

## 4.20: CONSANGUINITY AND INHERITANCE

### 20.1 Cohort Size

It was possible to ascertain the pattern of parental marriage in 201 sibships as shown in Table 20-1.

The symbols used in denoting marriage patterns and the subtypes of cousin marriages are found in Codes Used in Sibships Sequence and Codes Used in Marriage Pattern. The types of cousin marriage are explained in section 12 on consanguinity.

<b>Cohorts with Documented Marriage Patterns</b>			
	Patients	Sibships	Pedigrees
West Bank	289	201	175
Gaza Strip	259	142	105
Others	9	8	8
Total	557	351	288

**Table 20-1: The cohort of families with documented marriage pattern**

### 20.2 Marriage Patterns and Consanguinity

The marriage patterns in the series are depicted in Table 20-2. In the West Bank, consanguineous marriage was found in 80% of the total marriages and included 66% traceable cousin marriage and a much lower figure of 13.4% of untraceable 'extended family' marriage. In the Gaza Strip, the corresponding data were 89.5% for the total consanguineous marriages that is divided into 80.4% and 9% for the cousin and extended pedigrees marriages respectively (Table 20-1).

	Cousins		Family		Total Consang.		Same Locality		Not Related		Total	
<b>West Bank</b>												
<b>Genetic</b>												
<16	66	<b>74</b>	7	<b>8</b>	73	<b>82</b>	6	<b>7</b>	10	<b>11</b>	89	<b>100</b>
16+	41	<b>61</b>	14	<b>21</b>	55	<b>82</b>	6	<b>9</b>	6	<b>9</b>	67	<b>100</b>
Subtotal	107	<b>69</b>	21	<b>13</b>	128	<b>82</b>	12	<b>8</b>	16	<b>10</b>	156	<b>100</b>
<b>Non-Genetic</b>												
<16	9	<b>47</b>	4	<b>21</b>	13	<b>68</b>	4	<b>21</b>	2	<b>11</b>	19	<b>100</b>
16+	13	<b>65</b>	2	<b>10</b>	15	<b>75</b>	2	<b>10</b>	3	<b>15</b>	20	<b>100</b>
Subtotal	22	<b>56</b>	6	<b>15</b>	28	<b>72</b>	6	<b>15</b>	5	<b>13</b>	39	<b>100</b>
Total	129	<b>66</b>	27	<b>14</b>	156	<b>80</b>	18	<b>9</b>	21	<b>11</b>	195	<b>100</b>
<b>Gaza Strip</b>												
<b>Genetic</b>												
<16	51	<b>84</b>	7	<b>11</b>	58	<b>95</b>	3	<b>5</b>	0	<b>0</b>	61	<b>100</b>
16+	42	<b>86</b>	2	<b>4</b>	44	<b>90</b>	5	<b>10</b>	0	<b>0</b>	49	<b>100</b>
Subtotal	93	<b>85</b>	9	<b>8</b>	102	<b>93</b>	8	<b>7</b>	0	<b>0</b>	110	<b>100</b>
<b>Non-Genetic</b>												
<16	6	<b>67</b>	1	<b>11</b>	7	<b>78</b>	1	<b>11</b>	1	<b>11</b>	9	<b>100</b>
16+	8	<b>57</b>	2	<b>14</b>	10	<b>71</b>	1	<b>7</b>	3	<b>21</b>	14	<b>100</b>
Subtotal	14	<b>61</b>	3	<b>13</b>	17	<b>74</b>	2	<b>9</b>	4	<b>17</b>	23	<b>100</b>
Total	107	<b>80</b>	12	<b>9</b>	119	<b>89</b>	10	<b>8</b>	4	<b>3</b>	133	<b>100</b>
<b>All OPT</b>												
<b>Genetic</b>												
<16	119	<b>78</b>	15	<b>10</b>	134	<b>88</b>	9	<b>6</b>	10	<b>7</b>	153	<b>100</b>
16+	84	<b>72</b>	16	<b>14</b>	100	<b>85</b>	11	<b>9</b>	6	<b>5</b>	117	<b>100</b>
Subtotal	203	<b>75</b>	31	<b>11</b>	234	<b>87</b>	20	<b>7</b>	16	<b>6</b>	270	<b>100</b>
<b>Non-Genetic</b>												
<16	17	<b>55</b>	5	<b>16</b>	22	<b>71</b>	6	<b>19</b>	3	<b>10</b>	31	<b>100</b>
16+	21	<b>62</b>	4	<b>12</b>	25	<b>74</b>	3	<b>9</b>	6	<b>18</b>	34	<b>100</b>
Subtotal	38	<b>58</b>	9	<b>14</b>	47	<b>72</b>	9	<b>14</b>	9	<b>14</b>	65	<b>100</b>
<b>Total</b>	241	<b>72</b>	40	<b>12</b>	281	<b>84</b>	29	<b>9</b>	25	<b>7</b>	335	<b>100</b>

Consang.: Consanguineous. Percentages in bold.

