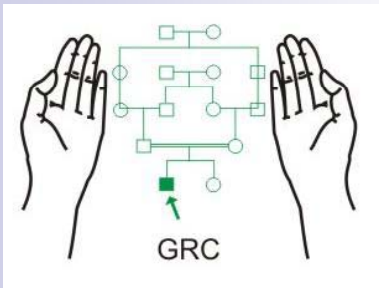


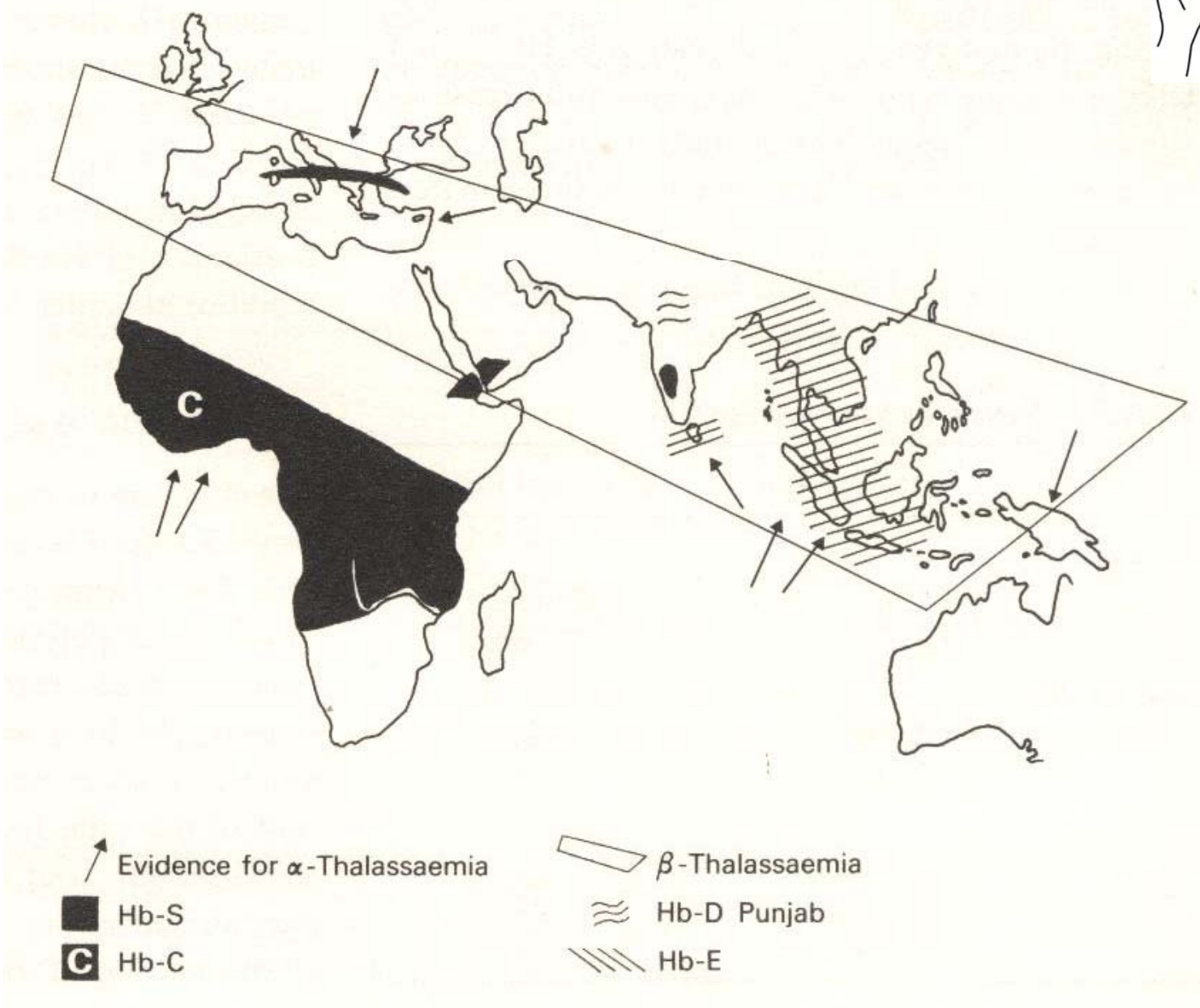
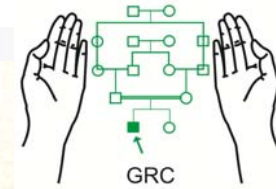
Epidemiology of Haemoglobin Disorders in Pakistan

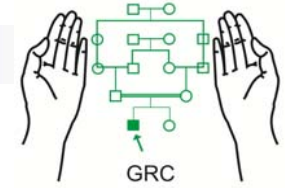


Maj Gen (R) Suhaib Ahmed, HI (M)
MBBS; MCPS; FCPS; PhD (London)

Genetics Resource Centre (GRC)

