Aetiological Classifications

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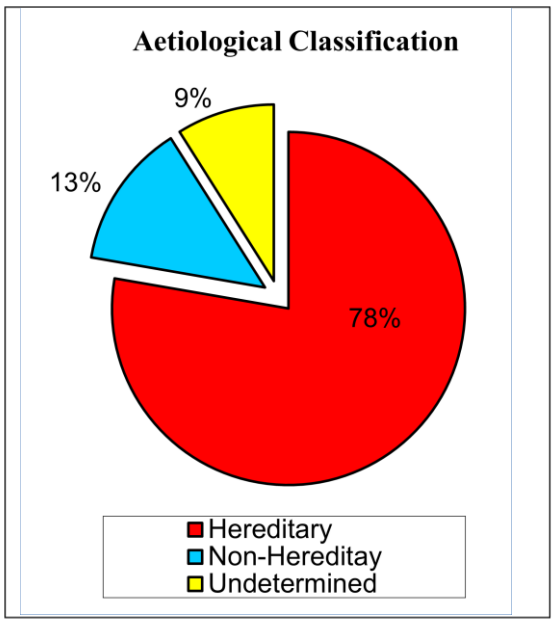
15.1 Introduction

In this study, among the total number of 669 patients, the aetiologies of the causative condition were as follows: (Figure 15.1)

1. Hereditary: This is the largest aetiological group comprising a total of 519 patients, 243 pedigrees and 310 sibships. (77.6%)
2. Non-Hereditary Conditions: This group comprises 90 patients and sibships with 89 pedigrees. (13.4%)
3. Aetiology Undetermined: This includes 60 patients with the same number of pedigrees and sibships. (9%)

Figure 15.1 Aetiological classification



The aetiological classification of cases by region is shown in Tables 15.1 and by gender in Table 15.2.

In the WB, the percentages of both the hereditary and non-hereditary conditions in the northern regions (Jenin, Qalqilya, Tul-Karem and Nablus) are equal. There is preponderance of hereditary conditions in the central regions (Ramalla, Jerusalem, and Bethlehem) and of the non-hereditary conditions in the southern regions of Hebron. (Table 15.3)

Subregional / Dwellings

There are wide variations in the proportions of hereditary and non-hereditary conditions according to the type of locality (i.e urban, rural or camps). Over 50% of both the hereditary and the non-hereditary cases live in villages (Table 15.3).

Table 15.1 Distribution of cases by aetiology and region

	West Bank		Gaza Strip		Others		Total	
Hereditary								
<16	163	***76.2***	141	***86.0***	6	***22.2***	310	***76.4***
16+	102	***76.7***	103	***82.4***	4	***66.7***	209	***79.5***
Subtotal	265	***76.4***	244	***84.4***	10	***33.3***	519	***77.6***
Non-Hereditary								
<16	26	***12.1***	9	***5.5***	5	***18.5***	40	***9.9***
16+	29	***21.8***	20	***16.0***	1	***16.7***	50	***19.0***
Subtotal	55	***15.9***	29	***10.0***	6	***66.6***	90	***13.5***
Undetermined								
<16	25	***0.9***	14	***1.2***	16	***3.7***	55	***1.2***
16+	2	***1.5***	2	***1.6***	1	***16.7***	5	***1.9***
Subtotal	27	***7.8***	16	***5.5***	17	***51.5***	60	***9.0***
Grand Total								
All age groups	347		289		33		669	
Total 16	214		164		***27***		***405***	
Total 16+	133		125		***6***		***264***	

Table 15.2 Gender in hereditary and non-hereditary cases

		West Bank		Gaza Strip		Total	
		No.	M:F	No.	M:F	No.	M:F
Hereditary							
All series	M	127	**0.9**	146	**1.5**	277	**1.1**
	F	138		98		242	
Subtotal		265		244		519	
School	M	78	**0.95**	73	**1.3**	152	**1.1**
Children	F	82		55		140	
Non-Hereditary							
All Series	M	25	**0.9**	19	**1.9**	49	**1.2**
	F	30		10		41	
Subtotal		55		29		90	
School	M	21	**2**	9	**4.5**	32	**2.5**
Children	F	10		2		13	
TOTAL		347		289		669	