**Table 20-2: Marriage patterns by aetiological cohort and region in the sibships**

### 20.3 Consanguinity by Aetiological Cohort

There are differences in the degrees of consanguinity between the genetic and non-genetic cohorts. In the WB, the figures are 82% vs 72% and in the GS 92% vs 74% respectively. (Table 20-3)

	West Bank			Gaza Strip		
	Cousins	Family	Total cons.	Cousins	Family	Total cons.
<b>Genetic</b>						
<16	74	7.9	82	83.6	11.4	95
16+	61	21	82	85.7	4.1	90
Subtotal	68.6	13.5	82	84.5	8.2	92.7
<b>Non-Genetic</b>						
16	47	21	68	66.6	11	77.7
16+	65	9.5	74.5	57	14.2	71.4
Subtotal	56	15	71	60.8	13	74.8

Cons.: consanguinity. Family: distant family, untraceable on pedigree chart.

**Table 20-3: Percentages of consanguinity amongst the Genetic and Non-Genetic Groups by region**

### 20.4 Consanguinity over the Decades

The rate of consanguineous marriage over the 60 years leading to the study, and ending in 1997, by region are presented in 3 age cohorts; namely the sibships of children <15, the sibships of young adults between 15-30 years and sibships of patients over 35 years of age. (Table 20-3)

### 20.5 Types of First Cousin Marriages (Table 20-4, Figure 20-3)

The frequency of the types of first cousin marriages in the OPT (section 12), revealed that type A formed 35.4% (n= 83 sibships) of all cousin marriages in both regions. This was followed in frequency by type B at 13% (27 sibships) in the WB. In the GS, type C was the second most common marriage at 10.5% of the total (11 sibships). Marriages from the paternal

side were 42% (99 sibships) and from the maternal side was 20% (47 sibships). (Figure 20-1, Table 20-4)

Age	Cousins	Family	Total	Same Village	No Relation	Total	
<b>WB</b>	<15	106 <b>65</b>	19 <b>12</b>	125 <b>77</b>	9 <b>5.6</b>	28 <b>17</b>	162 <b>100</b>
	15-30	68 <b>64</b>	20 <b>19</b>	88 <b>83</b>	9 <b>8.4</b>	10 <b>9.3</b>	107 <b>100</b>
	>30	10 <b>56</b>	3 <b>17</b>	13 <b>72</b>	3 <b>17</b>	2 <b>11</b>	18 <b>100</b>
<b>GS</b>	<15	115 <b>85</b>	8 <b>6</b>	123 <b>91</b>	6 <b>4.4</b>	6 <b>4.4</b>	135 <b>100</b>
	15-30	75 <b>80</b>	5 <b>5</b>	80 <b>85</b>	10 <b>11</b>	4 <b>4.3</b>	94 <b>100</b>
	>30	15 <b>68</b>	4 <b>18</b>	19 <b>86</b>	2 <b>9.1</b>	1 <b>4.5</b>	22 <b>100</b>
<b>OPT</b>	<15	221 <b>74</b>	27 <b>9</b>	248 <b>84</b>	15 <b>5.1</b>	34 <b>11</b>	297 <b>100</b>
	15-30	143 <b>71</b>	25 <b>12</b>	168 <b>84</b>	19 <b>9.5</b>	14 <b>7</b>	201 <b>100</b>
	>30	25 <b>68</b>	7 <b>19</b>	32 <b>86</b>	3 <b>8.1</b>	2 <b>5.4</b>	37 <b>100</b>