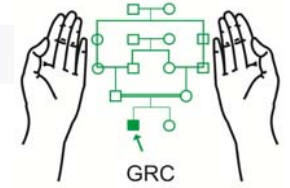
www.grcpk.com



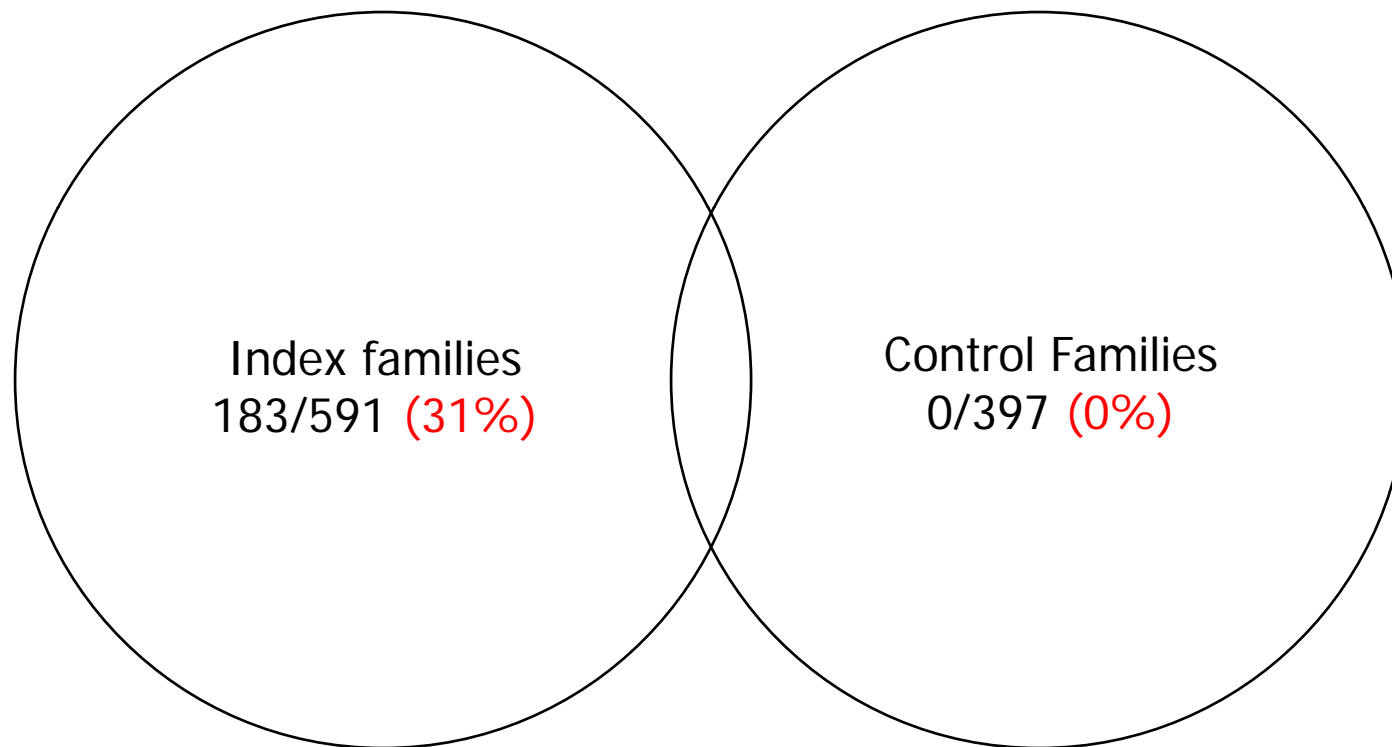


Haemoglobin Disorders in Pakistan

- β -Thalassaemia
- α -Thalassaemia
- $\delta\beta$ -Thalassaemia
- Abnormal Haemoglobins
 - Hb-S
 - Hb-E
 - Hb-D
- Miscellaneous Hb disorders

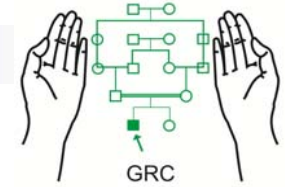


Distribution of Thalassaemia Genes in Pakistan



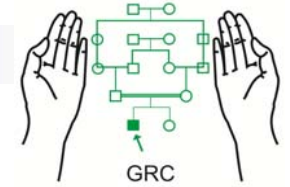
General Population
(5%)

(Ahmed et al, 2002)



β -Thalassaemia Trait in Pakistan

Disorder:	Ethnic group:	Type of study:	Place:	Subjects:	Methods used:	Carriers:	95% CI	Reference:
β -thalassaemia	Pathan	Population based	Peshawar	129	CEM Electrophoresis	5 (3.9%)	0.56-7.24%	Stern et al, 1968
β -thalassaemia	Mixed, all groups	Population based	Karachi	1224	CEM Electrophoresis	17 (1.4%)	0.73-2.04%	Hashmi and Farzana 1976
β -thalassaemia	?	Population based	Paris	67	CEM Electrophoresis	2 (3.0%)	1.08-7.08%	Coquelet et al, 1983
β -thalassaemia	Mostly Punjabi	Hospital based	Lahore	437	CEM Electrophoresis	42 (9.6%)	6.83-12.36%	Latif 1983
β -thalassaemia	Mostly Punjabi	Population based	Lahore	300	CEM Electrophoresis	5 (1.6%)	0.24-3.16%	Hameed and Chaudhry 1984
β -thalassaemia	?	Hospital based	Karachi	256	CEM Electrophoresis	16 (6.3%)	3.24-9.16%	Ihsanullah et al, 1985
β -thalassaemia	?	?	London	?	?	? (6%)	?	Modell and Berdoukas 1984
β -thalassaemia	Mixed, all groups	Population based	Rawalpindi	500	CEM Electrophoresis	27 (5.4%)	3.42-7.38%	Khattak and Saleem 1992a [@]
β -thalassaemia	Punjabi	Population based	Rawalpindi	245	CEM Electrophoresis	8 (3.3%)	1.14-5.46%	Khattak and Saleem 1992a [@]
β -thalassaemia	Pathan	Population based	Rawalpindi	201	CEM Electrophoresis	16 (8.0%)	4.26-11.74%	Khattak and Saleem 1992a [@]
β -thalassaemia	Mixed	Hospital based	Rawalpindi	1000	CEM Electrophoresis	39 (3.9%)	2.7-5.1%	Hassan et al, 1997
α -thalassaemia	Mostly Punjabi	Population based	Lahore	320	CEM Electrophoresis	3 (0.94%)	0.12-2.0%	Khan and Hayee 1986
α -thalassaemia	Mixed	Population based	Rawalpindi	500	CEM Electrophoresis	12 (2.4%)	1.06-3.74%	Zuhur-ur-Rehman et al, 1991



β -Thalassaemia in Pakistan

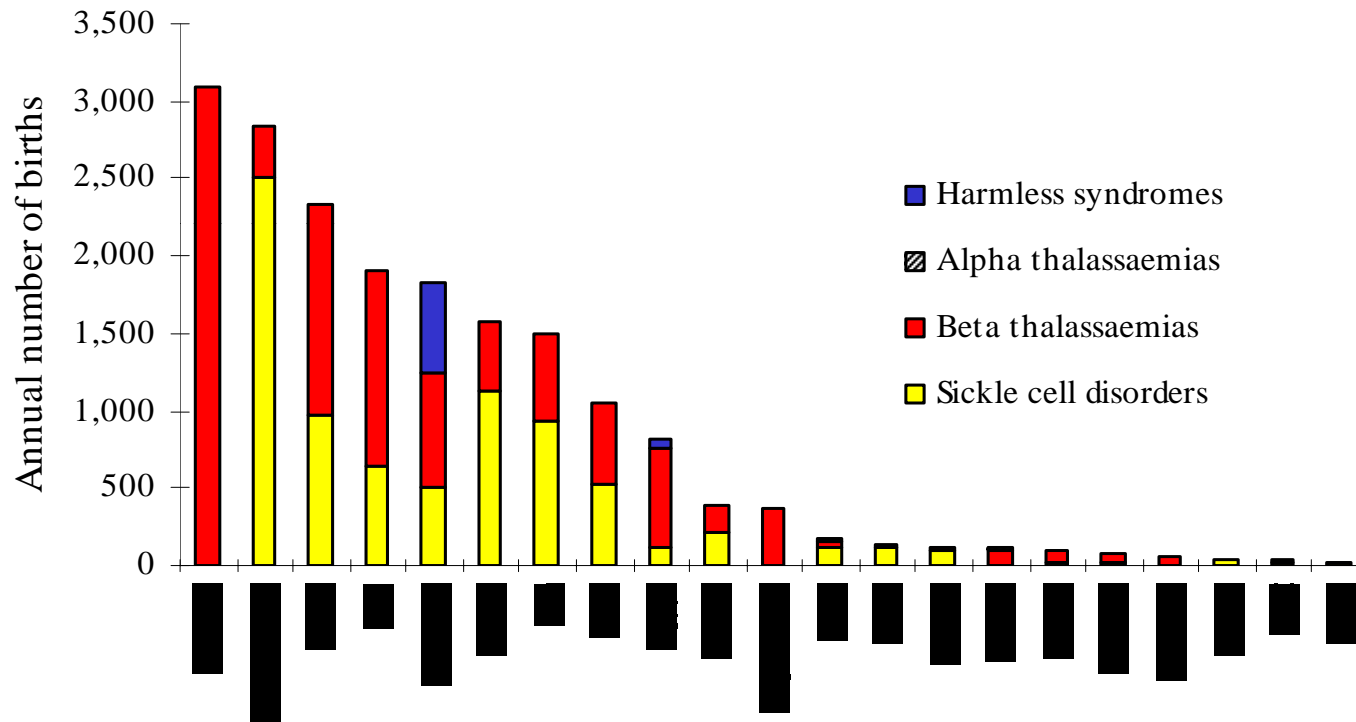
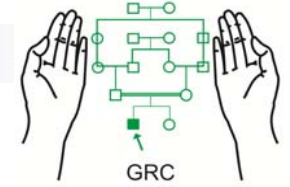
Thalassaemia Minor (Trait):

