18

Genetic Conditions: Results and Discussion

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Introduction

This chapter will address the common clinical conditions encountered in the childhood onset visual impairment survey between 1985-1987 in the West Bank and Gaza Strip. This includes epidemiological and clinical aspects with discussion. These are lens disorders (congenital cataract / aphakia and ectopia lentis); small eyes (both anophthalmia and microphthalmia); corneal conditions, both acquired and congenital; albinism, and the common retinal disorders both stationary and progressive.

18.1 Congenital Cataract

Congenital cataract (CC) is the commonest treatable condition in the series and the second commonest genetic condition. Appendix Table A18.1 lists all cases, their birth sequence, ratios, and mode of inheritance.

Patients and Sibships

The number of patients with cataract as a primary pathology was 132 forming 91% of the lens group (n= 145). (Table 18.1) The figure rises to 164 when cases with cataract as a secondary cause of pathology are added. The figure rises further to 185 when all cases with childhood onset cataract (but which did not contribute essentially to visual impairment) were added.

Age Distribution

Regionally, congenital cataract affected 22.4% and 20.7% of children in the WB and GS respectively. In the 16+ cohort, the percentage in the GS was double that of the WB at 19.2 and 10.5 % respectively. Wide age-cohort differences in the ratio of CC are found between the <16 and 16+ age groups in the WB and GS. In the <16, the ratio is 1.4:1 which is close to the population ratio of 1.78:1, whilst in the 16+, the ratio is reversed to become 0.58:1.

Gender
Male to female ratio in CC demonstrates male preponderance in both regions, especially in the GS where there are twice as many males as females. (WB 1.4:1, the GS 1.75:1)

Visual Acuities
Visual acuities in the CC patients on whom such figures were available (rather than an estimate ie other than WHO categories '6' and '7') were 4 (5%) in BL category '5', 21 (25%) in the BL category '4', 10 (12.2%) in the SVI category '3', 39 (47.5%) in the VI category '2' and 8 (9.8%) in the NVI category'1' (n=82). Cases in the combined SVI/BL category is 43% and 26% in the SVI/BL category (n=18/69)

Table 18.1 Patients families in the West Bank and Gaza Strip in cataract cases

	Patients with Cataract							
	Primary		Secondary		Others		Total	
WB	62	***47***	15	***52***	7	***64***	84	***49***
GS	58	***44***	11	***38***	4	***36***	73	***42***
Either	12	***9***	3	***10***	0	***0***	15	***9***
Total	132	***100***	29	***100***	11	***100***	172	***100***

Percentages in ***bold Italic***

Inheritance
Sixty one percent of CC cases are hereditary (n=81) and 9.8% are non-hereditary (n=13); this leaves 28.8% (n=38) of cases of undetermined aetiology. Excluding the latter group this brings the hereditary cases to 86% of the CC. The hereditary group comprises primarily genetic congenital cataract. The modes of inheritance in these patients are autosomal dominant (AD) in 11% (n=9); 84% autosomal recessive (AR) (n=68), 3% (n=4) were isolated cases and in 1 the aetiology was uncertain. Among the AR cases, 4 resembled autosomal dominant (AD) inheritance and an additional 4 cases were associated with AD myopia. (Table A18.1)

In comparison to the remainder of the CC series, the isolated group of patients included the largest proportion of cases recruited from the outpatient clinic which contained insufficient history, demography, and consanguinity data. Their inclusion in the study was necessary to provide additional information on the size of the problem of the various conditions, in particular lens disorders and their prevalence in the region.

Consanguineous marriage in these sibships was 81%. There were 94 patients (23.2% of the total study) in the <16 cohort with CC as a primary cause of visual disability and 110 (27%) when cases with CC as a secondary cause of blindness were included**.**

Prevalence
In the Palestinian population of the West Bank and Gaza Strip (this study) the prevalence in the 5-19 age cohort averaged 11.4/100,000 in both regions.

Mode of Inheritance
It was possible to establish the hereditary nature in 65% (94/145) of CC cases. Non-hereditary lens conditions formed 9.6% (14/145) of cases and in undetermined cases were 25.5% (37/145). When cases with the undetermined aetiologies are excluded, the percentage of hereditary conditions rises to 87% and non-hereditary to 13%.
Autosomal recessive mode of inheritance is the predominant mode with 76.6% confirmed cases, although this is more likely to be 85% when the possible AR / AD and isolated conditions are included as they are most likely to be recessive in origin. This leaves 9.6% (9/94) AD cases and 4.25% (4/94) chromosomal in origin.

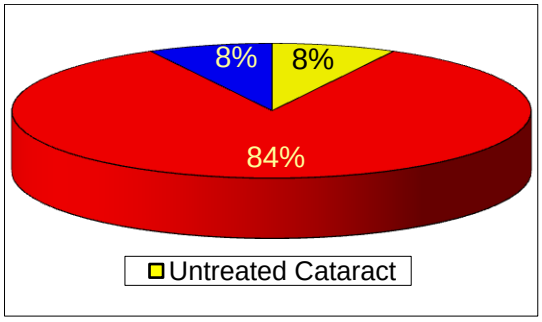
Aphakia
Aphakia was included under CC rather than as a separate entity. It was present in 109 patients (187 eyes) leaving 23 patients (134 eyes) with untreated cataract (both as a primary and secondary cause of blindness). This is in addition

to 12 other cases of aphakia belonging to other categories (whole globe 5, retina 4, cornea 2, and optic nerve diseases. (Figure 18.1)

Posterior Capsular Fibrosis

This was reported in 14 eyes. Several children underwent surgical capsulotomy with sufficient visual improvement to enable their transfer to sighted schools with the appropriate visual aids.

Figure 18.1 Proportions of aphakia and untreated cataract



Congenital cataract was also found in patients with ectopia lentis (n=15, 7.4%), congenital glaucoma (CG) (n=12, 6%), retinal dystrophies (n=10, 5%) and microphthalmos (n=10, 5%). This tops up the number of patients with lens related conditions to 202 patients (30.2% of the series), 112 of the patients were aphakic. (Tables 18.2, 18.3)

Associated Systemic Conditions

The commonest associated feature with congenital cataract in the survey was mental retardation / subnormaility. The distribution of this in the various congenital and cataract cases is shown in Tables 18.2 and 18.3.

Discussion

The diverse aetiologies and different definitions used to identify congenital cataract have led to difficulties in evaluating this condition in epidemiological studies.

In addition, the figures in this survey are nearly 3-fold those reported some 6 years later in 1993 (6.9%). This indicates that the recommendations put forward at the time of this study by the author of ensuring proper refractive correction, and transferring pupils to normal schools had been implemented. Also the possible improvement in cataract surgery outcomes with more prescription of glasses from an earlier age. [(1)]

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The lower numbers of the 16+ in the WB may be explained as an under representation due to the absence of those patients who would have been working in contrast to the GS where it was easier to achieve a better cover of cases (10.4% versus 20.8%), yet the total proportion in the whole study is very close in both regions (20.5% and 21.5% respectively). (Table 18.1)

The proportion of CC in the survey (WB 26.6%, GS 22%) makes it the commonest avoidable blindness. The figures are fairly close to those reported in Turkey [(2)] and very similar to those reported among the Palestinians in Israel (21%) [(3)] This is somewhere in between those reported in Thailand and the Philippines (44%), [(4)] and the lower figures (<10%) in some other countries, including the Established Market Economies countries and many of the developing countries. [(5), (6), (7), (8), (9), (10)]

Globally, it has been estimated that congenital cataract is the cause of blindness in 190,000 children (14% of the total childhood blindness). There is a wide variation in the prevalence, ranging from nil in Scotland [(5)] to 39% in Jamaica. [(11)] The incidence is variable and ranges from 1 to 3/10,000 live births or 10 per million of the total population in low-income countries. [(12)]

Lowest figures are from the industrialised countries where they have shown a marked decline since the 19th Century reaching 0% in 1986 as a result of improved rubella immunisation, early detection and improved

surgical techniques. [5], [6], [7], [8], [9], [13] Highest figures are from the developing world, in particular the Caribbean, Africa and to a lesser extent Asia. [11], [14], [15], [16], [17], [18] In India, wide interregional variations have been reported ranging between 2.9% in Uttar Pradesh to 23.6% in Kerala. [19] In the Nordic countries the prevalence was 36 per 100,000. The occurrence rate for dense bilateral and all unilateral cases were both 14 per 100,000 each [20]. In another study it was reported as ranging from 15-41/100,000 and in a small study in Sweden with an incidence rate of 12-23/ 100,000 live births. [21]

The higher proportion of CC of undetermined aetiology encountered in epidemiological studies is reflected in this study in the <16 cohort and is due to a lack of detailed history. Congenital cataract of hereditary aetiology formed 54% of the cases whilst in the 16+ cohort, it amounted to 92.5% as it was easier in these to obtain full detailed history and establish the mode of inheritance, especially as more affected siblings are born. It is, therefore, most likely that hereditary aetiology is very high in all age groups.

Rubella cataract is a rarity in this study and also in Lebanon, Saudi Arabia, Cyprus and Nigeria, as rubella is usually contracted at pre-childbearing age in these countries. Rubella cataract in Nigeria remains a major cause (19%) with only 5 of the 26 cases being genetic in aetiology. [22]

These figures differ from other Muslim countries who also have a high rate of consanguinity such as Uzbekistan where not only the percentage of familial cases of CC was lower (49%, 72/147), but there was a much higher proportion of the AD mode of inheritance than in this study (28% AD, 31% AR and 13% undetermined). Other differences between our study and that of Uzbekistan, include the proportion of the sporadic cases of CC which formed 44% (65/147) of the series compared to 25% in this study, associated microphthalmia at 22% compared to 5% and ectopia lentis 7% (10/177) compared to 9% from the total lens conditions. [10]

The visual morbidity in the aphakic congenital cataract patients in the WB and GS is high, with over 60% in the VI/SVI and 26% in the SVI/BL category. This is the result of amblyopia from long-term neglect and the absence of wearing aphakic correction. It is also, to a lesser extent, secondary to post-operative complications, in particular posterior capsule fibrosis, and in a few patients from surgical complication such as glaucoma and retinal detachment. During the course of the study, glasses were prescribed and the posterior capsular fibrosis was treated surgically, resulting in improvement in a proportion of these patients, some of whom were transferred to sighted schools. Similar findings were reported in the developing countries such as India where uncorrected aphakia and amblyopia contributed to 12.3% of blindness. [23]

Multidisciplinary efforts and organisation are required to combat the problem of amblyopia. Visual morbidity resulting from CC has considerably improved in industrialised countries in recent decades with optimised after care of aphakia and complications from a very early stage, before the onset of intractable amblyopia.

Nevertheless, the problems encountered in the rehabilitation process in developing countries are considerable. Diagnosis may not be made until well into childhood and even when made, referral for surgery may not be contemplated until beyond the age of cortical plasticity. In addition advances in paediatric anaesthesia have not reached many of the developing countries. Periodic post-operative and orthoptic care is lacking and frequently proper follow-up of these children is difficult for economic and logistical reasons. In addition, surgical techniques used such as extracapsular techniques or lens aspiration, without posterior capsulectomy, have created the problem of posterior capsule opacification, some of which will proceed to secondary glaucoma. Optical correction for these children is therefore suboptimal.

Table 18.2 Associated conditions with congenital cataract as a primary condition

Sex	Age	Findings
West Bank		
F	15.9	Very slow mentation, very shy
M	10.8	Slow mentation, cryptorchidism
M	3.7	Bat ears, extra digit, cryptorchidism, bright
M	7.2	Mentally subnormal
Gaza Strip		
F	19.6	Mentally subnormal
M	16.9	Hypoplastic maxilla, slurred speech [a]
M	7.2	Mentally subnormal, extra digit, bulgy sternum, undescended testes
F	2.9	Mentally subnormal, Down syndrome
F	8.9	Allergic rhinitis
Retinal dystrophies		
West Bank		
M	4.1	Trichomegaly, nails abnormality
M	41.7	Mentally retarded, spastic, unilateral CDH, small for age
3 M	12-15	Mentally subnormal
F	10	
Region uncertain		
M	7.8	Prominent first incisor
Congenital glaucoma		
West Bank		
F	3.2	Limbs weakness
M	6.0	Spastic
Region uncertain		
M	0.8	Mentally retarded
M	0.9	Mentally retarded, homocystinurea
F	9.4	mentally retarded, epileptic; grand and petit mal seizures
Other Conditions		
West Bank		
M	7.4	Mentally subnormal
F	13.4	Very bright child, IDDM

[a] Cataract absent in the other affected siblings
IDDM: Insulin dependent diabetes mellitus

Table 18.3 Mental subnormality in patients with cataract

As a primary / secondary	Cohort size	Total		Hereditary cases	
Primary	132	8	***6***	5	***62***
Primary and secondary	164	10	***6***	7	***70***
Total cases	185	18	***19***	13	***72***

Percentages in ***bold Italic***

18.2 Ectopia Lentis

Ectopia lentis is a small subgroup of lens conditions (EL) (n=13), 9 were from the WB and 4 from GS with a ratio of 2.25:1. The M:F ratio was 1.6:1 but in the GS, all cases were male. The group consisted of 9 sibships from 7 pedigrees. All the conditions associated with EL were AR and are shown in Table 18.4)

This condition is usually inherited as part of several syndromes such as homocystinurea and Marfan syndrome. Simple ectopia lentis is usually inherited as an AD trait but recessive conditions are also known to occur and have been reported in 19 patients in 2 Arab families in Jordan. [24] In this study, one sibship exhibits the simple form (3 patients) and in another 3 EL was associated with high myopia. The remainder of the cases are syndromatic and include a new association with infra-temporal quadrantic iris anomaly, dysmorphic features and one of the siblings suffers from arthritis of the ankle and fingers in one hand. Another patient also had cryptorchidism, shawl scrotum, mental subnormality and minor skeletal abnormalities [25] The rest are part of homocystinurea and Marfan syndrome.