15.2 Classification

In 60 patients it was not possible to ascertain the aetiology. (Table 15.5) The lack of available family information and pedigree charts in this group was an important factor in this shortfall; 55 of these patients were recruited from the out patients at St John Ophthalmic Hospital. Also, the lack of detailed information made it impossible to compile data on the marriage patterns and consanguinity. Conditions of undetermined aetiology formed 13.3% and

Table 15.5 Undetermined conditions

Possible genetic aetiology	50	(83.0%)
Possible non genetic aetiology	5	(8.3%)
Prenatal factors (1)		
Postnatal factors (4)		
Either prenatal or genetic	2	(3.3%)
Postnatal or genetic	1	(1.6%)
Undetermined	2	(3.3%)
Total	60	100%

Table 15.3 Distribution of aetiological groups in West Bank's sub-regions

	North		Centre		South		U/D		Total	
Non-hereditary	18	***32.7***	20	***36.4***	12	***21.8***	5	***9.1***	55	***100***
Hereditary	85	***32.1***	124	***46.8***	39	***14.7***	17	***6.4***	265	***100***
Total	103	***32.2***	144	***45.0***	51	***15.9***	22	***6.9***	320	***100***
% Non-Hereditary	***17.5***		***13.9***		***23.5***		***22.7***		***17.2***	

Percentages in ***bold italic.*** U/D: region undetermined

Table 15.4 Distribution of aetiological cohorts by type of dwelling

	Villages		Towns		Camps		U/D [a]		Totals	
West Bank										
Non-hereditary	31	***56.4***	20	***36.4***	3	***5.5***	1	***1.8***	55	***100***
Hereditary	148	***55.8***	79	***29.8***	24	***9.1***	14	***5.3***	265	***100***
Subtotal	179	***55.9***	99	***30.9***	27	***8.4***	15	***4.7***	320	***100***
% non- hereditary		***17.3***		***20.2***		***11***		***6.7***		***17***
Gaza Strip										
Non-hereditary	6	***20.7***	7	***24.1***	15	***52***	1	***3.4***	29	***100***
Hereditary	73	***29.9***	95	***38.9***	66	***27***	10	***4.1***	244	***100***
Subtotal	79	***28.9***	102	***37.4***	81	***30***	11	***4***	273	***100***
% non-hereditary		***7.6***		***6.9***		***19***		***9.1***		***11***
Both regions*										
All aetiologies	269	***40.2***	226	***33.8***	111	***17***	63	***9.4***	669	***100***
% non-hereditary		***14.3***		***13.4***		***16.7***		***7.7***		***14.2***

[a] Including others from undetermined (U/D) regions. Percentages in ***bold italic***

15.6% of the pedigree and sibships respectively.

The age groups in the undetermined cases are predominantly in the < 16 cohort (n=56) (9.6% of the total series). The M:F ratio is 2.3:1 in the WB and 2.5:1 in GS. The ratio resembles that of the non-hereditary postnatal cases in the < 16. The regional distribution of patients in this group was; WB, 27; GS, 16; undetermined from either regions 17.

In this group the main site of pathology was the lens in 66.6% (n=40) followed by the whole globe 18% (n=11). The main conditions diagnosed in this group were; congenital cataract (n=40); buphthalmos (n= 9); and others (n=11).

Hereditary Aetiology and Conditions

Heredity formed the major bulk of cases in this survey. Of the 669 patients with bilateral visual disorders, 517 cases were hereditary in origin, that is 77.6%. Of these, 265 patients (51%) are in the WB and 244 (47%) in the GS. A further 10 (2%) are patients whose families live in Israel or are from either the WB or the GS but where the exact origin is uncertain

The M:F ratio for the WB hereditary series (n= 163) is identical to the sex ratio in the general population at 1:1 in the <16. In the 16+ cohort the ratio 0.79:1 (n=102). (Table 15.2) The latter ratio resulted from a female excess of 12 patients. In the GS, the ratio in the <16 is 1.39:1 (n=141) and in the 16+, 1.64:1 (n=103). This is the result of an excess of 23 and 25 male patients in each cohort respectively. The overall ratio, however, in the total hereditary group is 1.14:1 combining the <16 at 1.17:1 and the 16+ at 1.1, similar to the ratio in the general population.