Punjabi:	4.6 %
Pathan:	5.2 %
Baluchi:	8.0 %
Sindhi:	4.3 %
Mohajirs:	5.3 %
OVER ALL:	5.1 % (8 million)

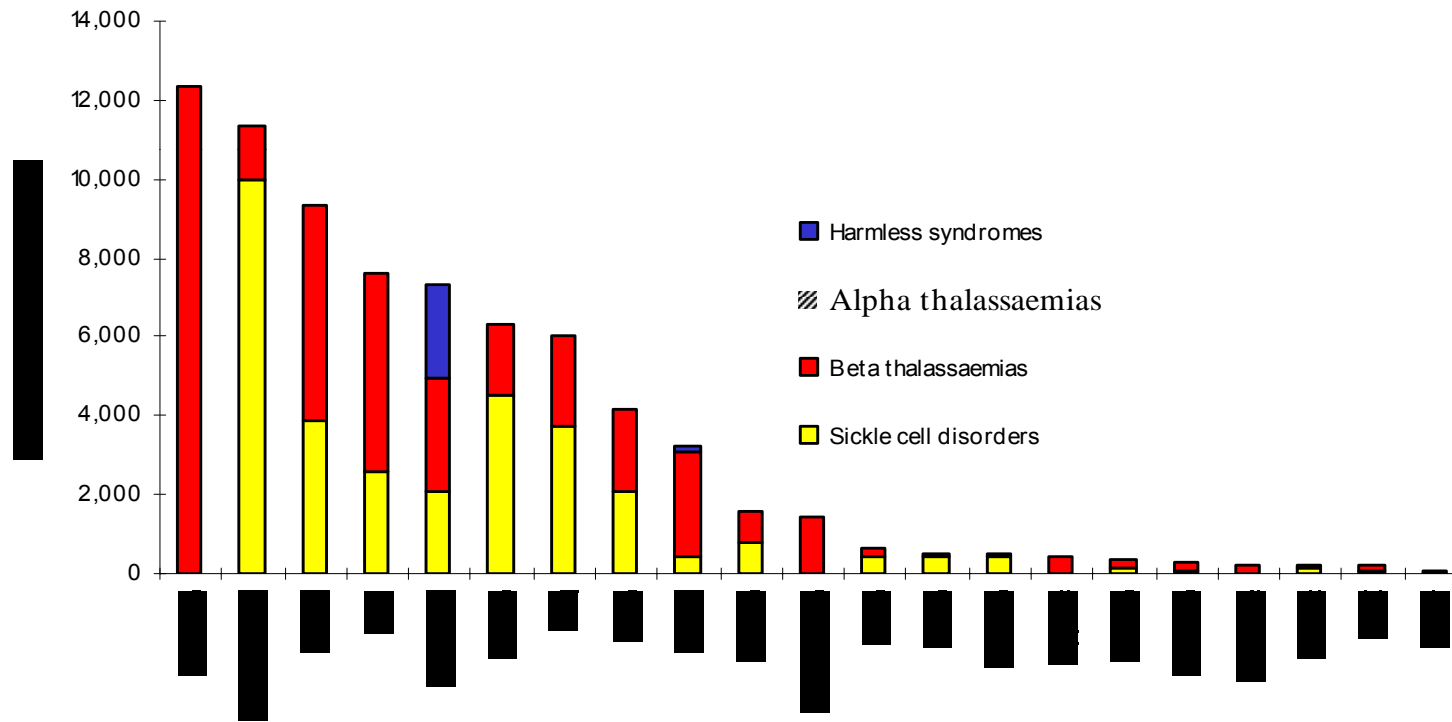
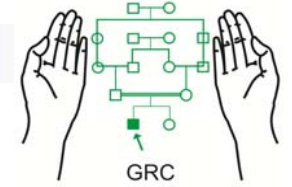
Thalassaemia Major:

Annual births:	5000
Total number:	50,000

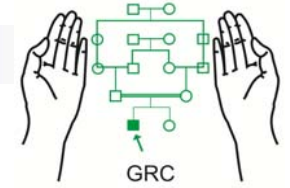
(Ahmed 1998)