18.3 Congenital Glaucoma

Demography

Congenital glaucoma encompasses 68 patients,

32 from the WB, 29 from the GS, 6 unidentified and 1 from Israel. These patients originate from 45 pedigrees, 20 from the WB, 18 from the GS and 7 from either region of the OPT. There were an additional 2 patients in whom buphthalmos was a secondary pathology.

Age Distribution

The age distribution in the CG cohort is 43 patients <16 years and 25 adult patients; a ratio of 1.72:1.

Gender

There are a total of 40 males and 28 females in the CG group giving rise to a M:F ratio of 1.43:1 for the total and 1.38:1 for the < 16. Among those whose family history is known (n=62), the ratio drops to 1.2:1 (1.1:1 general population, 0.9:1 in the CG sibships (n=224 sibs). Ratios between the two regions are comparable including male predominance except in the <16 cohort in the WB where it is 1:1.

Table 18.4 Conditions associated with ectopia lentis

Condition	No.	%	Sibships
Isolated AR ectopia lentis	3	***23***	1
High myopia	3	***23***	2 [a]
Infra-quadrantic iris anomaly, dysmorphic features, unilateral arthritis in ankle and fingers in one.	2	***15.9***	1
Syndromatic: hypoplastic scrotum, undescended testicles, feminine complexion, course scalp hair (absent in other siblings), flat feet, educationally subnormal (brother undescended testicles) - (Plates 26 to 29)	1	***7.7***	1
Marfanoid features	1	***7.7***	1
Homocystinurea	3	***23***	3 [b]
Total	13	***100***	9

[a] Same pedigree. [b] two pedigrees, 2 cousins from 1 pedigree.

Visual Acuities

Visual morbidity in this series is considerable. Prognosis is very poor whether left alone or if treated surgically. **(**Table 18.5) Both trabeculotomies and trabeculectomies were performed in this series but all procedures showed diminishing success rates with time although the latter was the most successful. [(26)] In many cases, corneal decompensation ensued with normalisation of the IOP soon after surgery and with a tendency for some eyes to become atrophic. In 1 case of simple infantile glaucoma, which was followed closely by the author of this study, corneal decompensation developed 7 months after an uneventful surgery and soon after, corneal opacification ensued. The initial high intraocular pressure and higher cup:disc ratios were found to be predictive factors for failure of the first procedure in a recent study on a similar population and the former was the only independent predictive factor for failure as the final outcome. In addition, the absence of family history carried a better prognosis. [(27), (28), (29)]

Table 18.5 Visual acuities in congenital glaucoma

	Total series		5 to 19	
WHO Visual Category	No.	*%*	No.	*%*
NPL '5'	14	***20.6***	7	***22.6***
Blind '4'	21	***30.9***	10	***32.3***
Total blind				
Category '7'	15	***22.1***	5	***16.1***
SVI ('3')	3	***4.4***	2	***6.5***
SVI/BL ('3', '4', '5', '7)				
VI ('2')	8	***11.8***	4	***12.9***
Category 6'	1	***1.5***	0	
NVI ('1')	5	***7.4***	3	***9.7***
n/a	1	***1.5***	0	***0.0***
Total	68	***100***	31	***100***

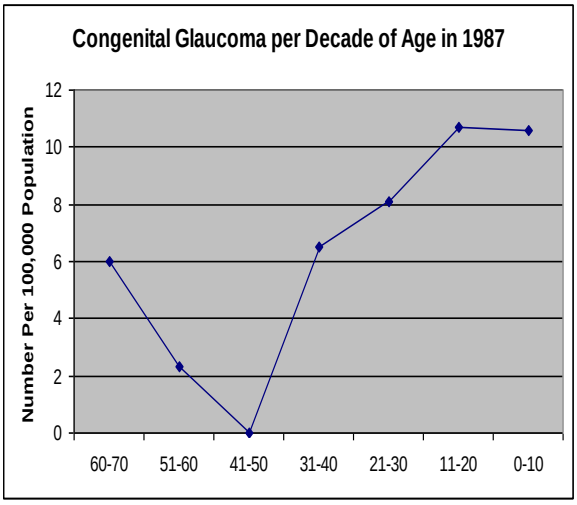
Not surprisingly, therefore, we find a high proportion of severe visual disability and

blindness in the series with 79% of congenital glaucoma falling into the SVI/BL category, two thirds of whom have NLP.

Clinical Characteristics

It is possible that 50 cases (74%) are primary CG (PCG) and 10 (15%) are ACS including 7 with Peter's anomaly and 2 with Reiger's syndrome.

Figure 18.2 Congenital glaucoma per decade in the West Bank and Gaza Strip.



One case is probably non-genetic.

There is considerable ocular morbidity in these conditions which made ascertainment of clinical details and type difficult. Twenty two eyes were phthisic or atrophic and 1 removed, 7 with corneal scarring and probable Peter's anomalies. [30]

It is possible that 50 cases are primary infantile glaucoma (PIG) and 10 are anterior cleavage syndrome including 7 of probable Peter's anomaly and 2 of Reiger's syndrome. One case is probably non-genetic. The severe ocular morbidity made ascertainment of clinical details and type difficult; 22 eyes were phthisical or atrophic and 1 removed. In 80% of cases, it presented at, or soon after, birth with the classical features of buphthalmos.

Inheritance

It was possible to establish the hereditary nature of CG in 57 cases; in 9 information was not available and in 2, the condition was non hereditary. In the hereditary cases, AR mode of inheritance was the norm in 90% of cases with known family history, and 3 were isolated cases. The percentage of affected sibs to the total sibship averaged 27.7%. The ratio within the gender was 32% and 24% of the affected male and females to respectively.

Prevalence

Congenital glaucoma (CG) ranks third amongst the causes of childhood blindness and is the second major congenital condition treated surgically. It represents 10.2% of patients in the whole series. The prevalence of CG in all the OPT is 5/100,000 (WB 3/100,000, GS 6.6/100,000). In the <16, the figures are 6, 4, 8 / 100,000 respectively.

In this study, however, incidence rates average 1:28,000 in the OPT (WB 1:34,000 and GS 1:22,000). It is difficult to explain this low rate in comparison to the rest of the region as it is found in both the <16 who are well represented in the schools cohorts and adults.

The number of CG cases per 100,000 in the WB and GS showed an increase between the 1950s and the 1970s when it levelled off (Figure 18.2).

Associated Findings and Conditions

Several additional conditions were associated with CG. These are enumerated in Table A18.2 together with the family sequence and other data.

Discussion

Male preponderance ranging from 1.55:1 to 1.9:1 have been reported in the various studies, [13), (31] although it was absent in the non-gypsy population of Slovakia which was 1:1. [31] Male preponderance and the lower than expected number of affected sibs in the familial cases have raised questions on the validity of AR inheritance mode. This, together with the transmission of disease in successive generations, is suggestive of AD inheritance.

Some light has, however, been shed on this in recent molecular genetic studies and is attributed to the high inbreeding in these communities where there is a high chance of marriage between homozygous and heterozygous subjects. In this study, only 1 sibship showed pseudodominance and heavy consanguinity in this community supports the argument that pseudodominance in CG is not an independent phenomenon. [32] As an observation, the ratio of males to the total numbers of males is higher than the equivalent percentage in females at 32% and 24%. [33]

The marked visual morbidity in this series and poor prognosis, whatever the surgical procedure used, explains the high proportion of severe visual disability and blindness in the series with 79% of cases falling into the SVI/BL category, two thirds of whom have NLP depicts a comparison between this series and the Slovakian study. [31] The initial high intraocular pressure and higher cup: disc ratios were found to be predictive factors for failure of the first procedure in a recent study on a similar population and the former was the only independent predictive factor for failure as the final outcome. In addition, the absence of family history carried a better prognosis. [27], [28], [29]

The AR mode of inheritance of CG in the West Bank and Gaza Strip survey is in line with the pattern documented in other parts of the Middle East. The percentage of affected sibs is 27.7% which is indicative of the recessive mode. The variable penetrance is well demonstrated in these sibships. The AR mode of inheritance was noted in 90% of sibships where family data were available (and most likely to be AR) and 3 cases were sporadic.

The largest group in this subcategory is that of isolated. Consanguinity ranging from first to third cousin marriages were recorded in 28/32 sibships (87%), 79% of whom were first cousin marriages. This is higher than the Saudi Arabian figures of 68%. An additional 3 were from the same locality and in 1 sibship only was no relationship found. Parental consanguinity has been reported in several studies on CG. [27], [32], [34]

Congenital glaucoma formed the third commonest disorder in the series amounting to 10.2% of cases in the series where cases of unknown localities. (WB 9.2%, GS 10%, excluding cases of unknown localities). (Chapter 14) It occupies a midway position between Jordan (15%) and Saudi Arabia (17%) on the one hand, and Lebanon, Cyprus (6% each) and Uzbekistan 4.7% on the other hand [14], [10], [35], [36],, [37] The former 2 countries have the highest recorded rates in literature after Nigeria and followed by the Dominic Republic and Peru. [22], [38], [39] Incidence rates in Europe ranged from 1:1,250 (the highest reported) in Slovakian Gypsies and 1:5,000 (Switzerland) to as low as 1:22,000 in Slovakia, averaging 1:10,000. [13] (Table 18.6)

The incidence rate in the Middle East is 1:2,500 compared to the rest of the world which is generally less than 1:10,000. [13], [40]

Incidence rates in the West Bank and Gaza Strip in this survey (averaged 1:28,000 in the OPT, WB 1:34,000 and GS 1:22,000) are difficult to explain in comparison to the rest of the region as found in both the <16 who are well represented in both the schools and in the 16+ cohorts. The number of CG cases per 100,000 in the WB and GS showed an increase between the 1950s and the 1970s when it levelled off (Figure 18.2). This pattern is also reflected in worldwide trends which demonstrated an increase in the incidence of PCG in the 1930s till the 1970s raising the share of this condition in childhood blindness from 10 to 20%, followed by a decline after the 1970s. [13]

Associated conditions with CG are scarce in literature, which makes the West Bank and Gaza Strip unique in the frequency of associated conditions with congenital cataract.

Table 18.6 Comparison of congenital glaucoma in the survey and Slovakia

	This study	Slovaks	Sinti
Sample size	68	87	118
Families	50 (45[a])	81	41
Prevalence	OPT 1/25,000 WB 1/28,000 GS 1/16,000	1/51,000	1/1,250
Incidence	OPT 1/28,000 WB 1/34,000 GS 1/22,2000	1/22,000	1/2,120
M:F Ratio	1.38:1/1.2:1[b]	1.55:1	1:1
Course	Severe	Severer in Sinti than non-Sinti	
Prognosis	Poor	worse in Sinti than non Sinti	
Bilaterality	100%	73%	100%
Diagnosis at Birth	80% birth	6 months	82% birth
Inheritance	87% A/R	-	highly probable A/R
Familial	76%	12%	85%
Sporadic Cases	23.5%[c]	88%	15%
Consanguinity	87%	5.9%	45%

[a] Number of extended genetic families. [b] Ratio of patients with known pedigree information.
[c] In 3 cases, the ratio of affected/total siblings was 1:5 or less. In another 3, ratios were 1:8, 1:10, and 1:11.

18.4 Small Eyes (Microphthalmia/ Anophthalmia

Small eyes, microphthalmos, (as defined by the WHO are eyes with a corneal diameter of less than 11mm), and form the fourth largest genetic group of conditions.

Age Distribution in MC
Children formed 62% of the series (23/37), 9 in the WB and 14 in the GS.

Gender in MC
Male predominance in observed in all the groups. (Table A18.3)

Inheritance
Of the total group of 60 patients, 53 (88%) were hereditary, 7 (12%) were prenatal. Sixty three percent of sibships showed a definite familial occurrence (>1 affected sibling in the family). (Table A18.3)

Prevalence and Incidence of MC
Microphthalmia and anophthalmia account for 5.1% and 0.4% respectively with marked regional variations being significantly higher in the GS (7.3%) than the WB (3.0%). This is due to a large pedigree that comprises 5 sibships with 10 patients. The mutation rate, however, is only marginally higher as demonstrated by the ratio of pedigrees between the two regions. The associated ocular findings in the GS were also higher (9%) and compares to published figures for the regions in 1993 (8.7%); [(1)] however, these were based on the compiled data of this author which was archived at SJEH. (Tables 18.7, 18.8)

Clinical Types and Regional Distribution

The total number of patients with MC is 60. This includes those in whom the condition was the primary site of pathology (n=38) and secondary contributor to the visual impairment (n=28). The primary cohort formed 4.3% of the WB cohort, 7.6% of the GS cohort and 5.5% of the total cohort. (Table 18.7). All MC cases, however, form 8%, 10.7% and 9% of the total Occupied Palestinian Territories series in both regions.