As hereditary conditions form 77.6% of the total series, analysis of the data will follow closely the findings demonstrated in the total series addressed previously. Apart from 1 case which was chromosomal.(

Hereditary lens disorders is the second commonest genetic group is lens disorders with 94 cases forming 18.1% of the total genetic cohort. This leaves 14 (9.6%) cases of non-hereditary aetiology and 37 (25.5%) cases of undetermined aetiology. (Table 15.6)

Excluding the latter, hereditary conditions form 87% of the lens cases. The hereditary group comprises primarily genetic congenital cataract with 81 patients (86%) followed by ectopia lentis with 13 patients (14%). An account of the clinical aspects of this group is found in chapter 17.

Other hereditary conditions included congenital glaucoma, small eyes (microphthalmos and anophthalmos, and congenital hereditary corneal oedema (chapter 17).

Table 15.6 Proportions of lens conditions and congenital cataract

Age	Nos.	%	Hered.		Non-hered.		UD	
All Lens categories								
All	*145*	***21.7***	*94*	***65***	*14*	***9.6***	*37*	***25.5***
<16	*105*	***26***	*57*	***54.3***	*11*	***10.5***	*37*	***35***
Cong. Cataract (including aphakia)								
All	*132*	***19.7***	*81*	***61.4***	*14*	***10.6***	*37*	***28***
<16	*94*	***23.2***	*46*	***49***	*12*	***12.7***	*37*	***39 .4***
All Cataract (primary and secondary pathology)								
All	*153*	***22.8***	*100*	***63.4***	*15*	***9.8***	*38*	***34***
<16	*111*	***27.4***	*61*	***55***	*13*	***11.7***	*38*	***34***

Hereditary retinal conditions constituted 97% of the retina cases with the commonest conditions being retinal dystrophies, albinism and high myopia 4.8% (n=22). (Tables 15.7 and 15.8)

In the GS, this was as high as 99% of all the retinal conditions.

There is an obvious male preponderance in the GS (ratio 1.5:1) with the reverse observed in the WB (ratio 0.7:1), averaging in both regions at 1:1.

Table 15.7 Retinal dystrophies in the anatomical 'retina' category

	West Bank				Gaza Strip				Total Series			
	M	F	Total	M:F	M	F	Total	M:F	M	F	Total [a]	M:F
All Retina	72	95	167	0.8:1	84	58	142	1.4:1	156	153	317	1:1
Genetic	68	92	160	0.7:1	83	57	140	1.5:1	151	149	306	1:1
% Genetic	***94***	***97***	***96***		***99***	***98***	***99***		***97***	***97***	***97***	

Table 15.8 Pedigrees and sibships in the genetic retinal series

	Pedigrees						Sibships					
	WB		**GS**		**Total**		**WB**		**GS**		**Total**	
All Retina	96	***91***	44	***42***	147	***100***	113	***60***	68	***36***	188	***100***
Genetic	89	***84***	42	***40***	136	***100***	106	***60***	66	***37***	177	***100***
% Genetic	**93**		**95**		**93**		**94**		**97**		**94**	
S'ship/Pedig [a]	**1.18**		**1.55**		**1.28**		-		-		-	-

Percentages ***bold italic*** [a]: ratio of sibships/pedigrees

Non-Hereditary Conditions

Number of cases

Of the 699 cases in the survey, the aetiology in 90 (3.3%) cases was acquired. Of those, 55 cases (61%) were from the WB forming and 29 (39%) from the GS. This forms a ratio of 1.9:1 which is only slightly higher than the ratio of the population in the two regions.

Tables 15.1 to 15.4 illustrate the distribution of the pedigrees, sibships, and patients among the hereditary and non-hereditary disorders.

Age

There is a preponderance of adults in this category with an <16 and 16+ ratio of 0.8:1. This is the reverse of the equivalent ratio in the hereditary condition which is 1.48:1.

Gender

The sex ratio in this group (1.19:1) is comparable to the ratio in hereditary conditions.

Causes

The causation of the 90 cases of non-hereditary conditions span the whole spectrum of non-hereditary factors as follows (Figure 15.3): -

A) Prenatal factors with 24 patients (27%).
B) Perinatal factors (including neonatal) with 10 patients (11%).
C) Postnatal factors, the largest group with 55 patients (61.8%).
D) Uncertain non-genetic, 1 patient.