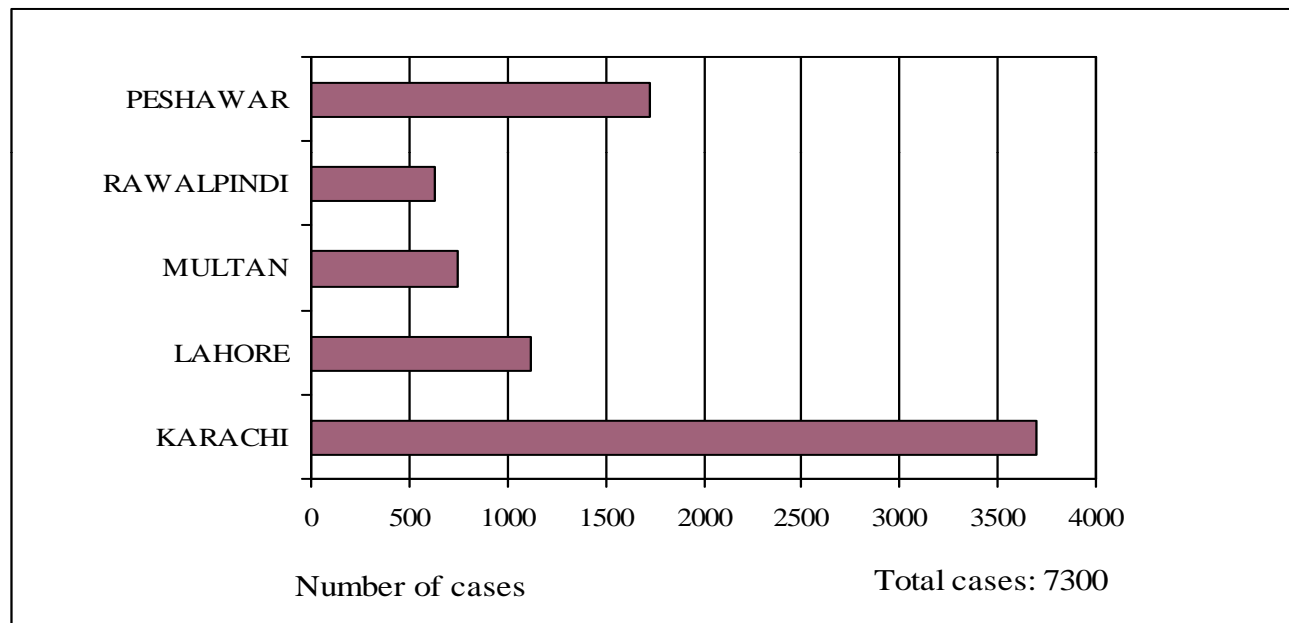
(WHO 1999)



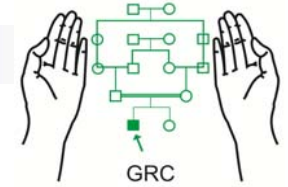
(WHO 1999)



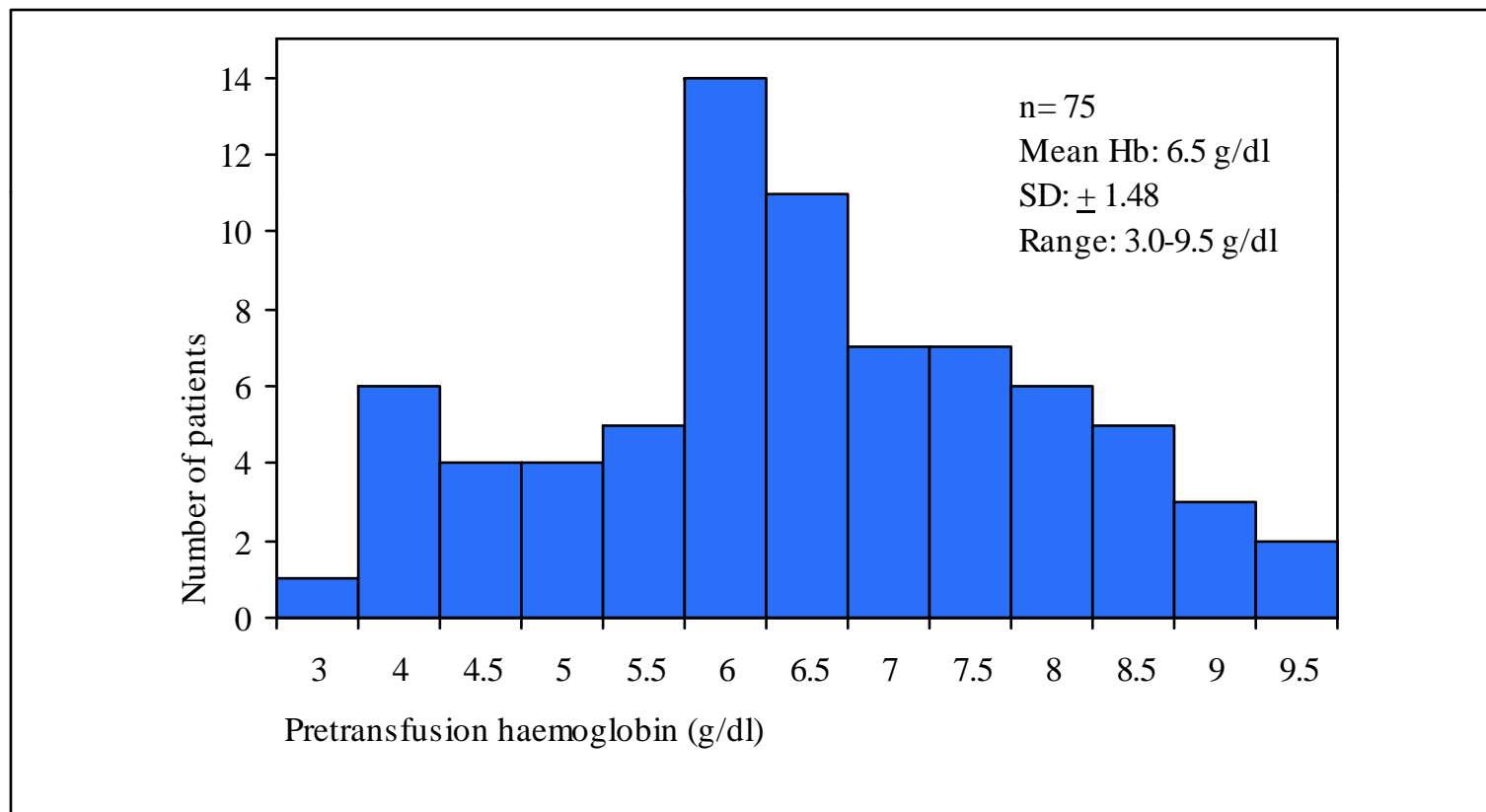
Registered Cases of Thalasaemia in Pakistan



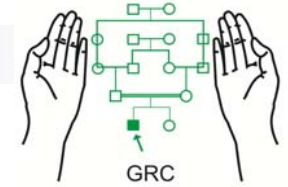
(Ahmed 1998)