On the basis of aetiology MC can be grouped into three categories:

Group A: MC is the primary cause of blindness (WHO anatomical classification) in 33 patients. The VA is in the SVI/BL category in 30 patients (91%) with 23 blind (70%) and 17 (51%) with NLP. Three patients from 3 unrelated sibships had anophthalmia. Five patients from one pedigree from the WB have an appearance of anterior cleavage syndrome (ACS). Colobomas were part of the microphthalmia in 7 patients (21%). In 2 patients out of 3 from one sibship from the GS, total absence of the iris identical to aniridia was seen with ACS. Group A also showed a wide interfamilial and intrafamilial variability in the phenotypic expression in the MC patients with a clinical picture that varies from a rudimentary eye bud that can be detected moving behind the conjunctiva, to a well-formed eyeball.

Group B MC is a secondary pathology contributing to the visual problem in 20 patients. In the majority of these patients (n=16, 80%), CC was the primary pathology, and in the remaining 4 (20%), uveal coloboma was the primary cause of visual loss. SVI/BL in this group was present in 9 cases (47%), Blind in 5 (26%) with none in the NLP category. Seven (37%) were in the VI category. (<6/18 to 6/60).

Group C MC in the non-hereditary cases were present in 7 cases. Six of the patients were blind; half with NLP.

Associated Finding and Conditions

Cataract and Microphthalmia

The overlap between cataract and microphthalmia was such that 11% of children in the SVI/BL category. both diagnoses in Uzbekistan. [10]

Other Features

Six patients (6/38) with MC had other associations and special features. (Table A18.3)

Group B was not associated with other systemic associations or unusual features. Patients and other siblings sequence are depicted in the box under each case. For siblings sequence refer to Table A18.3.

Special abilities (AR inheritance, first cousin marriage). One sibship was unique in this characteristic. All were of above average intelligence. One had exceptional auditory abilities whereby he could cycle around town despite NLP vision; the brother had superior photographic memory in addition to suicidal tendency; he had jumped twice from a high window**.**

Marfanoid features: (above average height, high arched palate), and anterior open bite. (AR, second cousin marriage).

Muscular-skeletal associations: (a) Muscular dystrophy, hands weakness; (b) kyphoscoliosis, (had surgery on one foot); and (c) telecanthus. An isolated case from a first cousin marriage.

Mental retardation plus: deafness and failure to thrive; feeble cry, spasticity, microcephaly, and myotonic jerks (IUI, unrelated parents).

Male predominance was almost equal in both groups averaging 1.55:1. This was not observed in Sweden where bilaterality was found in 53-60% of patients with other malformations and 27% of patients with isolated microphthalmia. [41] This is in contrast to the West Bank and Gaza Strip where cases encountered in both groups were bilateral, however, the selection criteria could have created a bias as all cases registered in the study had to be bilaterally visually impaired.

Visual morbidity in this study was worse than other series with 63% of cases in both subgroups having NLP, versus 20% in Uzbekistan. [10]

Mental retardation plus: deafness and failure to thrive: feeble cry, spasticity, microcephaly, and myotonic jerks (IUI, unrelated parents).

Table 18.7 Microphthalmia patients, and sibships

	Patients	Sibships	Pedigrees
Hereditary			
MC as a primary cause of blindness			
WB	13	9	8
GS	20	10	6
subtotal	33	19	14
WB:GS[b]	0.7	0.9	1.3
MC as a secondary cause of blindness			
WB	13	5	4
GS	6	5	3
subtotal [a]	20 [a]	11	8
Total	53	30	22
WB:GS[b]	2.2	1.0	1.3
Non-hereditary (all prenatal)			
WB	2	2	2
GS	5	5	5
total	7	7	7
WB:GS[b]	0.4	0.4	0.4
All MC cases			
WB	28	16	14
GS	31	20	14
Total [a]	60	37	29
WB:GS [b]	0.9	0.8	1
Grand total [a]	60	37	29
WB:GS[b]	1.75	1.5	1.2

[a] Includes 1 patient from either region.
[b] Average WB/GS population ratio is 1.78:1

Discussion

Male predominance was almost equal in both groups averaging 1.55:1. This was not observed in Sweden where bilaterality was found in 53-60% of patients with other malformations and 27% of patients with isolated microphthalmia. [41] This is in contrast to the West Bank and Gaza Strip where cases encountered in both groups were bilateral, however, the selection criteria could have created a bias as all cases registered in the study had to be bilaterally visually impaired.

Visual morbidity in this study was worse than other series with 63% of cases in both subgroups having NLP, versus 20% in Uzbekistan. [10]

Data on the prevalence of MC worldwide is scarce. Figures on the birth prevalence of microphthalmia and anophthalmia, based on population-based registers, are 14 and 3 per 100,000 births respectively. Large regional differences exist in the proportion of congenital malformations in blind school children ranging from 10.7% with microphthalmia, 2.3% with anophthalmia, and 1.3% with coloboma. [42], [43] The prevalence of severe visual loss from these abnormalities is estimated to affect between 0.4 and 16.2/100,000 children; the underlying cause could not be identified in 84.2%. [42] The prevalence of microphthalmia (as a primary pathology, Group A) in the WB and GS are 10 and 38 per 10,000 (averaging 2/100,000 in both regions). The figures are higher when both types are included (35 and 58 per 10,000). This is considerably higher than the estimated prevalence of 1.9/10,000 in Uzbekistan and those derived from birth registries from France, Sweden and California (0.4 to 5.9 / 10,000). [10]

In blind schools, the condition formed 23% (129/671) of the total children examined in Uzbekistan, [10] including a significant proportion with associated cataract. No cases of microphthalmos were reported in the Jordanian study, [36] but were present in 1.9% (4/208) of the Lebanese series, [37] 6.7% (6/89) in Cyprus [35] and 5% (21/439) in the recent UK study. [7] Figures from Uzbekistan were in line with those reported in other parts of Southern Asia. [10]

It has been suggested that 23% of children with microphthalmia or anophthalmia have chromosomal anomalies and 30% have other major malformations in comparison to a possible 5-6% in this study. In group A, AR inheritance was the norm, but AD mode was suggestive in a third of cases in Group B. [44]

Table 18.8 Prevalence of microphthalmia / anophthalmia conditions.

Region	Prevalence		Incidence
	<19	Total Series	1 in 1000s
Group A			
West Bank	2	1	56
Gaza Strip	4	4	23
OPT	4	2	27
Group B			
West Bank	2	1	51
Gaza Strip	2	0	64
OPT	2	1	55
All MC Cases			
West Bank	5	3	22
Gaza Strip	7	5	15
OPT	5	4	18

18.5 Hereditary Corneal Conditions

This is a small group of conditions with 14 patients from 9 sibships.

Phenotypes
Two entities were found in the series. one is an isolated congenital cornea oedema and the other Peter's like anomalies. They are distributed as follows:

a. Congenital corneal oedema, 4. (Table A18.4)
b. Peter's or suspected Peter's anomaly, 10. These can be divided into:
   i. Uncomplicated Peter's anomaly (without glaucoma).
   ii. Definite Peter's anomaly with CG: 3 cases.
   iii. Suspected Peter's with complicated CG.

Congenital Corneal Oedema (CCO)

Four cases belonged to 2 unrelated sibships, with 2 patients each. Gender comprised 3 females and I male, a ratio of 1:3. In one sibship (CE-02), both patients were mentally retarded and in both AR mode was obvious. Vision in these patients was severely compromised with all patients in the SVI/BL category (Table A18.4)

18.6 Hypopigmentation

Prevalence
Albinism made up 28 of the genetic retina cases out of the total 315 retina cases, thus forming, as a primary pathology, 2.3% (n=8) of the total series in the WB and 6.6% (n=19) in the GS, averaging 4.1% in both regions. These patients belonged to 12 sibships (WB 5, GS 7) and 11 pedigrees. Including other affected members of the sibships who were not examined (WB 18/45 GS 20/60), the total is 38 affected out of the 105 siblings, that is a ratio of 0.33:1. Prevalence based on the numbers of all the affected in the sibships studied per 100,000 populations were at least WB 1.7 (n=19), GS 3.5 (n=21) and OPT 2.4 (n=40). (Table A18.5)

Gender
Male/female ratio in the total hypopigmentation series was 1.25:1 with marked variation between the two Palestinian regions. In the WB the ratio was 0.3:1 (n=8) and in the GS 2.2:1 (n=19).

Clinical Types and Associated Conditions
Three clinical entities are identified in Table A18.5

.

a. Oculo-cutaneous albinism (9 patients).
b. Ocular albinism (9 patients).
c. Others (2 cases).

Visual Morbidity in Hypopigmentation

Twenty (57%) of the patients with hypopigmentation were visually impaired (category '2'), 4 (14%) had SVI (category '3') and a further 4 had good visual acuity (category '1'). The remaining (14%) 4 were in category '6' which were moved to category '2'.

Inheritance of Hypopigmentation Cases

Of the total group of 60 patients, 53 (88%) were hereditary, 7 (12%) were prenatal. Sixty three percent of sibships showed a definite familial occurrence (more than 1 affected sibling in the family). Patients sequence within the sibships in the three groups is shown in Table A18.5.

Discussion

Hypopigmentation, in particular albinism, are common conditions but their true prevalence is not reflected in the series. The majority of these cases have sufficient vision for education in ordinary sighted schools. The true prevalence of the condition per 100,000 people is bound to be higher than 1.7 (n=19) in the WB and 3.5 (n=21) in the GS with the average of 2.4 in both regions of the OPT (n=40) because the majority of these cases attend normal sighted schools. The percentages of albinism is lower than those reported in other Arab countries [37], [45] but compares well to Sri Lanka, [46] possibly for the above reason.

The association with skin lesion and night blindness in the patient from the GS has not been reported previously in the literature. The inheritance was most probably AR in all sibships including the sibship with only males affected (6 affected males out of 12 siblings) especially as there was a distant connection with another sibship who had both affected males and females.

Three syndromatic cases were found in the series. One patient with OCA had night blindness and reduced ERG together with scattered spots of skin fibrosis). The other was an albinoid who had congenital blindness, possibly LCA with large head circumference and delayed milestones. The third patient was albinoid combined with Waanderburg-like features including white forelock.

18.7 Retinal Dystrophies

Retinal dystrophies comprised 250 patients out of the 304 patients with hereditary retinal conditions, thus forming 80% of the total retina series. These patients were spread out over 109

Table 18.9 Retinal dystrophies: numbers, gender and ratio by region

	West Bank				Gaza Strip				Whole Series				WB/GS	
	M	**F**	**Both**	**M:F**	**M**	**F**	**Both**	**M:F**	**M**	**F**	**Both**	**M:F**	**RD**	**Population [a]**
<16	38	45	83	0.8	37	27	64	1.4	77	74	151	1	1.30	1.67
16+	25	36	61	0.7	18	19	37	0.9	43	56	99	0.8	1.65	1.79
Total	63	81	144	0.8	55	46	101	1.2	120	130	250	0.9	1.43	1.76
Pedigrees				80				25				109	3.2:1	
Sibships				98				46				148	2.1:1	
S:P [b]				1.2				1.8				1.4		

[a] Ration of the value in the WB to the GS. [b] S:P ratio: Ratio of sibships to extended genetic families

pedigrees / 148 sibships. (Table 18.9) There are more sibships per pedigree in the GS (ratio 1.8) than in the WB (ratio 1.2:1). (Table 18.9) The various phenotypes are listed in Table A18.11. The prevalence of RD per 100,000 population in the <16 population in the WB, GS and the total region was 18, 24 and 21 respectively and in the total population the prevalence was 13, 17 and 15. (Two cases of atypical syndromatic CRD in association with optic atrophy, one of whom also had Friedreich Ataxia, cardiomyopathy, and vitreous condensation have not been included in the above figures).

Stationary Cone Disorders (Achromatopsia / Rod-monochromatism)

Patients and Prevalence

Achromatopisa (Rod monochromatism) cohort comprised 33 patients who fell within 12 pedigrees and 19 sibships. Table 18.10 shows their distribution between the WB and the GS and demonstrates the preponderance of the condition.

Table 18.10 Patients, sibships and pedigrees in achromatopsia

	WB	GS	Total [a]	WB:GS ratio[i]
Patients	9	23	33[a]	0.4:1
Pedigrees	5	6	12	0.86:1
Sibships	7	11	19	0.64:1

[a] This figures includes one additional case from either regions. [b] The ratio of the general population between the WB and GS is 1.78:1.

The prevalence of achromatopsia per 100,000 including all reported cases was 1 in the WB and 3.6 in the GS averaging 2 in both regions. The figures in the <16 are 1.5, 5.5 and 3.