Pathologies in Non-Hereditary Conditions

Whole globe pathologies formed the main group of conditions in the non-hereditary causes with 31 patients constituting 35% of cases. This is followed by corneal conditions comprising 16 cases (18%) and thirdly by optic nerve disorders with 14 cases (16%), whilst lens disorders had 11 cases (12%) and retinal conditions 9 cases (10%).

A breakdown of all non-hereditary cases are listed in Table A15.1. (Chapter 17 Appendix)

Figure 15.3 Aetiological factors in non-hereditary conditions

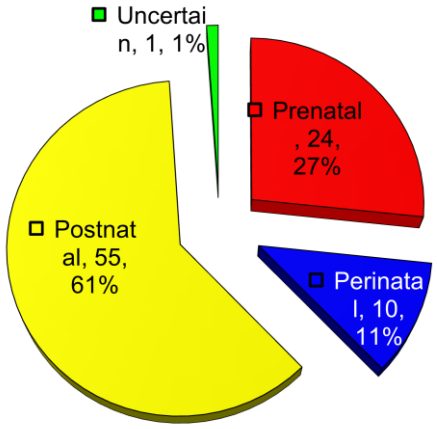


Table 15.9 Intrauterine causes

1.	Intrauterine infections (IUI)	
	a. Congenital Toxoplasmosis	3
	b. Congenital Rubella	1
	c. Undetermined type of IUI	10
2.	Possible IUI	5
3.	Possible drug intake	3
4.	Either IUI or drug intake	1
5.	Undetermined IU Factors	1
	Total	24

Visual acuities in the prenatal group of patients were severely compromised with 71% (n= 17) blind and nearly two thirds of the blind having NLP. The visual acuities in cases with lenticular aetiology varied between categories '2' and '3'

Table 15.10 Visual acuities in prenatal conditions

Category '5' (NLP)	10
Category '4' (blind)	7
Category '3' (SVI)	1
Category '2' (VI)	3
Category '1' (NVI)	1
Others	2
Total	**24**

Prenatal Factors

Among the 24 cases of prenatal aetiologies, the majority are most probably secondary to intrauterine infection constituting 79% of the prenatal cases and making this factor the most important cause for prenatal conditions which amounts to 3.6% of the total series of 669. In most cases of the undetermined type of intra uterine infections, it was not possible to ascertain the exact cause although CMV virus infection is a likely possibility. There were 3 cases with possible drug intake in the first trimester (Table A15.1).

Visual Acuities

Anatomical Sites

The lens was the main site of pathology and found in 50% of the prenatal cases, followed by the whole globe in 33%. The main clinical conditions in this subgroup are CC followed by microphthalmos.

Demography

There is a significant preponderance of prenatal conditions in the WB versus GS with a ratio of 15:1.

The contributory factors in the patients studied are enumerated in Table A15.1)

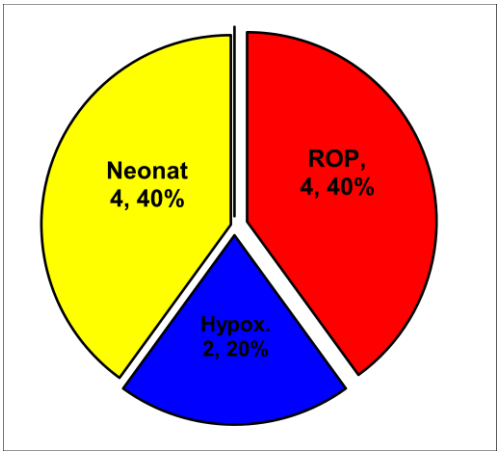
Perinatal and Neonatal Causes

This is a very small group consisting of 10 patients only. Four of these patients were in the WB and three in the GS. The number of females in the GS was double that of males (2 and 1). Two thirds (n=4) of the perinatal problems were caused by ROP and the other third (n=2) were from birth hypoxia. (Figure 15.4)

There were only 4 cases where the cause of blindness was due to factors occurring in the first month after birth. One was described as due to ophthalmia, two due to harmful topical medications (one of which was iatrogenic as a result of a medical error), and the fourth case was secondary to surgical complications in the first month (neither the nature of the condition nor of the surgery were clear). Anatomical sites of the pathologies were retina in 4; phthisis bulbi, 2; corneal pathology, 2; and optic atrophy, 1.