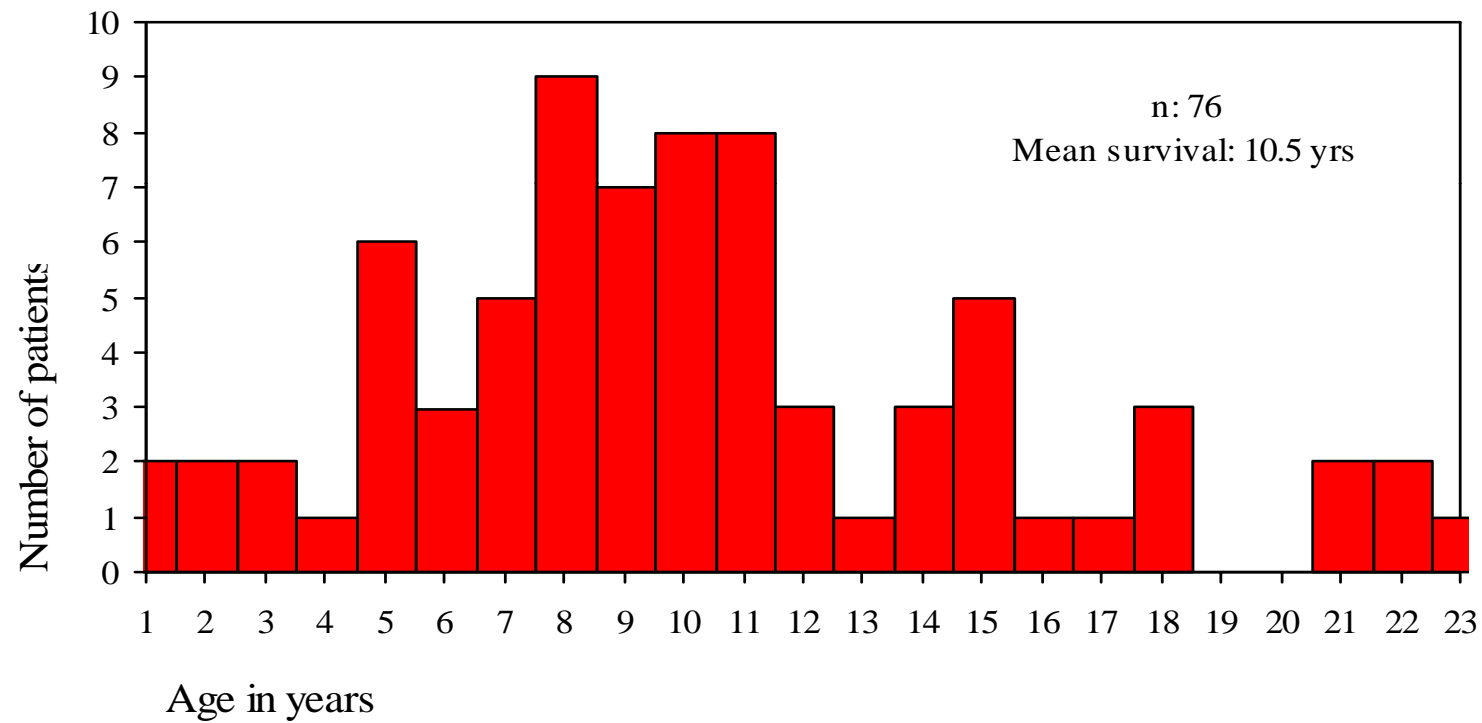
Mean Pre-transfusion Hb in Thal Major in Pakistan



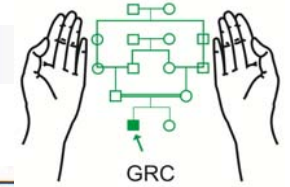
(Ahmed 1998)



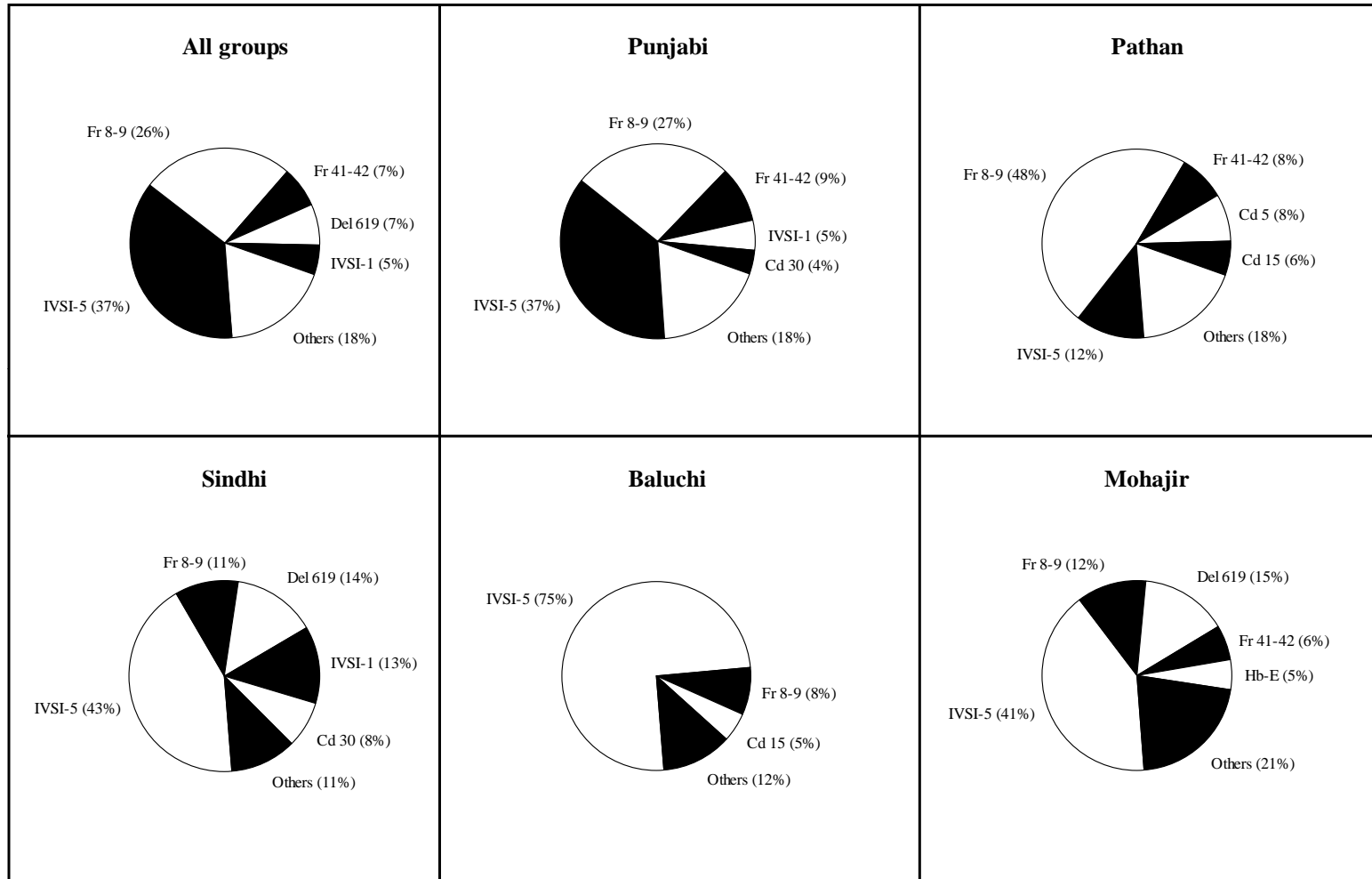
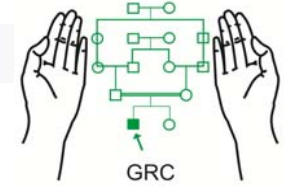
Survival Pattern of Thal Major in Pakistan