Gender

Gender differences in achromatopsia are shown in Table 18.10. Male to female ratios are 0.3:1, 0.8:1 in the WB and GS respectively. (Table 18.11)

Visual Acuities in Achromatopsia

Nearly three quarters of the achromatopes were visually impaired (category '2'), 2 were in the NVI category '1' and the remaining 7 had either SVI or were blind. The lowest visual acuity was 2/60 and the mode was 6/60. The mean visual acuity was approximately 6/36. (Table 18.12)

Table 18.12 Visual acuities in achromatopsia

WHO Visual Impairment Categories							
	1	**2**	**'**	**4**	**5**	**7**	**SVI//BL**
No.	2	24	4	3	0	0	7
%	***6***	***73***	***12***	***9***	***0***	***0***	***21***

Associated Conditions

There were no associated findings in any of the achromatopsia cases; however other siblings exhibited the following: extra digit, 1 male; deaf-mutism, 1 female; and mental retardation, 1 female. The remainder were educationally

Table 18.11 Gender and age distribution of achromatopsia by region

	West Bank				Gaza Strip				Total OPT				WB/GS	
	M	**F**	**Both**	**M:F**	**M**	**F**	**Both**	**M:F**	**M**	**F**	**Both**	**M:F**	**Cases**	**Population[a]**
<16	2	5	7	0.4	7	8	15	0.9	10	13	23	0.8	0.47	1.67
16+	0	2	2	-	3	5	8	0.6	3	7	10	0.4	0.25	1.79
Total	2	7	9	0.3	10	13	23	0.8	13	20	33	0.7	0.4	1.76
Pedigrees				5			6				12		0.86:1	
Sibships				7			11				19		0.64:1	
S:P [b]				1.4:1			1.8:1				1.6:1			

[a] Ration of the value in the WB to the GS. [b] S:P ratio: Ratio of sibships to extended families

normal and, if anything, performed above average academically.
(http://Jalili.co/educatt.pdf)

Inheritance

Achromatopsia inheritance was AR in 100% of cases.
sequence and ranks of siblings (Table A18.7)

Progressive Cone and Cone-Rod Dystrophies

Patients and Pedigrees

The total number of patients affected in the progressive types of photoreceptors disorders, cone dystrophies, (CD) and cone-rod dystrophies (CRD) was 70 thus forming 28% of retinal cases. Of these, 27 came from the WB, 42 from the GS. The M:F ratio averaged 1:1. (Table 18.11) These patients who suffered from progressive cone and cone-rod disorders were distributed among 20 pedigrees forming 40 sibships. Of these, 18 sibships (13 pedigrees) were from the WB, 21 sibships from the GS (6 pedigrees) and 1 uncertain.

Prevalence of Cone Disorders

The prevalence of CD and CRD combined per 100,000 population in the WB, GS and both combined was 4, 9, 6 in the <16 and 2, 7, and 4 in all ages respectively. For CRD and CD individually, the figures are 1, 7.7 and 3.5 for the former and 1, 0.73, 0.9 respectively. This represents a WB:GS ratio of 0.6:1.

Age Distribution and Gender

Ages in cone and CRD ranged from 3 months to 53 years, the M:F ratio being close to that of the general population except for the 16+ group. (Table 18.11)

Visual Acuities in Cone Disorders

These varied between visual impairment (category '2'), 28 cases, SVI (category '3'), 11 cases, blindness (category '4'), 29 cases; I case with NLP (category '5); and 1 cannot see (category '7'). (Table 18.14)

Table 18.14 Visual acuities in the clinical subtypes of retinal dystrophies

RD Type	Cohort	WHO VA Category						Total
		1	2	3	4	5	7	
RM	33	***6***	***73***	***12***	***9***	***-***	***-***	***100***
CD	12	***-***	***92***	***0***	***0***	***8***	***-***	***100***
CRD	47	***-***	***30***	***19***	***34***	***2***	***2***	***100***
LCA	94	***-***	***1***	***9***	***64***	***9***	***5***	***100***
RCD	21	***2***	***2***	***2***	***14***	***1***	***-***	***100***

Percentages in ***bold*** **Italic** VA: visual acuity
RD: retinal dystrophy

Table 18.13 Progressive cone dystrophies (cone degeneration and cone-rod dystrophies by gender, age and region

	West Bank				Gaza Strip				Whole Series				W:GS	
	M	F	Both	M:F	M	F	Both	M:F	M	F	Both	M:F	CR	Population [a]
<16	8	9	17	0.9	14	12	26	1.2	22	22	44	1	0.65	1.67
16+	3	7	10	0.4	10	6	16	1.7	13	13	26	1	0.63	1.79
Total	11	16	27	0.7	24	18	42	1.3	35	35	70	1	0.64	1.76
Pedigrees			13				6				20			
Sibships			18				21				40			
S:P [b]			1.4				3.5				2		2.2:1	0.85:1

[a] Ratio of the value in the WB to the GS. [b] S:P ratio: Ratio of sibships to extended genetic families

Penotypes Cone Disorders

Three progressive types of cone disorders were identified including cone degenerations without electrophysiological evidence of rod involvement, cone-rod dystrophies and congenital amaurosis of the cone and rods. Each of these categories is further subdivided into syndromatic and non-syndromatic versions. This is in addition to the stationary form, achromatopsia. (Tables A18.7)

Inheritance of Cone Disorders

Among the 70 patients, 67 (96%) were inherited in an AR manner. In 2 (3%) an AD mode was suspected and in 1 (1%) the mode was uncertain.

Clinical Aspects Cone Disorders

These are highlighted in Table A18.7 which also show patients' sequence within their sibships and the ratio of affected to total number of the sibship together with the mode of inheritance..

Rod-Cone Dystrophies

Prevalence of RCD

The prevalence of RCD per 100,000 populations was 10.5, 3.6 and 8.2 in WB, GS and the total OPT. (Table A18.16)

Visual Acuities

These ranged between NVI (category '1') to NLP in the following proportions. (Tables 18.17)

Clinical Types of RCD

According to their time of onset, they can be divided into 2 subcategories; congenital (infancy) onset and childhood onset. The distribution, sex ratios and pedigrees/sibships in the each subgroup and both combined are shown in Tables 18.6, A18.8.

Visual Acuities

These ranged between NVI (category '1') to NLP in the following proportions. (Table 18.14)

Inheritance

All cases were inherited in AR mode.

Birth Rank and Sequence of Patients

Table A18.9 lists the rank and sequence of RC patients, and the ratio of affected to the total number of the sibships.

Table 18.15 Rod and rod-cone dystrophies by age, gender and region

	West Bank				Gaza Strip				Whole Series				WB/GS	
	M	F	Both	M:F	M	F	Both	M:F	M	F	Both	M:F	RC	Population [a]
<16	21	26	47	0.8	8	6	14	1.3	30	33	63	0.9	3.4	1.67:1
16+	16	24	40	0.7	4	4	8	1	20	29	49	0.7	5.0	1.79:1
Total	37	50	87	0.7	12	10	22	1.2	50	62	112	0.8	4	1.76:1
Pedigrees				48			9				60			3.3:1
Sibships				57			10				69			5.7:1
S'ship/Ped. ratio[b]				1.2			1.11				1.15			

[a] Ratio of the value in the WB to the GS. [b] S:P ratio: Ratio of sibships to extended genetic families

CD: Cone-rods. CRD: Cone-rod dystrophies.
CACR: Congenital amaurosis of the cone-rod. (61)
RM: Rod-monochromatism (achromatopsia)
LCA: Leber congenital amaurosis
RC: Childhood onset rod-cone dystrophies including one case of stationary night blindness

Table 18.17 WHO visual acuities in 109 cases with RCD in %

VA	Congenital [a]	Childhood [b]	**Total [c]**
NVI '1'	-	*9.5*	*1.8*
'2' VI	*1.1*	*9.5*	*2.7*
SVI' 3'	*10.2*	*9.5*	*9.2*
BL '3' '4'	*72*	*66.6*	*72*
NLP '5'	*10.2*	*4.7*	*9.2*
'6' [d]	*0*	*0*	*0*
'7' [e]	*5*	*0*	*9.2*
Total	*100*	*100*	*100*
SVI/BL	*99*	*81*	*95.4*

[a] Congenital onset RCD
[b] Childhood onset RDC
[c] Total WB & GS may contain other cases of uncertain region
[d] Category '6' Can See
[e] Category '7' Cannot See

Table 18.16 WB:GS ratios of <16 cases, genetic families and M:F in RD.

RD Type	Cohort	WB: GS Ratios [a]			M:F Ratios		
		<16	Sibship	Pedigee [b]	WB	GS	OPT [c]
Cone and Cone Rod disorders							
CD	12	1	4	5	2	2	2
CRD	47	0.3	0.35	1	0.5	1.3	1
CACR	11	WB only			1	-	1
RM	33	0.47	0.64	0.86	0.4	0.6	0.4
Rod Cone disorders							
LCA	88	3.6	5.7	5.3	0.85	1.4	0.9
RC	21	1.5	6.5	6.5	0.8	1.4	1
Total RD							
	250	1.3	2	3.2	0.8	1.4	1

Disscussion

This study is marked by a heavy emphasis on retinal dystrophies which stemmed from being the largest and most interesting group of disorders encountered in the survey in the presence of some fascinating arrays of new findings in large pedigrees. [47] Minute clinical details were studied and analysed. The study shed light on several new conditions and associations. Among these were cone-rod dystrophy with amelogenesis imperfecta where there were 34 cases from 3 pedigrees with the youngest ever reported case of bull's eye. [48], [49] [50] [51] [52] [53] These data have been left out of this study for future reporting.

There was a female preponderance in the WB that is possibly caused by the predominantly female residential schools in that region which could have skewed the results, although this is partly balanced by the boys only school, Al-Ala'iyya. However, this may well also reflect a true preponderance of blindness in girls in this region. This is especially so as the gender disparity persists in the patients recruited from the outpatients (0.7:1) in all the age groups and is absent in two of the conditions; namely CD and CACR, [54] where the ratio compares to that of the general population. There are also variations in female preponderance within the conditions. In RM, the number of females is nearly double that of males and is found across the board in both regions in patients, sibships and pedigrees.

In line with the recognized clinical characteristics of retinal dystrophies, [47], [55], [56], [57], [58] [59] cone disorders have better visual, acuities than rod disorders, with the widest spectrum of visual acuities being exhibited by CRD. Rod monochromatism (achromatopsia) scores the best of acuities with the worst being in the congenital form of blindness, LCA. (Table 18.14)

Prevalence Subtypes

It has long been recognised that RD forms the largest group of conditions attributable to childhood blindness and constitutes the bulk of

conditions in countries where infections and malnutrition have been eliminated. [60] In the Middle East, a similar preponderance has been reported including Jordan. [10], [14] [35], [36], [37], [1] In this study, RD are common in both Palestinian regions. However, the higher number of patients affected in the GS per sibship has given rise to a preponderance of patients with RD in the GS, well depicted in the WB:GS ratio of 1.43:1 (<16, 1.3:1; 16+, 1.65:1). This is despite the significantly higher numbers of pedigrees and sibships in the WB (WB:GS pedigrees ratio 3.2:1, sibships 2:1).

The prevalence, based on the total number of patients encountered per 100,000 were at least 13 in the WB, 17 in the GS and 15 in both regions combined. A more meaningful figure is that of the <16 in the GS as the UNRWA blind school is the only blind institute in the Strip and the social worker knew all cases not enrolled in the school and those on the waiting list for admission when they reach school age.

Worldwide data, in particular in the Middle East, on the proportions and prevalence of the various subtypes of RD are lacking. [47], [55], [56], [57] [58], [59] In this study, regional variations in the prevalence of various types of retinal dystrophies are found which show that CRD and RM are predominantly GS conditions, but RC disorders and cone-rod congenital amaurosis (CACR) are WB conditions. (Table 18.15)

The preponderance of cone disorders including achromatopsia in the GS, is found in a number of patients and sibships but not in pedigrees. This is the result of the presence of one large extended family with syndromatic CRD with multiple sibships and 30 affected patients. There are also higher numbers of female patients in the 16+ cohort in the WB.

The number of pedigrees in the WB is 2-fold that of the GS, that is above the population ratio between the two regions (1.78:1). These figures are reversed when it comes to sibships ratio (0.75:1) and patients' ratio 0.54:1 (<16= 0.46:1, 16+= 0.67:1). This preponderance is also seen in the stationary type (RM). In contrast, RCD are preponderant in the WB at 4:1 (<16= 3.3:1) in both patients and pedigrees. (Table 18.15)

Molecular Biology

This work, with its detailed genealogy, also presented valuable material for the molecular biologist and has resulted in several new findings including the detection of increased band sharing in DNA fingerprints in inbred populations and more recently a new locus was found on chromosome 2q11 at which recessive amelogenesis imperfecta and CRD were found to cosegregate [51], [61] More recently the genetic mutation has been isolated. [50], [62]

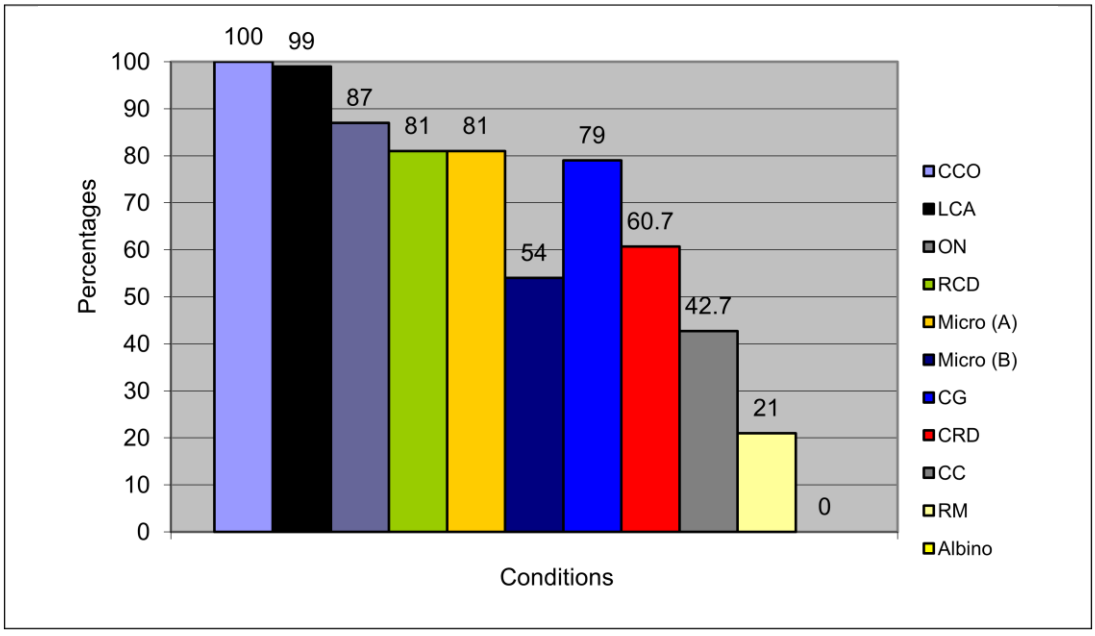
18.8 Vitreo-Retinopathies

This is an heterogeneous group of conditions where vitreoretinal pathology is the hallmark of the condition. Each pedigree has its characteristic features with marked intra sibship variability in the extended pedigree. The group comprised 12 patients belonging to 7 sibships, part of 6 pedigrees. These are mainly concentrated in the WB with 10 of the patients coming from there. Only one pedigree with 1 sibship originates from the GS. Five of the patients belonged to a single pedigree with 2 sibships. There is also male predominance with 9 out of the 12 patients being males. Ten of the patients were <16.

