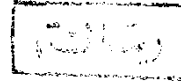


**A Genetic study of Colobomatous
Eye Anomalies**

Thesis

Submitted in Partial Fulfillment of the MD Degree

In
Genetics



By

Hanan Ibrahim El Bastawisy Hamouda

M.B., B.CH., M.Sc.

616.042

H. J

Supervised by

52926

Prof.Dr. Mohamed Ahmed Awad-Allah

Prof. of Pediatrics and Genetics
Faculty of Medicine- Ain Shams University

Prof.Dr. Samia A. Temtamy

Prof. of Human Genetics
National Research Centre-Ministry of
Scientific Research & Technology

Prof.Dr. Mouchira Abd-ElSalam

Prof. and Head of Human Genetics Department
National Research Centre, Ministry of
Scientific Research & Technology

Dr. Karam Abdel-Alim

Assistant Prof. of Genetics
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University



1994

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

”إِنَّا خَلَقْنَا الْإِنْسَانَ مِنْ نُطْفَةٍ أَمْشَاجٍ نَبْتَلِيهِ
فَجَعَلْنَاهُ سَمِيعًا بَصِيرًا

صدق الله العظيم

سورة الانسان (٢١)



ACKNOWLEDGMENT

ACKNOWLEDGEMENT

I wish to express my sincere gratitude to Prof.Dr. Mohamed Ahmed Awad-Allah, Professor of Pediatrics and Genetics, Ain-Shams University for continuous guidance, unlimited support and helpful criticism.

I would like to thank Prof.Dr. Samia Ali Temtamy Prof.Dr. of Human Genetics, National Research Centre to whom my gratitude is beyond expression, for her valuable advice, sincere assistance, close supervision, unforgettable instructions throughout the whole work.

Many thanks and great respect are presented to Prof.Dr.Mouchira Abd El Salam, Head of Human Genetics Department-National Research Centre for her great interest and generous guidance throughout the cytogenetic work as well as during writing the thesis.

I would like also to thank Dr. Karam Abdel-Alim Assistant Prof. of Genetics, Ain-Shams University, for his help and supervision.

I would like to extend my appreciation to Dr. Shadia Ibrahim Abdel-Sayed Assistant Prof. of Ophthalmology, Research Institute of Ophthalmology for the ophthalmic examination and photography of all studied cases.

I wish to record my deepest thanks to all my colleagues in the Human Genetics Department-National Research Centre for accepting me as one of them sharing them their laboratory and their advise and support throughout the whole thesis.

Lastly but not least, Iam indebted to the patients and their parents for their co-operation regardless of their direct subjective benefit. Hope that the knowledge gained through their collaboration will help to ameliorate the life of their fellows in the future.

*To My Parents
(Good bless Their Souls)
No Word can be Sufficient to express mylife lasting
respect and gratitude*

*And
To the Only one In this World Whom
I cann't express my feeling towards
his support, care, and kindness,
"My Brother"*

CONTENTS

	Page
I. INTRODUCTION	1
II. REVIEW OF LITERATURE.....	3
- Anatomy of the eye ball	3
- Embryology of the eye	6
- Anomalous closure of the embryonic cleft	21
- Types of eye colobomas	30
- Etiology of colobomatous eye anomalies	49
III. AIM OF THE WORK	112
IV. PATIENTS AND METHODS	113
V. RESULTS	125
VI. DISCUSSION	185
A. Isolated eye anomalies	187
1. Isolated aniridia	187
2. Coloboma of iris and choroid	189
3. Isolated ocular coloboma	190
4. Coloboma of the optic nerve	191
B. Eye anomalies as part of known genetic syndromes	193
1. Goltz syndrome	193
2. Bavinck syndrome	201
3. Rieger syndrome	205
4. Aniridia, ectopialentis, abnormal upper incisors and MR syndrome	207
5. Distal symphalangism with unilateral coloboma and microphthalmia	210
6. Aniridia plus syndrome	212
7. Toriello-Carey syndrome	214
8. Fraser syndrome	216

	Page
9. Hypomelanosis of Ito	217
10. Walker-warburg syndrome	218
11. Sommer syndrome	220
12. Anophthalmia, microcephaly, hypotonia, hypogonadism, failure to thrive and developmental delay syndrome	222
C. Chromosomal Abnormalities	226
1. Chromosome 13-trisomy	227
2. t(7;14) (q 13.2,q12)	231
3. Chromosomal breaks	234
VII. SUMMARY AND CONCLUSION	236
VIII. REFERENCES	239
ARABIC SUMMARY	---