Table 20-3: Consanguinity per 15-year age cohorts

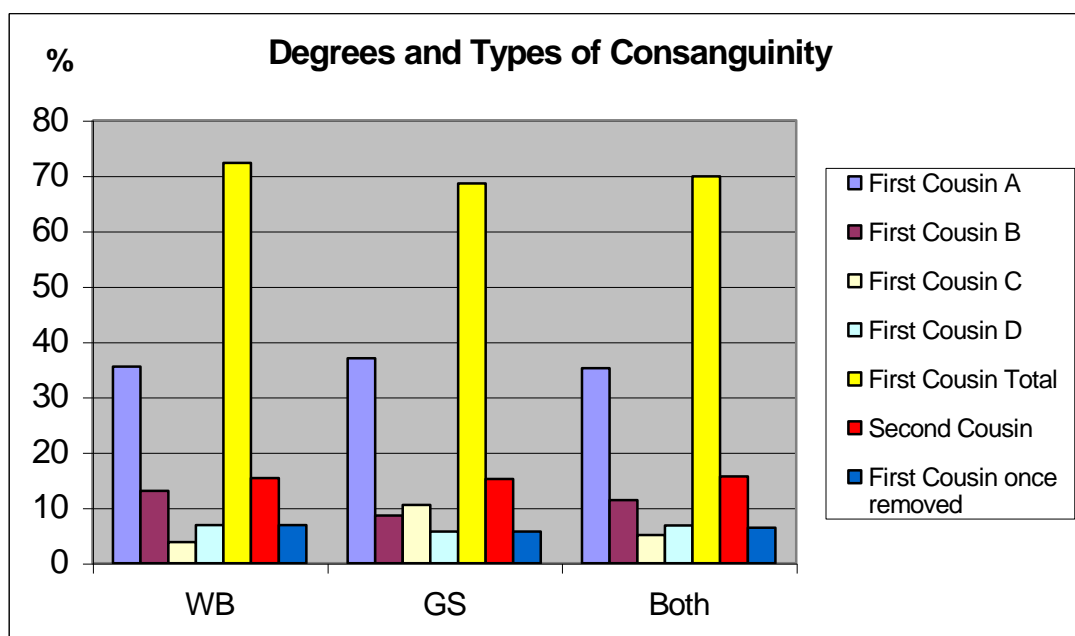


Figure 20-1: Graphics presentation of the types of consanguineous marriages

Cousin Marriages	WB		GS		OPT	
First Cousin (type A)	46	<b>35.4</b>	37	<b>35.2</b>	83	<b>35.2</b>
Double first cousin	1	<b>0.8</b>	0	<b>0</b>	1	<b>0.4</b>
First Cousin (type B)	17	<b>13.1</b>	9	<b>8.6</b>	27	<b>11.4</b>
First Cousin (type C)	5	<b>3.8</b>	11	<b>10.5</b>	12	<b>5.1</b>
First Cousin (type D)	9	<b>6.9</b>	6	<b>5.7</b>	16	<b>6.8</b>
First Cousin (either A or C)	3	<b>2.3</b>	1	<b>1.0</b>	4	<b>1.7</b>
First Cousin (either B or D)	4	<b>3.1</b>	0	<b>0</b>	4	<b>1.7</b>
First Cousin (type unknown)	9	<b>6.9</b>	8	<b>7.6</b>	18	<b>7.6</b>
<b>Subtotal first cousin all types *</b>	<b>94</b>	<b>72.3</b>	<b>72</b>	<b>68.6</b>	<b>165</b>	<b>70</b>
First Cousin once removed	9	<b>6.9</b>	6	<b>5.7</b>	15	<b>6.4</b>
Second Cousin	20	<b>15.4</b>	16	<b>15.2</b>	37	<b>15.7</b>
Second Cousin once removed	3	<b>2.3</b>	4	<b>3.8</b>	8	<b>3.4</b>
Third Cousin	2	<b>1.5</b>	5	<b>4.8</b>	7	<b>3.0</b>
Cousin details unknown	2	<b>1.5</b>	2	<b>1.9</b>	4	<b>1.7</b>
<b>Subtotal Other cousin marriages</b>	<b>36</b>	<b>27.7</b>	<b>33</b>	<b>31.4</b>	<b>71</b>	<b>30</b>
TOTAL	130	<b>100</b>	105	<b>100</b>	236	<b>100</b>
Paternal Side Marriages	54	<b>41.5</b>	49	<b>46.7</b>	99	<b>41.9</b>
Maternal Side Marriages	30	<b>23.1</b>	15	<b>14.3</b>	47	<b>19.9</b>

\* Includes 3 and 4 sibships with double first cousins from the WB and GS respectively.

**Table 20-4: Types of first cousin marriages per region**

## 20.6 Consanguinity in Clinical Conditions

The degrees of consanguineous marriage in the various clinical conditions are shown in Table 20-5. The highest consanguinity is found in retinal dystrophies, microphthalmos and albinism, reaching >80% followed by CG

(72%). The least are in anterior segment disorders (18.2%) followed by idiopathic nystagmus (28%).