18.9 SVI/BL in Common Ocular Conditions

Figure 18.3 depicts the severity of visual loss in the common conditions encountered in the blind school survey by condition. In descending order of the severity of visual impairment are: congenital corneal oedema, LCA, optic nerve disorders, microphthalmia, congenital glaucoma, cone-rod dystrophies, congenital cataract, achromatopsia and albinism.

Figure 18.3 Proportion of SVI/BL in common clinical conditions



18.10 Associated Conditions

This study demonstrated the wide range of associations in the various genetic conditions and their variability. Some sort of association existed in 32% of the series (38% including medical problems). The proportion of additional morbidity, hearing, or mental deficiency in the visually impaired in the UK ranged between one-third and one-half of the total cohorts. [63], [64] Mental retardation is the most important and commonly defined association reported in conjunction with CB in many studies including the UK, the Nordic countries and Germany. [7], [63], [64], [65] It was present in 27% of the UK study [7] and 60% in the Nordic countries in those with the severest visual impairment; many of these children had multiple impairments due to brain injury such as cerebral palsy and epilepsy. [63], [64] In these countries, mental retardation is explained by periventricular keratomalacia in the majority of cases. [65] In this study, mental retardation was present in 7.6% of the total cohorts and found in a wide range of disorders showing certain patterns that are worth noting.

It was manifested predominantly in the two commonest groups of disorders namely; congenital cataract and rod-cone dystrophies. In CC, mental retardation was found in 10% of the total series but the figure rises considerably to 71% and 60% when CC is associated with retinal dystrophies and CG respectively; in other words, in syndromatic conditions. Rod disorders on the other hand were stigmatised by the frequency of associations and subnormal mentation. Submentation in this group reached as high as 12% of the total RC series with some 25% of the childhood onset cases having some degree of mental subnormality.

Although CG cohorts showed a wide spectrum of associations in 30% of the patients (20/68), mental retardation did not present as a part of the conditions; the mental deficiency in the two CG cases was acquired from a post systemic infection in one case and was part of an AR inherited mental retardation coexisting with CG; the sibling's sister had the same pattern of mental retardation but without having CG. The same is applicable on the microphthalmia series where mental retardation only existed in 1 patient of 3 suffering from anophthalmia. It is interesting to

note that another 3 siblings of this patient who also had anophthalmia, died from different causes. The rest of the retinal dystrophies, which were very rich in their systemic associations did not show any significant association with mental abnormalities; CDs escaped any association with submentation, as did patients with CRD. The latter, apart from the pedigrees with BBS, encompassed one pedigree only with 2 siblings out of 3 having subnormal mentation. In fact, CRD patients, especially CRDAI, were characterised not only by normal mentation but also with above average school performance (Table A18.3)

In summary, RCDs and CC, especially syndromatic cases, have the highest proportion of mental impairment, especially when there are several associations, and in syndromatic cases. This is in contrast to the European data where mental deficiency was associated with brain injury as a consequence of prematurity, frequently with multiple impairments, such as cerebral palsy and epilepsy. [63], [64] Epilepsy was present in 5 cases only in the series, 3 of whom are RCDs.

Table 18.18 Prevalence of common blinding conditions in the study

Hereditary Condition	WB	GS	All OPT
	Per 100,000 population		
Hereditary conditions	32	50	39
Congenital cataract	6	10	8
<16 years	10.5	12	13
Congenital glaucoma	3.6	6.4	5
Microphthalmos	1	3.8	2
Microphthalmos	3.5	5.8	4.4
Albinism	1.6	3.3	2.2
High myopia	1	3.8	2
Retinal dystrophies All ages	13	17	15
Under 16	18	23	21
Cone degeneration	1	0.73	0.9
Cone-rod dystrophies	1	7.7	3.5
All progressive cone disorders	3.2	8.4	5
Congenital rod-cones	6.8	4	7.1
Rod-cone disorders	10.5	3.6	8.2
Rod monochromatism	1	4	2.2

Prevalence of Common Conditions

The prevalence is worked out by combining the numbers of the patients registered and examined in the study with other affected members with the same condition extracted from the history and pedigree charts. The results are enumerated in Table 18.18.

Demonstrable differences and similarities exist between the WB and GS in the M:F ratio in several conditions. Tables A18.10, A18.11 depict the conditions according to their male and female preponderance and gender ratios in both regions. The general trend is a male preponderance in the GS and female preponderance in the WB.

18.12 Other Aspects of the Survey

Clinical Details of Retinal Dystrophies

The comprehensive review of the clinical findings in retinal dystrophies, including their presentations, symptoms and clinical features combined with electrophysiological and electrodiagnostic findings were compiled during the study. This information has been removed from this study and will be published separately. [48], [49], [50], [51], [52], [53], [54], [61], [66]. [67]

Dental Associations

In addition to the ophthalmic screening, a comprehensive dental screening shed light on the dental problems and helped in establishing the diagnosis and pattern of the dental associations in this group. The discovery of an association between CRD and amelogenesis imperfecta, a rare condition of enamel defect, has already been addressed elsewhere. [48], [49], [50], [61], [62]

Red Filters Trials in Photophobia

The efficacy of red transmittance 550 nm as compared to ordinary dark or non-tinted glasses was assessed in 24 diagnosed cases of these conditions (cone-rod dystrophy 14, rod-cone dystrophy 2, rod-monochromatism 5 and central areolar dystrophy 3). Independent observers evaluated improvements in; (a) visual acuity on Sheridan Gardiner testing in normal daylight illumination; (b) photophobia as assessed by reduction in blinking and orbicularis spasms; and (c) subjective comfort. Twelve out of 14 (86%) cases of cone-rod dystrophy and 3 out of 5 (60%) of patients with rod monochromatism demonstrated marked improvement on all three parameters with red as compared to dark glasses. Only 2 cases (14%) of cone-rod dystrophy preferred dark tinted to red glasses. There was no improvement in the three cases of central areolar choroidal dystrophy, or in the two cases of rod-cone dystrophy. In spite of the small sample size, it seems that patients with cone-rod dystrophy, especially in its early stages, would benefit from red glasses which help by cutting down the short and middle wave length radiation. Red glasses attenuate the ambient illumination that would otherwise saturate the patient's rods, and thus prevent them from seeing in normal daylight illumination.
(http://jalili.co/covi/redfilter.pdf)

Educational Performance

School marks as an indication of intelligence were collected where available. This was done despite the limited sample and the possible bias that could have resulted from the selection procedure whereby results made available for the study skewed towards the better performers. This by itself worked as an indicator for the IQ levels in these conditions, and in particular congenital RC dystrophies (LCA). (Table A18.9) list the available school grades of 83 pupils (44 from the WB and 38 from the GS) and demonstrates a pattern where patients with certain conditions achieve higher academically and vice versa.

The sample shows a whole range of educational abilities with the very bright and high performers, such as those patients with albinism and the syndromatic CRD, in particular the type associated with AI. This also includes the 2 cases with CACR, one of whom is musically gifted. The rest of the CACR series are educationally subnormal. This is in contrast to the rod-cone types of retinal dystrophies, which score worse; the observations are supported by the clinical observations whereby this condition harbours a very high predominance of mental retardation.

Congenital glaucoma follows cone conditions in terms of better educational performance. Congenital cataract cases are a mix of good and poor performers. It is interesting to note that all the CC associated with small eyes (8/20) performed better than the rest of the CC sample. Congenital cataract patients show a wider range of IQs but it is worth noting that all patients with small eyes (n=8/20) are educationally better than the rest of the sample.

The optic nerve group showed a disparity between the two syndromatic and acquired cases and the two post inflammatory/meningitis cases.

In the small eyes group, at the top came a male patient with rudimentary globe the second was the eldest of two sibs whose brother is educationally subnormal as seen from the marks. Both siblings suffer from a syndromatic type of

Table 18.19 Comparison of school performance by gender

Gender	Nos.	Mean Total	Arabic/ English	Science / Maths	Arts/ Craft	History	Sports
Males	43	66	66	66	75	71	76
Females	39	65	68	68	73	67	78

microphthalmia associated with high myopia and cataract. The worst performer was a girl with anophthalmia.

No gender differences in performances existed except marginally in humanities/history. (Table 18.19) To the best of my knowledge no such aspect exists in the literature for comparison. (http://jalili.co/covi/educatt.pdf)

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Chapter 18 Appendices

Appendix 1

Table A18.1 Patients' sequence, ratios, and mode of inheritance in congenital cataract

Patient No.	Sequence *	Ratio**	Cons. †	Mode Φ
West Bank				
CC-02-1-1 to 5	**MFM**f**MM**	5:6	NR	AR
CC-02-2-1	**F**[a] m**F**fmfm	2:7	C1A	AR
CC-02-3-1	**M**[a] fm-m-m-m-	1:2	NR	AR
CC-03-1-1	cmfcc**F**afp	1:4	R-SF	IUD?
CC-04-2-1& 2	a**F**m-m**M**f-mf	2:8	C1D	AR
CC-04-1	**M**fff**M**[b] ff	2:7	R-SF	AR
CC-05-1-1	f-mf-f-m-m-m-mff**F**	1:11	SV	AD
CC-05-2-1 to 6	mf-m-**FMMF**c**M**cfm**M**	6:11	NR	AD
CC-06-1-1	fmm**F**mfmfm	1:9	SV	IUI
CC-08-1-1	fccmfmm**F**mm	1:8	C2	?AR
CC-10-1-1	n/a	1:4	C1	AR
CC-12-1-2	mc**F**cffcfmm**M**m	2:9	C1A	AR
CC-13-1-1	mfmm-{m-m-}mcc**F**ffm	1:8	C1hA	IU?
CC-14-1-1	f**F**mfmfmfc	1:8	C1A	SX
CC-15-1-1	mm-f**M**mf-fmfm	1:8	C1hA	SX
CC-16-1-1 to 3	**F**f**M**ffm**M**	3:7	C1A	AR
CC-18-1-1	mcmmfffmm**F**	1:9	R-SF	IUI
CC-19-1-1	mmmm**M**cfc	1:6	NR	UD
CC-20-1-1 to 3	f-f-f-f-ff-f**MM**f-c**F**mm	3:7	C1A	AR
CC-21-1-1	{f-}[c] mffmf**M**c{f-}fcf-[d] m	1:11	C2A	IUI
CC-22-1-1 & 2	f[m-][e] **F**f**MF**-[f] f**F**f	4:8	R-SF	AR
CC-23-1-1	f-ff-f[m][g] **M**mm-mfcm{f} [h]	1:9	C1B	IUI
CC-62-1-1-my	ffff**M**[i]	1:7	UA	n/a
Gaza Strip				
CC-01-1-1 to 4	**F**f**M**mmm**MM**mffc	4:11	C1A	AR
CC-01-2-1 to 4	f-**MF**m**F**m**M**cmfm**M**[j]	5:11	C1A	AR
CC-01-3-1 & 2	**MF**	2:2	C1A	AR

CC-07-1-1 to 5	f-[k]**MMF**f-[k] m**M**m**M**m	5:10	C1A	AR
CC-11-1-2	mfc**MMc**	2:4	C1A	SX
CC-11-2-3	**M**f-f-**M**f-f-f-m**M**mc**F**	4:11	C1C	AR
CC-17-1-1	ffm**F**mfmm	1:8	C1C	IUI
CC-24-1-1, 2	Mf**MM**f-[L]	2:5	SV	AR
CC-25-1-1, 2	mmf-ff**F**msmc**F**[p]	2:9	C1A	AR
CC-26-1-1, 2	**FM**mmff	2:6	C3	AR
CC-27-1-1	**M**{f}cmfmmfff[m]	1:9	SV	SX
CC-28-1-1	m**MMF**	3:4	C1B	AR rAD[v]
CC-28-2-1	fmm**M**[p] fmff	1:8	NR	AR rAD?
CC-30-1-1	**F**[n] ffmmm	1:7	R-SF	AR
CC-30-2-1 to 3	m**F-FMMF**mf	4:7	C1hA	AR
CC-30-3-1 & 2	mf**F**ff**M**f	2:7	C2A	AR
CC-30-4-1	cff**M**	1:3	C2A	AR
CC-45-1-1& 2	fffmf**FM**	2:7	NR	AD
CC-47-1-1	mmf(**F**f-)|fmfmf [o]	1:10	C2	? IUI
CC-28-1-1 & 2	m**MMF**	3:4	C1B	AR rAD?
CC-48-1-1	UUUUUUUU**F**[q]	1:9	UA	IUI
CC-29-1-1	**MF**???[r]	2:?	n/a	AR
CC-46-1-1	ff{m}f({**M**[s]})mf{f}[t]	1:8	C2hA	IUI
SY-03-1-1	m-[d] smmsmffmfm**F**	1:10	NR	CH

* Refer to codes used in sibships notation section 6.3 for the key to symbols used. ** Affected to total living siblings or living and dead siblings if affected with the same condition. † Cons.: consanguinity, refer to section 6.4 for key. Φ Mode of inheritance.[a] Parents of 02-1. [b] Case 04-2's parent [c] infancy death, spina bifida, [d] post pyrexia mortality. [e] [m-] premature. [f] died age 5 yrs. [g] proteinurea. [h] squint. [i] not in sequence. [j] died 6m of small pox [k] died age 13 days and 4 weeks from gastroenteritis. [L] mother with CC, non-consang. [m] hemiplegics, grandmother has MC, a 1st cousin with harelip. [n] mother of CC-30-2. [o] died in labour. [p] father of 28-1. [q] all U are normal, father has CC. [r] the rest n/a. [s,t] ONH coloboma: [s] bilateral, [t] unilateral CC in in the same sibship [v] rAD: resembles AD inheritance. SX: Simplex: isolated or sporadic. UA: data unavailable.