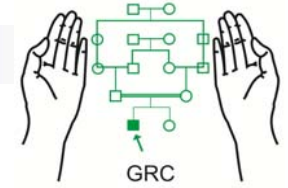
(Ahmed 1998)



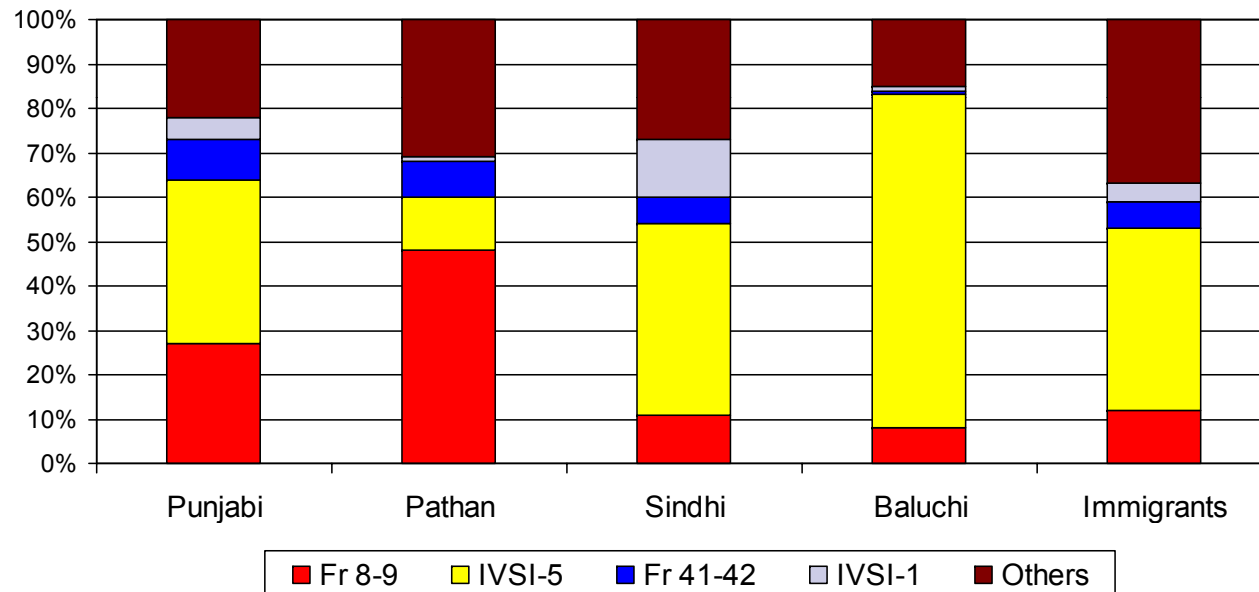
Mutation	Punjabi	Pathan	Sindhi	Baluchi	Mohajir	All
Common mutations						
IVSI-5 (G-C)	107 (27.2%)	27 (12.9%)	114 (43.9%)	131 (76.2%)	75 (41.4%)	454 (37.3%)
Fr 8-9 (+ G)	146 (37.2%)	103 (49.1%)	29 (11.2%)	14 (8.1%)	23 (12.7%)	315 (25.9%)
Del 619 bp	14 (3.6%)	4 (1.9%)	36 (13.9%)	2 (1.2%)	29 (16.0%)	85 (7.0%)
Fr 41-42 (-TTCT)	36 (9.2%)	18 (8.6%)	16 (6.2%)	1 (0.6%)	11 (6.1%)	82 (6.7%)
IVSI-1 (G-T)	19 (4.8%)	4 (1.9%)	33 (12.7%)	2 (1.2%)	7 (3.9%)	65 (5.4%)
Uncommon mutations,						
Cd 15 (G-A)	14 (3.6%)	13 (6.2%)	5 (1.9%)	9 (5.2%)	8 (4.4%)	49 (4.0%)
Cd 30 (G-C)	15 (3.8%)	1 (0.5%)	19 (7.3%)	3 (1.7%)	4 (2.2%)	42 (3.5%)
Cd 5 (-CT)	11 (2.8%)	16 (7.6%)	0 (0.0%)	1 (0.6%)	2 (1.1%)	30 (2.5%)
Fr 16 (-C)	6 (1.5%)	8 (3.8%)	6 (2.3%)	6 (3.5%)	3 (1.7%)	29 (2.4%)
Cap+ 1 (A-C)	9 (2.3%)	8 (3.8%)	0 (0.0%)	0 (0.0%)	3 (1.7%)	20 (1.6%)
Hb-E	3 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (5.5%)	13 (1.1%)
Cd 30 (G-A)	3 (0.8%)	2 (1.0%)	0 (0.0%)	2 (1.2%)	4 (2.2%)	11 (0.9%)
IVSII-1 (G-A)	6 (1.5%)	1 (0.5%)	0 (0.0%)	1 (0.6%)	2 (1.1%)	10 (0.8%)
Rare mutations						
-88 (C-T)	1 (0.3%)	2 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.3%)
IVSI-1 (G-A)	1 (0.3%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	2 (0.2%)
Fr 47-48 (+ ATCT)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.2%)
Fr 126-131 (-17 bp)	0 (0.0%)	2 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.2%)
Cd 39 (C-T)	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
IVSI minus 25	0 (0.0%)	0 (0.0%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Total	393 (100%)	210 (100%)	260 (100%)	172 (100%)	181 (100%)	1216 (100%)



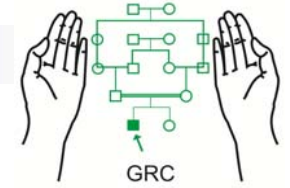
(Ahmed 1998)