LIST OF TABLES

	Page
1. General findings in (8) patients with trisomy-13 .	75
2. Ocular findings of both eyes of (8) patients with trisomy-13	76
3. Comparison of normal development and abnormalities in trisomy-13 in different stages of gestation ...	77
4. AD syndromes associated with ocular colobomas	98
5. AR syndromes associated with ocular colobomas	99
6. XL syndromes associated with ocular colobomas	100
7. Syndromes associated with colobomatous anomalies .	101
8. Most commonly used symbols and abbreviations in cytogenetic nomenclature	119
9. Main clinical data of studied cases	127
10. Genetic data of studied cases	136
11. Comparison of genetic and clinical data of aniridia cases	140
12. Clinical features of Rieger syndrome cases	142
13. Features of studied cases of Walker-Warburg syndrome	145
14. Chromosomal abnormalities observed in (7) out of (30) studied cases	147
15. Characteristic features of Goltz syndrome and actual features present in our proband	196
16. Comparison of Bavinck's cases features and our studied cases	203

	Page
17. Difference in clinical features between ZamZam et al.(1988) case and our case no.4	208
18. Comparison between Sommer et al., cases and our studied case of Sommer syndrome	221
19. Comparison between Al-Frayh et al. case and our case no. 30	224
20. Comparison of clinical features of our case with the previously described cases of Patau syndrome.	228

LIST OF FIGURES

	Page
1. Section of eye ball	5
2. Transverse section through the forebrain of a 22-day embryo	8
3. Normal eye development	8
4. Development of iris and ciliary body	12
5. Persistent irido-pupillary membrane	18
6. Diagrams showing the transformation of the optic stalk into the optic nerve	18
7. Changes in the position of the eyes	20
8. Diagrammatic representation of the development of typical colobomas	29
9. Showing genetic sheet used in registration of proband's data	115
10. Showing pedigree symbols & abbreviations used ..	120
11. Pedigree of case no. 10 & 11	149
12. Pedigree of case no. 15 & 16	149
13. Pedigree of case no. 19	150
14. Pedigree of case no. 20	150
15. Pedigree of case no. 24, 25 & 26	151
16. Pedigree of case no. 12	151
17. Pedigree of case no. 17	152
18. Pedigree of case no. 22	152
19. Pedigree of case no. 1	153

	Page
20. Pedigree of case no. 2	153
21. Pedigree of case no. 14	154
22. Pedigree of case no. 3	154
23. Pedigree of case no. 13	155
24. Pedigree of case no. 27	155
25. Pedigree of case no. 4	156
26. Pedigree of case no. 9	156
27. Pedigree of case no. 5	157
28. Pedigree of case no. 23	157
29. Pedigree of case no. 7	158
30. Pedigree of case no. 8	158
31. Pedigree of case no. 6	159
32. Pedigree of case no. 21	159
33. Pedigree of case no. 29	160
34. Pedigree of case no. 30	160
35. Pedigree of case no. 18	161
36. Pedigree of case no. 28	161
37. Shows dysmorphic facial features in case (1)- Goltz syndrome	162
38. Showing dysmorphic features of case no. 1	162
39. Shows bilateral split feet of case (1)	163
40. Shows typical iris coloboma in case (2) Bavinck syndrome	163
41. Shows facial profile of case 2 and her father ...	164

	Page
42. Shows facial features of case (3) Rieger syndrome	164
43. Shows iris coloboma, cataract, absence of iris pattern and telangectasia in case 3	165
44. Low insertion of thumbs in case 5 (Aniridia plus syndrome)	166
45. Shows same case (5) at 4 years of age	166
46. Shows aniridia in case (5)	167
47. Shows retinal pigment epithelial degeneration in same case (5)	167
48. Facial features of case (6) WWS	168
49. Brachycephaly in profile of case (6)-WWS	168
50. Brain CT-scan showed lissencephaly and shunt operation for dilated ventricles in case (6)-WWS.	169
51. Coloboma of left upper eye lid of case (7)	170
52. Right cryptophthalmos in case (7)	170
53. Ambiguous genitalia in case (7)	171
54. Family with AD-aniridia, case no. 10, 11	171
55. Normal fundus appearance	172
56. Left optic disc coloboma in case (14)-Bavinck syndrome	172
57. Dysmorphic facial features and musculo-skeletal dysplasia in case -18	173
58. Dysmorphic features in case -18	173
59. Characteristic facies of case (22)	174
60. Characteristic facial features of case 27 Rieger syndrome	174

	Page
61. Showing characteristic features of case (28)	175
62. Showing anteriorly displaced anus in case (28) ..	175
63. Shows facial features of case (29)	176
64. Normal female karyotype 46, XX	177
65. Showing normal male karyotype 46, XY	178
66. Karyotype of case no.(4): 46, XY dup.(17q) (q12) and constriction at 5q13	179
67. Karyotype of case no.(4): 46, XY, constriction at 5q33	180
68. Multiple chromosomal breaks in case (11)	181
69. Karyotype of case no.(18): 46, XX, t(7,14) (q13.2, q12)	182
70. Karyotype of case no.(18): 46, XX, del (5)(q35) .	183
71. Karyotype of case no.(28): 47, XX, (+13)	184