PCG and gene abnormalities is the initial step in the establishment of the pathophysiology of the disease ***(Badeeb et al., 2014).***

Aim of the Work

To identify mutations in CYP1B1 gene in cases of primary congenital glaucoma, and its correlation to disease severity and surgical outcome (phenotype genotype correlation).