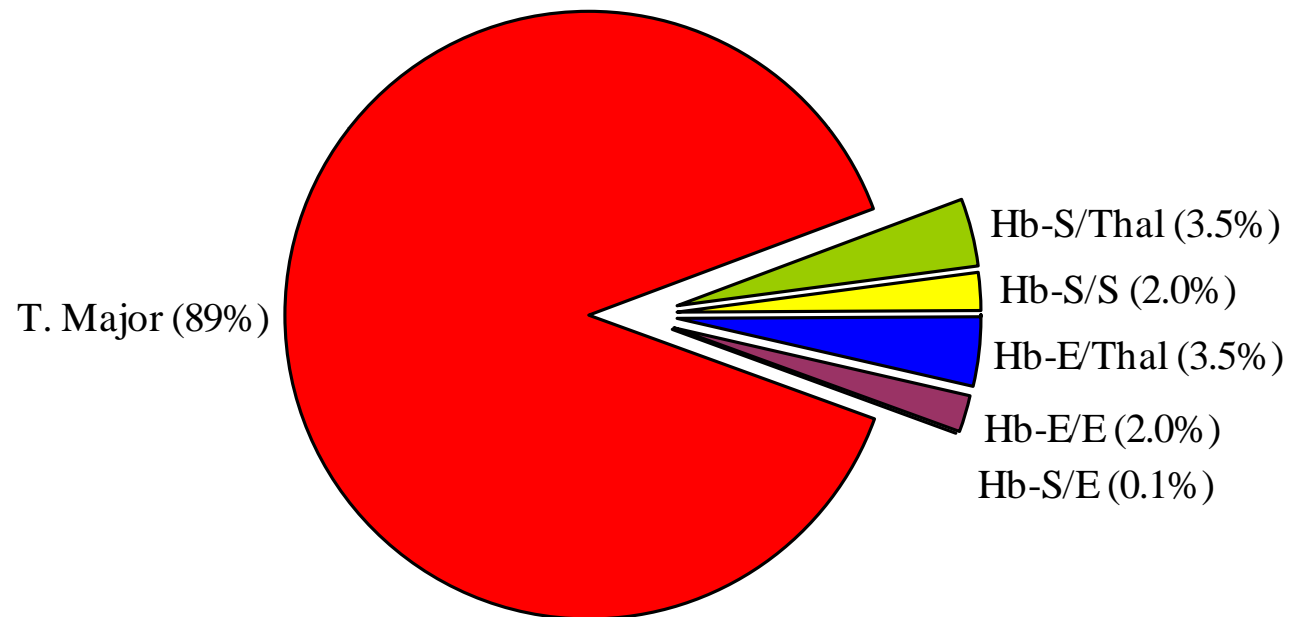
β -Thalassaemia Mutations in Pakistan



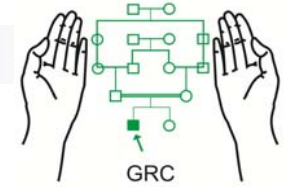
(Suhaib Ahmed et al, BJH 1996)



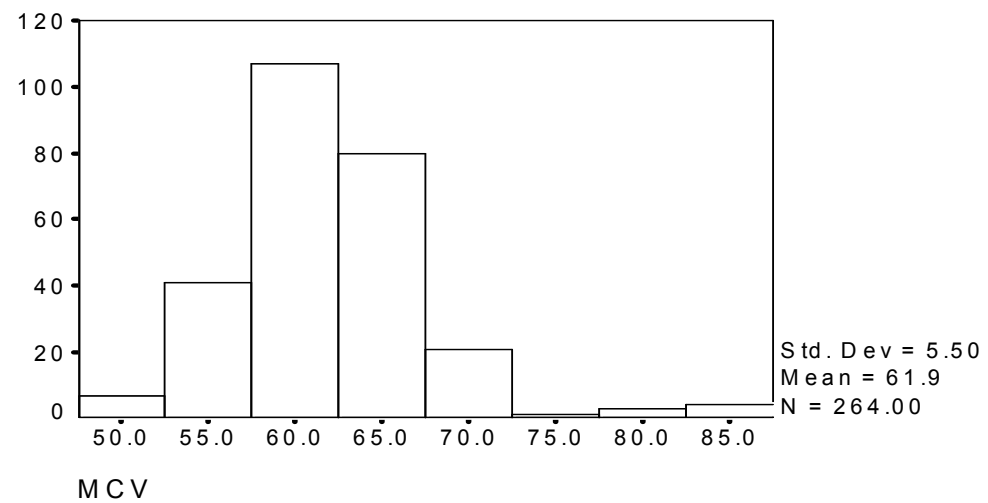
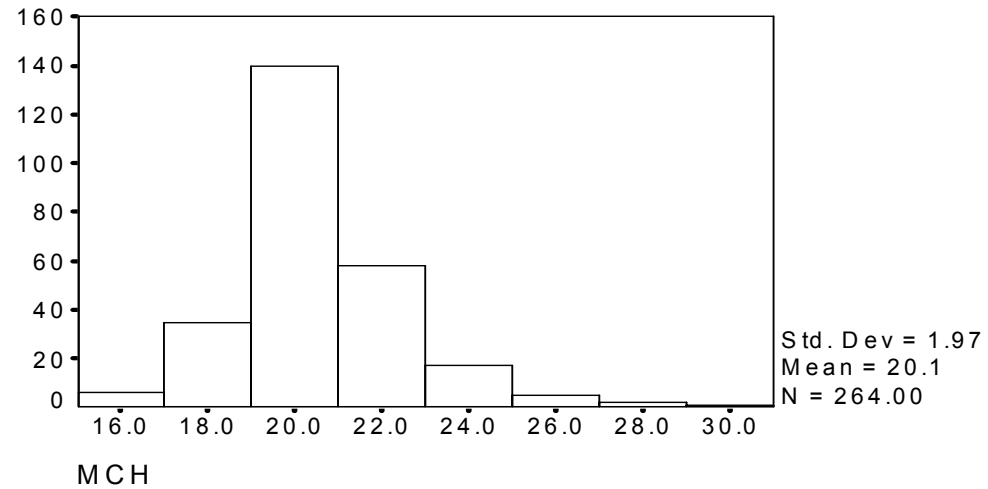
Abnormal Haemoglobins in Pakistan



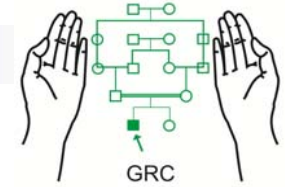
(Suhaib Ahmed 1998)



MCV and MCH in Thal Trait



(Ahmed 1998)

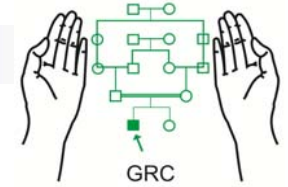


α -Thalassaemia in Pakistan

- $-\alpha^{3.7} \alpha / \alpha \alpha$ 8.3%
- $-\alpha^{3.7} \alpha / -\alpha^{3.7} \alpha$ 2.0%
- $-\alpha^{4.2} \alpha / \alpha \alpha$ 0.2%
- Anti $-\alpha^{3.7} \alpha \alpha \alpha / \alpha \alpha$ 0.9%
- $-\alpha^{\text{SEA}} -\alpha^{\text{SEA}} / -\alpha^{3.7} \alpha$?
- Non deletional α -thal ?

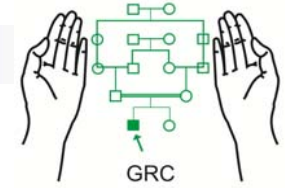
Ahmed 1998; Khan et al, Hemoglobin 2003; 27: 161-6.