Table A18.2 Congenital glaucoma: associated finding and patients' sequence

Case No.	Gender/age	Siblings *	Ratio	Clinical comments
1) Above average intelligence				
CG-10-1-1	F 23 WB	m**F**mmmf**M**ff	2:9	CC, ? Rdet, Lt. preshesis
CG-14-1-1	M 6 GS	c**M**ff	1:3	? Peter's, staphyloma, corneal graft
CG-31-1-1	M 21 WB	{f-}**M**f**M**f[m-s]ff~f **	2:9	PCG
CG-26-1-1&3	F 15, M 23 WB	**M**cmff**F**c**F**f**M**	4:8	PCG: (1) gross, Rdet. (3) Rt mild, CC, IDDM
CG-04-1,2,3	F 11, 16 GS	f-ffm-ff**FF**ff**F**cm	3:12	PCG:(2) high myopia
2) Deafness				
CG-23-1-2	M 31 WB	**M**Mccffmc**F**f-**f	2:7	PCG, Rt phthisis, Lt. prosthesis, 70% deaf,
CG-19-1-1	F 39 WB	**F**mfffmm-**fmfm	1:10	? PCG: cystic globe, Rt phthisis, deaf.
3) Syndromatic				
(A) 1. hypoplastic maxilla. 2. Abnormal dentition upper jaw. 3. Long fingers with short nails. 4. Allergic rhinitis				
CG-15-1-1	F 11 WB	n/a	n/a	?PCG: Rt diffuse cor. op., Lt clear cornea
(B) 1. trichomegaly. 2. nail abnormality.				
CG-26-1-4	M 5 WB	**M**cmff**F**c**F**f**M**	4:8	Dense cor. op., subluxated CC, ?LCA
4) Atopy **(a) Allergic rhinitis**				
CG-07-1-1&2	F 3 GS F 10 GS	m**F**fcm**F**	2:5	? PCG (1) ?Peter's (2) photophobic, clear cornea, dense cataract
CG-27-1-1	F 8 WB	ffmm**F**f**F**	2:7	PCG: central cor. op.,
(b) Food allergy				
CG-06-1-2	F 8 GS	**F**m**F**fmcf	2:6	? PCG, ?Peter's anomaly
(c) Drug allergy (see CG-26-1-3 above)				
5) Paraplegia				
CG-23-1-1	F 18 WB	m**M**ccffmc**F**f-***f	2:7	PCG, phthisis
6) Significant personality and mood disorder				
CG-09-1-2	M 16 GS	mff**M**f**F**-ff**M**Mffcc	4:12	PCG: Rt. atrophy.CC
CG-06-1-1	F 11GS	**F**m**F**fmcf	2:6	?PCG, ?Peter's anomaly.
CG-04-1-1	F 17 GS	f-ffm-ff**F**f**F**cm	3:12	PCG
7) Subnormal mentation				
CG-05-1-1	M 16 GS	ffm**M**mmf-fmmm	1:11	Burnt out CG, phthisis, Lt. leucoma adherence (acquired)
CG-21-1-1	M 9 WB	cmc{f} **M**[a] fm	1:5	PCG: mentally retarded, sister also retarded
[a] Mental retardation noted post pyrexial illness age 11 month				
8) Buphthalmos cases without associated findings				
CG-01-1-1	M 13 GS	n/a	-	CG
CG-02-1-1	F 10 WB	n/a	-	CG
CG-03-1-1	M 2 WB	f**FM**	2:3	PCG

Table A18.2 Congenital glaucoma: associated finding and patients' sequence

Case No.	Gender/age	Siblings *	Ratio	Clinical comments
CG-03-2-1	M 28 WB	fm**M**) fmf	1:7	PCG
CG-03-3-1	F 20 WB	m**F**-mfm{ff}f	2:8	PCG
CG-08-1-1,2	M 16 WB M 19 WB	Mmm**MM**	2:5	PCG: (1) cataract (2) atrophia bulbae
CG-09-1-1	M 17 GS	mff**M**f**F**-ff**M**ffcc	4:12	?PCG: Rt. cor. op., Lt. phthisis
CG-10-1-2	M 13 WB	m**F**mmmf**M**ff	2:9	Bilateral phthisis bulbae
CG-12-1-1	M 14 WB	ff**M**mfmf-f	1:8	PCG:Rt. buph, Lt. phthisis
CG-13-1-1	M 5 GS	f**M**p	1:2	PCG: central cor. op., (scar)
CG-16-1-1	F 9 WB	smfm[a]fcm[a]mmf **F**m [b]	1:11	ACS, Reiger. Rt phthisis
[a] squint. [b] delayed speech.				
CG-17-1-1	F 36 GS	f-m[a] f-f-m**F**[m][b] mmm[c]**M**[d] **M**	3:10	? PCG: Rt. prosthesis, Lt. cor. op.
[a] glaucoma age 44yr. [b] Mental retadation, [c] Unilateral Road traffic accident. [d] glaucoma age 12 yrs.				
CG-18-1-1	M 22 OPT	fmff**M**m**M**f	2:8	PCG, CC
CG-22-1-1, 2	F 3 WB M 9 WB	**M**m**F**	2:3	PCG: (1) buphthalmos (2) CC
CG-24-1-1	F 12 WB	mf**F**m	1:4	PCG: Rt phthisis, Lt high iop. ChR scars
CG-25-1-1	M 3 WB	c**M**M-	2:2	?ASD / Peter's anomaly (atypical), ?PCG cornea decompensation
CG-26-1-2	F 13 WB	**M**cmff**F**c**F**f**M**	4:8	PCG: gross buphthalmos
CG-27-1-2	F 4 WB	ffmm**F**f**F**	2:7	?PCG, ?CCO: Rt. corneal haze, Lt. cor. op.
CG-28-1-1	M 2 WB	**M**	1:1	PCG
CG-29-1-1, 2 & 3	F 14 GS, M 17 GS M 31 GS	m**M**-mmmmm**M**f**M** **F**	4:10	PCG (3) Rt. phthisis
CG-29-2-1	F 9 GS	**F**	1:1	PCG
CG-31-1-2	M 24 WB	{f-}**M**f**MF**[m-f-]ff~f	2:9	PCG
CG-32-2-1 & 2	F 17 WB F 30 GS	**M**[b]-f-[c]**F**mmmf **F**cf m cc	3:9	(2) Reiger, Rt. presthesis
[a] Father of of 32-1. [b] died from RTA. [c] died age 3 months.				
CG-34-1-1	M 9 OT	n/a	-	PCG
CG-35-1-1	F 3 OT	n/a	-	PCG, myopia
CG-37-1-1	M 3 OT	n/a	-	PCG
CG-38-1-1	M 4 OT	n/a	-	PCG: L>R
CG-36-1-1	M 5 OT	n/a		CC
CG-40-1-1	M 9 GS	n/a		PCG
CG-41-1-1	M 3 GS	n/a		PCG: buphthalmos
CG-42-1-1	M 3 GS	n/a		PCG: buphthalmos
CG-43-1-1	M 3 OT	n/a		PCG
CG-44-1-1	M 1 GS	n/a		PCG
CG-45-1-1	M 4 WB	n/a		?PCG
CG-46-1-1	M 3 GS	An affected sister	-	Large cθ , high iop

Table A18.2 Congenital glaucoma: associated finding and patients' sequence

Case No.	Gender/age	Siblings *	Ratio	Clinical comments
CG-47-1-1	M 5 GS	n/a	-	cd 14/12.5
CG-32-1[a]	M 60 WE	fff**M** (the Father)	1:4	ACS
CG-30-1-1, 2	M 22 GS F 24	f-[**] mf**FM**	2:5	ACS/Peter's anomaly: essential iris atrophy
AS-02-1-1	M 8 GS	ff-f-mff**M**ff-msf	1:7	Peter's anomaly + CC. global weakness
ACQ-56-1-1	M 16 WE	**M**mmffmmmccm	1:8	Phthisis, cor. op., prosthesis (Trauma)

* Refer to codes used in sibships notation section 6.3 for the key to symbols used.
** Affected to total living siblings or living and dead siblings if affected with the same condition. *** Infancy death. (1), (2) indicate patient number from the first column when more than one person is involved. ACS: anterior cleavage syndrome. eye;. CC: congenital cataract. CCO: congenital corneal oedema. cθ: corneal diameter. ChR: chorioretinal. Cor. Op.: corneal opacity; decomp: decompensation. Gl: glaucoma. Lt.: left. PCG: primary congenital glaucoma.;Rdet: retinal detachment. Rt.: right eye. RTA: road traffic accident.

Table A18.3 Patients with small eyes: sequence, ratio and age (microphthalmia and anophthalmia as a primary pathology causing blindness

Reference No.	Sequence *	Ratio**	Age
Anophthalmia			
MC-02-01-1	[c]cc{s**M**[vi]}cc(**F**)mccmcfc**M**-**F**-cmm**M**-f	5:8	38
MC-11-01-1	ffm**F**m-m**M**-fcc [g]	2:8	11
MC-05-01-1 to 3	**F** [*]ff**M**fm**F**f	3:7	12-26
Microphthalmia			
CB-04-01-1 [a]	mm-**F**m**M**	2:5	35
MC-01-01-1	m-m-f-f-f**FM** [b]	2:7	20
MC-03-01-1	ffm**M**cff	1:6	5
MC-04-01-1,2,3	[d] m**MF**mfc**M**cmccp	3:7	6-15
MC-05-02-1	f**M**	1:2	8
MC-05-03-1, 2	**FF**mm	2:4	3
MC-05-04-1 to 5	**M**f**M**[i] m**FM**[ii]**F**mmm-	5:10	18-33
MC-05-05-1	fff**F**	1:4	3
MC-06-01-1	mf-**F**-mmffm**M** [e]	2:9	17
MC-07-01-1	fmm[mm][f] ffmff**F**f	1:12	8
MC-09-01-1	**Mf**m	1:3	5
MC-09-02-1	fmfmm**M**mfmfm	1:11	13
MC-10-01-1,2	ccccc**MF**mff	2:5	5, 6
MC-12-01-1, 2	fm**MF**cf	2:5	7, 9
MC-13-01-1	mm**F**ff-ccc	1:5	7
MC-15-01-1	fmc**M**[iv]ff	1:5	8
MC-16-01-1	f**M**fffc [h]	1:6	15
MY-04-01-2	m-ccm-f**M**cccmcmfs**F**[iii]mfcc	2:8	20
ON-02-01-1	m[m][j] m**F**[vii]	1:4	3
ASD-01-01-1 to 4	**MM**-fm-**F**-**F**c**F**-**MM**fm**F**	8:12	8-19
ASD-01-02	m**M**[k]m**M**mf	2:6	45
	52:118	1:2	

* Refer to codes used in sibships notation section 6.3 for the key to symbols used.
** Affected to total living siblings or living and dead siblings if affected with the same condition. [a] First wife: 4:4 sibs, mentally retarded and mute. [b all] died ages 1yr, 2 yr, 2 m, 2 m. [c] All died in infancy from gastroenteritis, 3 yrs cause? 1 yr chest Infection. [d] father has mild MC (10.25 mm, VA 6/6). [e] all died age 6m of pyrexia, F- died 6m from measles. [f] [identical twins]. [g] died of cong. heart disease ? Patent ductus arteriosis. [h] from 2nd marriage. [j] [m] deaf-mute. [k] ASD-01-1 father.