Visual acuities were also severely affected in this category with 100% SVI/BL (NLP,5; BL, 3; SVI,1; and category '7', 1).

Figure 15.4 Perinatal causes



Postnatal Factors

This is the largest group of the acquired non-genetic cases with 55 patients, forming 62% of the non-hereditary conditions and 8% of the total series. Twenty of these patients were under the age of 16 (36%) and 35 (64%) are adults. This group comprised 31 patients from the WB as opposed to 21 in the GS, thus producing a ratio of 1.5:1, which was fairly similar to the population ratio, taking into account the small size of the sample and the possible presence of a few scattered cases in the WB that had not been examined (population ratio 1.78:1). There were an additional 2 where the origin was not determined and one from Israel.

The M:F ratio in the various age cohorts in this group shows that with the exception of 16+ cohort in the WB, there is a male preponderance the highest being in the GS <16 cohort at 4:1, followed by the WB <16 cohort at 2.3:1 and finally the GS <16 cohort at 1.6:1. The WB 16+ cohort showed female preponderance with a ratio of 0.36:1.

In this aetiological group, 40% of cases belonged to the whole globe (n=22), 25.5% to the cornea (n=14), 20% to the optic nerve (n=11) and 9% to the retina (n=5). The 14 corneal cases were of corneal scarring and 1 was staphyloma. Eleven of these were 16+ and 3 <16. In the whole globe cases, 12 were phthisical/atrophic eyes and in 3, eyes had been removed.

Trauma accounted for 11 cases distributed between the WB (6) and the GS (5) (WB/GS ratio 1.2:1 compared to a population ratio of 1.78:1). M:F ratio was 1.2:1. Of these cases only 1 was from head injury and the rest were ocular including 4 from bomb explosion.

Blindness ranked very high at 83% of the total with 60% having NLP (n=33). The figure reaches 87% when combining the blind with the SVI.

Table A15.1 sums up all the conditions in the non-hereditary conditions.

Table A15.1 Breakdown of all the non-hereditary cases by category with percentages

Conditions	Nos.	% Subgroup	% Total
Prenatal (Intrauterine) Causes			
Intrauterine infection (IUI)			
Congenital toxoplasmosis	3	*12*	*3.3*
Congenital rubella	1	*4*	*1.1*
Undetermined IUI	10	*40*	*11*
Intrauterine infection suspect	5	*20*	*5.5*
Intrauterine medicine suspect	3	*12*	*3.3*
Undetermined IU factors	3	*12*	*3.3*
Subtotal IUI	**25**	***100***	***27.7***
Perinatal Causes			
ROP	4	*40*	*4.4*
Birth hypoxia	2	*20*	*2.2*
Ophthalmia neonatorum	1	*10*	*1.1*
Iatrogenic: Surgery, drops, and traditional medicine	3	*30*	*3.3*
Subtotal perinatal	**10**	***100***	***11.1***
Postnatal (Childhood) Causes			
Ophthalmia (epidemics), 1 small pox	4	*7.2*	*4.4*
Other ocular infections / inflammation	7	*12.7*	*7.7*
Measles	9	*16.4*	*10*
Trachoma	2	*3.6*	*2.2*
Vernal Catarrh	2	*3.6*	*2.2*
Unidentified ocular cause: cornea 3, secondary glaucoma 1, unidentified 1	5	*9.1*	*5.5*
Vascular	1	*1.8*	*1.1*
Ocular trauma	10	*9.1*	*11.1*
Subtotal postnatal	40	*72.7*	*42.2*
CNS causes			
Meningitis/encephalitis	6	*11*	*6.6*
Intracranial tumours	2	*3.6*	*2.2*
Intracranial thrombosis	1	*9.1*	*1.1*
Spontaneous subdural haemorrhage	1	*9.1*	*1.1*
Cortical blindness	1	*9.1*	*1.1*
Trauma - head injury	1	*9.1*	*1.1*
Undetermined CNS causes	2	*3.6*	*1.6*
Subtotal CNS Causes	14	*25.5*	*15.5*
Undetermined	1	*1.8*	*1.1*
Subtotal childhood causes	**55**	***100***	***61***
Grand Total	**90**		***100***