$\delta\beta$ -Thalassaemia in Pakistan

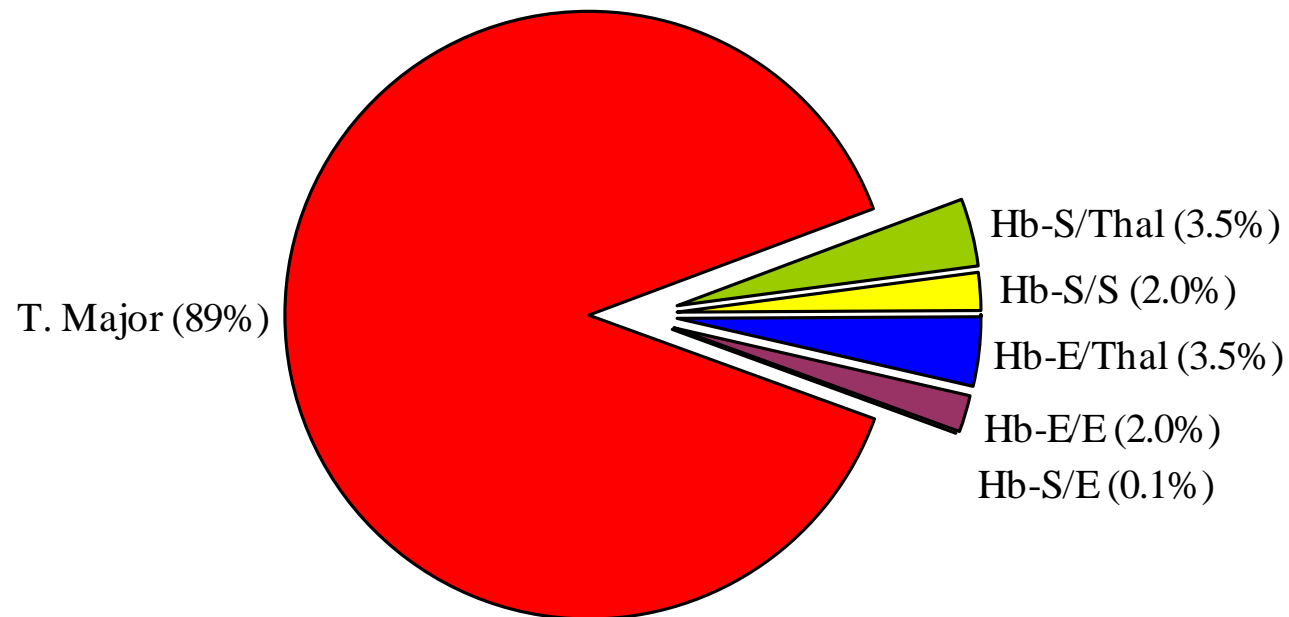


Sr.	Fam	Ethnic	Sex	Age	Trans	Spl	Hb	TRBC	MCV	MCH	HbF	HbA ₂	Mutation	Xmn-I
Heterozygous ($\Delta\gamma\delta\beta$)^o/Nor														
1.	1.	Pathan	F	30	No	-	11.5	5.15	73.2	22.3	15%	2.4%	($\Delta\gamma\delta\beta$) ^o /Nor	-/+
2.	2.	Punjabi	M	33	No	-	13.4	5.61	78.3	23.9	17%	2.9%	($\Delta\gamma\delta\beta$) ^o /Nor	-/+
3.	2.	Punjabi	F	28	No	-	10.4	4.48	72.1	23.2	15%	2.6%	($\Delta\gamma\delta\beta$) ^o /Nor	+/+
4.	3.	Punjabi	F	27	No	-	12.5	5.67	71.6	22.0	12%	2.8%	($\Delta\gamma\delta\beta$) ^o /Nor	-/+
5.	3.	Punjabi	M	6	No	-	11.3	5.91	64.0	19.1	12%	2.4%	($\Delta\gamma\delta\beta$) ^o /Nor	-/+
6.	3.	Punjabi	F	4	No	-	10.5	5.41	66.2	19.4	14%	2.3%	($\Delta\gamma\delta\beta$) ^o /Nor	-/+
Mean							11.6	5.37	70.9	21.7	13%	2.6%		
Homozygous ($\Delta\gamma\delta\beta$)^o/$\Delta\gamma\delta\beta$)^o														
7.	2.	Punjabi	M	8	No	+	10.5	5.50	63.3	19.1	100%	Nil	($\Delta\gamma\delta\beta$) ^o / $\Delta\gamma\delta\beta$) ^o	+/+
8.	3.	Punjabi	M	33	No	+	10.5	6.30	65.1	20.0	100%	Nil	($\Delta\gamma\delta\beta$) ^o / $\Delta\gamma\delta\beta$) ^o	+/+
9.	3.	Punjabi	F	2	Yes	++	5.0	2.27	71.8	22.0	70%*	1.3%	($\Delta\gamma\delta\beta$) ^o / $\Delta\gamma\delta\beta$) ^o	+/+
10.	4.	Punjabi	F	34	No	++	11.2	4.40	76.9	25.4	100%	Nil	($\Delta\gamma\delta\beta$) ^o / $\Delta\gamma\delta\beta$) ^o	+/+
11.	5.	Bohra	F	10	No	++	10.3	5.32	70.1	19.0	100%	Nil	($\Delta\gamma\delta\beta$) ^o / $\Delta\gamma\delta\beta$) ^o	+/+
12.	6.	Bohra	M	29	No	++	10.7	5.17	70.6	20.7	100%	Nil	($\Delta\gamma\delta\beta$) ^o / $\Delta\gamma\delta\beta$) ^o	+/+
Mean							9.7	4.82	69.6	21.0	100%	Nil		
Compound heterozygous ($\Delta\gamma\delta\beta$)^o/IVSI-5 (G-C)														
13.	6.	Bohra	F	3	Yes	++	8.0	3.8	72.3	21.3	20%*	1.3%	($\Delta\gamma\delta\beta$) ^o / β ^o	-/+

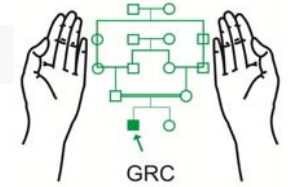
(Ahmed & Anwar 2005)



Abnormal Haemoglobins in Pakistan



(Ahmed 1998)



Thalassaemia Intermedia in Pakistan

Cause of Thalassaemia Intermedia:	n:	Mean age:	
		At 1 st transfusion:	At examination:
Xmn-I +/+ genotype	14	6 years	13 years
β^+ -mutation	6	3 years	8 years
β^+ -mutation and suspected coincident α -thal	6	11¼ years	18 years
Unidentified thalassaemia mutation	2	7½ years	12½ years
Confirmed coincident α -thalassaemia	2	9½ years	13½ years
Suspected coincident α -thalassaemia	9	9½ years	16 years
Total	39	7 years	14 years

(Ahmed 1998)