Table A18.4 Congenital corneal oedema cases from two unrelated sibships

Ref. No.	Sequence*	Ratio	Ages	VA
CE-01-1, 2	fm**FM**ffmf	2:8	21	3, 7
CE-02-1, 2	mf,(f-)mmffmfmcm**FM**[a]	2:12	16,17	4

Table A18.5 Hypopigmentations

Reference No.		Sequence *	Ratio	Clinical Aspects
Oculo-cutaneous Albinism				
ALB-02-1	WB	**F**-[a] **FM**f**F**	4:5	[a] failure to thrive died age 1 yr
ALB-06-1		**F**ffff**FF**m**M**f	5:11	
ALB-08-1		m**F**m-[b] m**F**f-fffcfmcc	2:11	[b] accidental death
ALB-03-1[c]	GS	**M**ffff**F**ff**MF**mca	3:11	[c] ? related to 04-1
ALB-04-1		ff**M**-ffff-**M**-**MMMM** [d]	6:12	[d] all males ?related to 03-1
ALB-07-1		m-mmfm**M**	1:6	Night blindness and skin lesions
ALB-09-1		**MF**ffmmmcm	2:8	
29:7,7 average 1:3				
Ocular Albinism				
ALB-01-1	GS	F**F**f**M**fmf**F**f**MF**c	5:11	tyrosinase +ve.
ALB-05-1		m**M**mf-f-cm-m**M**mm	2:10	ocular - partial with fair hair [a]
Albinoids				
SY-16-1	WB	**M**{**M**}mfm	2:5	albinoid fundus, blue iridis, Waanderburg features (+white forelock).
SY-23-1	GS	F**M**c	1:2	cong. blindness ?LA, large head circumference ?hydrocephaly, delayed milestones
10:27, average 1:2.7				

* Refer to codes used in sibships notation section 6.3 for the key to symbols used.
** Affected to total living siblings or living and dead siblings if affected with the same condition.
[a] Absent in the rest.

Table A18.6 Sequence and ranks of patients in Achromatopsia

Reference No.	Birth Sequence*	Ratio *
West Bank		
RM-03-1-1 & 2	fc**F**cc**F**ffm**F**f	3:9
RM-06-1-1	mf-[a] fmam**F**fmm	1:8
RM-06-2-1,2	n/a	2:?
RM-06-3-1	mm[b]m**F**m	1:5
RM-08-1-1	ff[f][c] **F**cmff	1:7
RM-10-1-1	mfff**F**cm{m}[d] f	1:6
RM-12-1-1,2	mfm**FM**	2:5
WB subtotal (excluding 06) 11: > 40 = 1:4.4		
Gaza Strip		
RM-01-1& 2	**M**m-ff-fmm**F**cfm	2:8
RM-02-1-1 to 4	mf**M**f**F**fffmm**MF**	4:12
RM-02-2-1	mmf**F**	1:4
RM-02-3-1	**F**afam[am]mf[am]fc c	1:6
RM-02-4-1	ff-**F**fff-mmm-	1:6
RM-02-5-1	ffmf**F**f	1:6
RM-04-1-1 to 5	**M**f-fmf-f-**MF**m-**MF**f**M**	6:9
RM-05-1-1	**F**{f}[e][f][f]**F**f	2:5
RM-07-1-1	n/a	1:?
RM-07-2-1, 2	mfff-f**MM**ac	2:6
RM-09-1-1	fm**F**m[f][g] m-f	1:6
GS subtotal (excluding 07) 22:> 68 = 1:3		
RM-11-1-1	ff**M**m	1:4

Total (excluding 06 & 07)34:> 112 = 1:3.5

Table A18.7 Cone-rod dystrophies

Patient No.	Sequence/Rank*	Ratio**	Age	Remarks
(A) Cone Dystrophies				
(1) Syndromatic: Hypoplastic maxilla, stuttering speech (West Bank)				
CD-05-01-1 to 4	**M** * fF**F**m**MM**	4:6	17 to 4	* unilat. cataract
(2) Non-Syndromatic (The Gaza Strip)				
CD-01-01-1-F	n/a	1:?	55	Father of 01-02
CD-01-02-1, 2	**FM**m**MFM-**	4:6	31, 16	
CD-02-01-1 & 2	ff**M*** mmf[sm]**M**	2:8	13, 4	* displaced teeth
CD-03-01-1	mfffm-f**M**m-fm	1:8	20	delayed walking
CD-04-01-1 & 2	**F**fffm**FF**mf-	2:8	18, 16	
Affected to total sibships and ratio in CD subtotal 14:36 = 1:2.7 excluding 01				
(B) Cone-Rod Dystrophies				
(1) Syndromatic				
(a) BBS: MSN, speech defect, extra digit, myopia (WB)				
CR-08-01-1 & 2	m{f}**M**f**M**f *	2:6	9, 5	* Left esotropia
CR-10-01-1	f-mf-m**F**(cf)[f]*ffp	1:5	7	* extra digits
(b) CRDAI – Congenital Onset with macular degeneration (GS)				
CR-01-01-1 to 3	**M**f**F**fm**MF**	3:7	22 to 10	
CR-01-02-1	ccmccm**M**ccc	1:3	8	
CR-01-03-1 to 4	{m}*mf**FF**m**MM**	4:8	8 to 0.9	* vernal catarrh
CR-01-04-1	m-**M***	1:1	50	* 01-05 ‘s parent
CR-01-05-1, 2	[sf]**F**m{mm-}m**M**	2:5	8, 2	
CR-01-06	f-f-f**F***m**FFMM**	5:6	32 to 22	* not assessed
CR-01-07	Ff**M**m	1:4	45	
CR-01-08	**FMF**	3:3	14 to 11	
CR-01-09	Ff**M**	1:3	0.6	
CR-01-10	**F**-mmfffm-f-f**M**mc	2:11	18	
CR-01-11	**F**fff**M**	1:5	2	
CR-01-12	**F**m**F**mm**M**	3:6	11 to 2	
CR-01-13	**MF**mfcmf	2:6	10, 9	
CR-01-14	f**M**f-mmf	1:6	12	
CR-01-15	m-ffm-f-f-f-cc**M**f	1:4	19	

CR-01-16	f-mffm**F**mm-mf	1:8	20	
CR-03-01-1	Fmm-m**M**fcf-f-m	1:6	18	
(c) CRDAI – Childhood Onset without macular involvement (GS)				
CR-02-01-1 to 3	**M**mf-**FF**cmcf	3:6	22 to10	
(d) CRD with Mental retardation (in 2/3 sibs)				
CR-04-01- 1 & 3	m**F**m-m-m-f-f-**M**f**F**mm	3:7	21-24	
Affected to total sibships and ratio in CRD 53:160 = 1: 3				
(2) Non-syndromatic				
CR-05-01-1	**M**f**M**	1:3	2	Childhood onset
CR-05-02-1	**M**fffmmmmm**M**	2:11	40	ew mutation
CR-06-01-1	m-fmmm-m-mmf**F**mcmc{f-}c	1:9	18	
CR-06-02-1	Cf**F**	1:2	1	
CR-07-01-1	**MF**mfmfm	2:7	11	
CR-11-1-1-	mff-**M**mm**M***[**F**]fmmm	4:12	21	* also mentally retaded
(C) Congenital Amaurosis of the Cone-rod (Only CD 05 from GS)				
(1) Syndromatic: with congenital hypertrichosis and trichomegaly				
CACR-01-01-1-F	M**F**fffmfmp	1:8	20	Cousins
CACR-01-02-1	fm**F**fmmmm	1:8	14	
(2) Non-Syndromatic with dull mentation				
CRCA-02-01-1	f**M**-fmff**M**m-ff	2:10	8	
CRCA-02-02-1 to 3	**F**m**M**f**M**f	3:6	9, 6, 3	
CRCA-02-03-1 to 3	f**M**fmm**F**mm**F**ffm	3:12	19 to 14	
CRCA-03-1-1 & 2	m(m-)ffmfm(**M**)**F**m	2:10	9, 6	
Affected to total sibships in CACR and ratio 11:36 = 1:3.6 (excluding CD 01)				

* Refer to codes used in sibships notation section 6.3 for the key to symbols used.
** Affected to total living siblings or living and dead siblings if affected with the same condition.

Table A18.8 Rod cone dystrophies: patients' sequence, ratios

Rod Disorders			
Patient No.	**Rank and Sequence ***	**Ratio****	
(A) Classical Leber's Congenital Amaurosis			
(1) Syndromatic (West Bank except RC-38 from GS)			
RC-01-1,2	**MF**m	2:3	Slow mentation
RC-38-1-1& 2	fm-fcmmmmmf**MF**fm	2:12	Slow mentation
RC-03-1-1 &2	{m}* **F****cc[f]^{c}cc**F****c	2:4	* cong.inguinal hernia **MSN
RC-02-1-1 & 2	ffmfc**FM ***	2:6	* mute, poor speech
RC-02-2	f*c**M-M*M**-fc**M-M**-mccm	1:5	* abnormal dentition
(2) Non syndromatic			
RC-04-1	m**M**mfc	1:4	All from West Bank except RC 14 and RC18 from GS) No. of affected to total sibships in LCA 25:77 = 1:3
RC-09-1	m**FF**fmfcf	2:7	
RC-13-1	mfm**F**fmc	1:6	
RC-15-1	fffc**F**	1:4	
RC-16-1	cmccfcaf**MM**c**F**a	3:8	
RC-40-1	f**MFM**mfc	3:6	
RC-53-1	n/a	n/a	
RC-14-1	**FF**mmffcmc**F**	3:8	
RC-14-2	missing	n/a	
RC-18-1	f-mm**MF**	2:4	
(B) Congenital Rod-Cones with Retinal Changes (All from WB except RC-10, RC-25 and RC-34 from GS)			
(1) Syndromatic/other associated			
RC-08-1	f-f-fcff-mcm**MF**c	1:5	Slow mentation, very shy
RC-11-2-1 & 2	**F**f-f**MF**cm	3:5	Slow mentation, very shy
RC-36-1	Mmf**M**	1:4	slow learner, poor memory
RC-34-1	**M-** ^{a}(sm)**F-** ^{a} **M** ^{ab}	3:4	^{a} delayed milestones ^{b} mentally retaded
RC-40-1- 1 to 3	f**M**^{ab} **FM**^{ac} mfc	3:6	^{a} undescended testes ^{b} slow mentation ^{c} bright, bat ears, extra digit in hand
RC-32-1-1 &2	**M***fmf**F**	2:5	* sits at corner with hands between thighs
RC-37-4- 1 to 4	**M***cmf**MFF**	4:6	*bad tempered, undisciplined
RC-33-1	Ccc**M***mfmmf-**F**- mmf**M**	3:10	* pectus cavus, long thin webbed digits, hyperextended

			joints, hypertelorism
RC-35-1- 1 to 3	M**M**fm**M*f**F***	3:7	* very obese
RC-11-1	fm-m**F**fmmfmf	1:9	prominent teeth
RC-21-1	c**F*M**(sf)	2:2	* cleft palate
RC-19-1-1 & 2	F**M**c**F***cfm-m	2:5	* atopy
RC-33-2	m-m(fccmf-fm**F***	2:7	
RC-10-1	f-mfff**MF***mmf**M**f	3:11	* excessive hands, feet sweating
RC-25-1, 1 to 5	**MF**fffmmf**F**f**MF**mfcf	5:15	All trichomegaly
(2) With no associations			
RC-05-1-1 to 3	ffm-ffcmf**MM**m**F**	3:10	
RC-07-1	fmfc**F**m**F**f	2:7	
RC-11-3	**F**m**F**	2:3	
RC-12-1	**FMF**f	1:4	
RC-16-1	cmccfcaf**MM**c**F**a	3:6	
RC-17-1-1	**M**	1:1	
RC-39-2	**F**	1:1	
RC-20-1	Fffm**FF**	2:6	
RC-21-2	ffm**F**f-m	1:5	
RC-22-1	N/a	n/a	
RC-23-1	F**MF**mff	2:6	
RC-24-1	cmm-**M**fm**M**c**F**m	3:8	
RC-27-1	c**M**m	1:2	
RC-30-1- 1 to 3	smacffmf**FFM**ccfm	3:10	
RC-30-2- 1 & 2	**MM**cccccc	2:2	
RC-30-3-1	mfmmffmmc**M**cccc	1:9	
RC-31-1- 1 to 3	**MM**mfssmmf**M**f	3:9	
RC-37-1-1 & 2	m-mf-ffm**MM**mmcm-	2:8	
RC-37-2-1 &2	m-mcmcf-**F**mmfcmm**F**	2:11	
RC-37-3-1	**F**	1:1	
RC-47-1	**M**m**F**m**M**	2:5	

No. of affected to total sibships ratio in cong. RC 83:231= 1:2.8

(B) Childhood onset rod-cone dystrophies			
RC-31-1	**M* M**mfssmmf**M**f	3:9	* mentally subnormal, hysteric
RC-40-1-1 & 2	F**MF*M**mfc	3:6	* dull mentation

RC-41-1	mmmf-**F**f-mf	1:6	MSN, slow speech, extra digit
RC-43-1	**M***mmf**F***M**ccfm	2:8	* obese. SNM, hypertelorism
RC-52-1	ffmm**M**fff	1:8	deaf, dull

Table A18.9 School Marks of 82 visually impaired pupils

Patients	Sex	Age[a]	VA[b]	Subjects Means				
				All [c]	Lang[d]	Scien[e]	H'man[f]	Arts
Hypopigmentation [g]								
ALB-05-1-2	M	5	3	96	90	95	100	100
ALB-07-1-1	M	10	1	89	75	89	91	95
ALB-08-1-2	F	12	2	85	80	88	85	83
Average hypopigmentation				89	82	91	92	93
Cone Disorders								
RD-CR-01-13-2	F	8	2	94	96	91	-	96
RD-CR-01-12-2	M	5	4	91	80	95	100	80
RD-CR-01-13-1	M	9	3	87	74	90	96	84
RD-CR-01-01-2	M	12	4	85	76	82	66	96
RD-CR-01-08-2	M	12	2	84	85	78	70	98
RD-CR-01-02-1	M	7	2	84	80	80	90	85
RD-CR-01-14-1	M	10	2	81	84	87	64	78
RD-CR-01-08-1	F	13	2	73	71	71	50	96
RD-CR-01-08-3	F	9	2	71	70	74	60	88
RD-CR-03-01-1	M	10	2	70	64	74	60	98
RD-CR-01-12-1	F	10	3	68	75	48	60	78

Table A18.9 School Marks of 82 visually impaired pupils

Patients	Sex	Age[a]	VA[b]	Subjects Means				
				All [c]	Lang[d]	Scien[e]	H'man[f]	Arts
Cone Degeneration								
RD-CD-04-01-2	F	15	2	82	75	85	76	91
RD-CD-02-01-1	M	12	2	79	65	82	80	80
RD-CD-04-01-1	F	16	2	78	81	68	72	86
Achromatopsia								
RD-cRM-08-1-1	F	22	2	87	84	86	94	82
RD-cRM-10-1-1	F	11	2	83	85	83	83	83
RD-cRM-03-1-2	F	10	2	69	79	67	66	75
Isolated Macular Degeneration and Vitreo retinopathy								
RD-MD-11-1-1	M	7	2	92	95	95	90	78
RD-MD-09-1-3	F	12	3	74	76	64	-	96
RD-VR-02-1-1	M	10	5	86	89	88	95	69
Cone rod Congenital Amaurosis								
CRCA-01-02-1	F	13	4	82	84	86	90	78
CRCA-02-03-2	F	17	3	67	60	-	57	73
CRCA-02-03-3	F	12	3	65	66	53	72	72
Average All the cone disorders				79	78	78	76	84
Acquired								
Control 13-1-1	M	9	1	88	80	85	-	96
ACQ-56-1-1-phth	M	15	2	82	85	77	89	74
ACQ-48-1-1-phth	F	16	1	73	67	79	64	80
ACQ-34-1-1	F	6	3	70	62	73	-	75
Average non genetic cases				77	73	79	77	81

Table A18.9 School Marks of 82 visually impaired pupils

Patients	Sex	Age[a]	VA[b]	Subjects Means				
				All [c]	Lang[d]	Scien[e]	H'man[f]	Arts
Congenital Glaucoma								
CG-08-1-1	M	15	4	83	82	86	71	86
CG-06-1-2	F	7	4	80	90	65	-	72
CG-09-1-1	M	16	5	78	76	72	83	79
CG-23-1-1-phth	F	16	3	78	80	84	77	75
CG-07-1-1-cc	F	9	4	77	70	84	78	60
CG-09-1-2-cc	F	22	5	72	60	64	88	70
CG-12-1-1	M	12	4	71	60	71	55	75
CG-10-1-2-phth	M	12	5	70	69	56	67	74
CG-32-2-1-2	F	16	2	60	48	72	50	81
CG-26-1-4-cc	M	4	5	59	59	70	57	41
CG-06-1-1	F	19	4	57	30	60	86	40
CG-10-1-1-cc	M	12	5	29	58	-	-	-
Average congenital glaucoma				68	64	70	71	67
Anterior Segment Dysgenesis (ASD)								
SD-01-1-2-mc_	F	12	3	69	75	66	67	69
ASD-01-1-1-mc_	M	18	3	65	64	54	47	86
ASD-01-1-3-mc_	M	9	3	63	48	65	58	80
Average ASD				65	70	68	71	66
Coloboma / Congenital Corneal Oedema								
CB-02-1-1-mc	F	15	2	68	65	69	65	71
CB-02-1-2-mc	M	11	3	72	68	75	50	87
CB-03-1-1	M	12	4	37	15	23	15	70
Average colobomas				56	63	62	67	62

Table A18.9 School Marks of 82 visually impaired pupils

Patients	Sex	Age[a]	VA[b]	Subjects Means				
				All [c]	Lang[d]	Scien[e]	H'man[f]	Arts
CCO-01-1	F	20	3	51	53	41	43	61
Small Eyes								
MC-06-1-1	M	16	5	87	85	89	91	82
MC-12-1-2-CC	M	7	2	78	100	90	100	40
MC-11-1-1	F	9	5	40	22	36	41	54
MC-12-1-1-CC	M	6	4	32	30	29	40	-
Average small eyes				62	59	61	68	59
Congenital Cataract								
CC-04-2-1	F	13	2	82	84	84	77	73
CC-22-1-2-my	M	18	2	78	59	81	81	94
CC-05-2-3-mc	F	12	4	75	66	69	76	76
CC-05-2-4-mc	F	9	3	74	70	69	75	71
CC-05-2-1-mc	M	12	2	73	54	80	60	85
CC-05-2-2-mc	M	11	1	72	65	68	68	87
CC-08-1-1	F	10	2	72	60	73	75	82
CC-23-1-1	M	15	2	52	21	51	34	67
CC-07-1-4	M	7	2	48	62	44	-	48
CC-19-1-1-dg	M	15	3	47	22	70	12	80
CC-30-3-1-mc	F	9	2	46	44	46	49	40
CC-30-2-2	M	9	2	44	40	43	49	45
CC-01-1-3	M	20	4	44	50	43	40	40
CC-28-1-1	M	9	4	43	42	43	44	47
CC-47-1-1-dg_vr	F	12	2	39	30	50	10	64
CC-18-1-1	F	12	5	36	25	32	44	43

Table A18.9 School Marks of 82 visually impaired pupils

Patients	Sex	Age[a]	VA[b]	Subjects Means				
				All [c]	Lang[d]	Scien[e]	H'man[f]	Arts
CC-30-3-2-mc	M	3	4	34	25	38	-	40
CC-26-1-1-my	F	10	2	34	31	36	33	35
CC-26-1-2-my	M	8	2	32	41	21	-	42
CC-25-1-1	F	8	4	23	32	10	-	-
Average congenital cataract				54	47	55	52	61
Myopia								
MY-05-1-1	F	11	4	81	80	78	70	90
MY-09-1-1	M	13	1	75	78	65	60	82
MY-08-1-1-cc	M	5	2	49	50	48	50	50
Average myopia				67	69	64	60	74
Optic Nerve								
ON-12-1-1-sy	M	17	4	87	81	93	90	88
ON-14-1-1	M	11	4	78	66	79	79	78
ON-15-1-1	M	9	2	61	45	45	75	65
ON-17-1-1	M	17	4	30	20	26	-	35
Average optic nerve				65	53	60	81	67
Rod Disorders								
RD-RC-25-1-3	F	13	4	53	60	53	36	50
RD-RC-06-1-1	M	5	4	40	46	35	-	35
Average rod disorders				44	53	44	36	43

[a] Age at examination [b] WHO visual categories [c] Average all subjects [d] Languages (Arabic and English) [e] Science subjects [f] Humanities [g] oculocutaneousalbinism.

Table A18.10 West Bank:Gaza Strip ratio of the prevalence of clinical conditions.

	School Age		**All Ages**		**Pedigrees [a]**	
	Ratio	Cohort	Ratio	Cohort	Ratio	Cohort
Equal Proportions						
Retinal Dystrophies	**1.7**	129	**1.4**	245	**3**	65
Cong. Cataract	**1.2**	56	**1.6**	120	**1.4**	70
WB Predominance						
Optic Nerve	**11**	12	**4**	23	**6**	21
Vitreo retinopathies	**9**	10	**5.5**	13	**6**	7
All Rod	**5**	60	**4**	112	**5.3**	57
LCA	**5**	50	**4**	94	**4.8**	39
Childhood onset	**1.3**	7	**5.6**	21	**6**	13
CACR	**6/0**	6	**11/0**	11	**6/0**	6
Uvea	**3/0**	4	**8**	6	**5/0**	5
Gaza Strip Predominance						
Small Eyes	**1.1**	17	**0.7**	37	**1.2**	18
Mac. Degenerations	**1**	12	**0.8**	22	**2.6**	11
All cones	**0.6**	49	**0.5**	103	**1.5**	30
CRD	**0.2**	24	**0.2**	47	**1**	10
RM	**0.5**	12	**0.3**	33	**0.8**	11
Cong. Nystagmus	**0.3**	4	**0.16**	7	**0.3**	4
Hypopigmentation	**0.3**	18	**0.4**	27	**0.4**	10
Myopia	**0.3**	12	**0.5**	24	**0.6**	13

Table A18.11 West Bank:Gaza Strip ratio of the prevalence of clinical conditions.

	School Age		All Ages		Pedigrees [a]	
	Ratio	Cohort	Ratio	Cohort	Ratio	Cohort
Equal Proportions						
Retinal Dystrophies	**1.7**	129	**1.4**	245	**3**	65
Cong. Cataract	**1.2**	56	**1.6**	120	**1.4**	70
WB Predominance						
Optic Nerve	**11**	12	**4**	23	**6**	21
Vitreo retinopathies	**9**	10	**5.5**	13	**6**	7
All Rod	**5**	60	**4**	112	**5.3**	57
LCA	**5**	50	**4**	94	**4.8**	39
Childhood onset	**1.3**	7	**5.6**	21	**6**	13
CACR	**6/0**	6	**11/0**	11	**6/0**	6
Uvea	**3/0**	4	**8**	6	**5/0**	5
Gaza Strip Predominance						
Small Eyes	**1.1**	17	**0.7**	37	**1.2**	18
Mac. Degenerations	**1**	12	**0.8**	22	**2.6**	11
All cones	**0.6**	49	**0.5**	103	**1.5**	30
CRD	**0.2**	24	**0.2**	47	**1**	10
RM	**0.5**	12	**0.3**	33	**0.8**	11
Cong. Nystagmus	**0.3**	4	**0.16**	7	**0.3**	4
Hypopigmentation	**0.3**	18	**0.4**	27	**0.4**	10
Myopia	**0.3**	12	**0.5**	24	**0.6**	13

Table A18.12 Gender differences in clinical conditions by region

Condition	WB [a]	GS [a]	WB:GS	Cohort
General Population ratios *n:1*				
< 19 years	*1.1*	*1.08*	-	-
> 19 years	*0.86*	*0.9*	-	-
All ages	*0.88*	*1*	-	-
Male Preponderance				
CC [b]	-	-	*1.8*	132
CG				
Total series	+	-	*1.5*	68
< 6	+	-	*4*	20
Small Eyes	+	*2, 1.4*		15, 22
Optic Nerve	*+, 1.8*	-		23
Myopia	-	+		24
Albinism	-	+	*19*	2.2
All rod disorders	-	+	*1.2*	22
RCD	-	+	*2*	2
Female Preponderance				
CG (6-18)	*+ 0.6*	*+ (0.9)*		WB, 15; GS,14
Achromatopsia	+	*0.3, 0.8*		33
Uvea	+	-	*0.6, 0*	6, 0
RD	+	-	*0.8, 1.2*	144
CD	+	-	*0.6*	8
CRD	+	-	*0.6. 1.2*	8
Albinism	+	-	*0.3*	8
All RCD	+	-	*0.7*	87
LCA	+	-	*0.9*	73
Childhood RP	+	-	*0.3*	17
CIN[c]	-	+	*0, 0.4*	7
Equal sex ratio (M:F ratios between 1.0 to 1.2)				
CD	+		*1*	12
RDes	+		*1*	151
Uvea	+		*1*	6
CRD	+		*1*	47
School Age				
Rod 6-16	+	-	*1*	60
CACR	+	-	*1*	11

Myopia	+	-	*1*	8
MC (6-18)	-	+	*1*	8
LCA	-	+	*1*	19
All cone		+	*1.1*	65

[a] Ratios in *Italic*
[+] Male or female preponderance

Appendix B

Abbreviations and symbols used in family sequence and degree of consanguinity

a	Abortion
c	Miscarriage
F, m	(lower case) non-affected male or female
F, M	(upper case) affected male or female
M, F (bold)	An affected male of female who was examined
M, **F (bold)**	The affected male or female in question when more than one is affected in the sibship.
n/a	Siblings sequence and pedigree information is not available
p	Pregnant
s	Still birth (followed by f or m if gender is known) e.g sf, sm, indicate a female still birth and a male still birth
U	Uncertain gender
[ ]	Twins such as [mm], [ff], [mf]
-	Minus sign following f, F, m, M indicate deceased sibling.
, * ~ ’	To denote specific information data in the preceeding symbol which is explained in the text
{ }	To denote specific information contained inside the bracket
?	’?’ preceding a symbol indicates uncertainty of the information that follows eg ‘?-‘ means possibly dead, ?m possibly male.
mfMcFf	Siblings not in sequence, when several symbols underlined

Abbreviations Used Referring to Types of Consanguinity

C*n*	Degree of cousin marriage eg C1 is first cousin and so on.
C1PM	Double first cousin (if both paternal and maternal)
NR	No relation
SV/ST	Same village/same town or locality
C*n*1h	Cousin once removed eg C1h is first cousin once removed.
P	Paternal
M	Maternal