	Cousins		Total Consang.		Same Location		Not Related		Total	
<b>Retina</b>										
Cone Degeneration	6	<b>100</b>	6	<b>100</b>	0	<b>0</b>	0	<b>0</b>	6	<b>100</b>
Rod-Monochromatism	16	<b>89</b>	16	<b>89</b>	0	<b>0</b>	2	<b>11</b>	18	<b>100</b>
Cone-rod	21	<b>78</b>	23	<b>85</b>	2	<b>7</b>	2	<b>7</b>	27	<b>100</b>
Leber's Amaurosis	32	<b>68</b>	39	<b>83</b>	6	<b>13</b>	2	<b>4</b>	47	<b>100</b>
Rod-Cones	42	<b>68</b>	52	<b>84</b>	6	<b>10</b>	4	<b>6</b>	62	<b>100</b>
CACR	4	<b>67</b>	4	<b>67</b>	2	<b>33</b>	0	<b>0</b>	6	<b>100</b>
Macular Degeneration	8	<b>89</b>	8	<b>89</b>	1	<b>11</b>	0	<b>0</b>	9	<b>100</b>
Vitreo-retinopathies	5	<b>71</b>	6	<b>86</b>	0	<b>0</b>	1	<b>14</b>	7	<b>100</b>
Albinism	7	<b>88</b>	7	<b>88</b>	1	<b>13</b>	0	<b>0</b>	8	<b>100</b>
Myopia	10	<b>83</b>	10	<b>83</b>	1	<b>8</b>	1	<b>8</b>	12	<b>100</b>
<b>Ant. Segment/Globe</b>										
Cong. Glaucoma	27	<b>75</b>	32	<b>89</b>	3	<b>8</b>	1	<b>3</b>	36	<b>100</b>
Cong. Cataract	30	<b>65</b>	35	<b>76</b>	4	<b>9</b>	7	<b>15</b>	46	<b>100</b>
Microphthalmos	13	<b>62</b>	17	<b>81</b>	3	<b>14</b>	1	<b>5</b>	21	<b>100</b>
Colobomas	3	<b>60</b>	5	<b>100</b>	0	<b>0</b>	0	<b>0</b>	5	<b>100</b>
Syndromatic	12	<b>55</b>	13	<b>59</b>	3	<b>14</b>	6	<b>27</b>	22	<b>100</b>
Ant. Segment Disorders	3	<b>50</b>	3	<b>50</b>	1	<b>17</b>	2	<b>33</b>	6	<b>100</b>
Idiopathic Nystagmus	1	<b>33</b>	2	<b>67</b>	0	<b>0</b>	1	<b>33</b>	3	<b>100</b>
<b>Non-Hereditary</b>										
Acquired Conditions	18	<b>56</b>	22	<b>69</b>	5	<b>16</b>	5	<b>16</b>	32	<b>100</b>
Optic Nerve conditions	10	<b>59</b>	12	<b>71</b>	1	<b>6</b>	4	<b>24</b>	17	<b>100</b>

Percentages in bold. Consang: consanguinity.

**Table 20-5: Consanguinity in the common clinical conditions**

Mode of Transmission	West Bank		Gaza Strip		All OPT	
Autosomal dominant	9	<b>3.4</b>	2	<b>0.4</b>	10	<b>1.9</b>
Suspected autosomal dominant	0	<b>0</b>	2	<b>0.4</b>	4	<b>0.8</b>
All possible AD	9	<b>3.4</b>	4	<b>0.8</b>	14	<b>2.7</b>
Autosomal recessive	229	<b>86.4</b>	226	<b>46.5</b>	462	<b>89.0</b>
Simplex (Undetermined mode) *	22	<b>8.3</b>	12	<b>2.5</b>	37	<b>7.1</b>
All possible AR	251	<b>94.7</b>	238	<b>49.0</b>	499	<b>96.1</b>
X-linked	3	<b>1.1</b>	0	<b>0.0</b>	3	<b>0.6</b>
Chromosomal	1	<b>0.4</b>	1	<b>0.2</b>	2	<b>0.4</b>
Undetermined	1	<b>0.4</b>	1	<b>0.2</b>	1	<b>0.2</b>
Total	265	<b>100</b>	486	<b>100</b>	519	<b>100</b>

\* AR mode is the most likely mode of inheritance.

**Table 20-6: Mode of transmission in 519 patients with hereditary conditions**

## DISCUSSION

### 22.19 Marriage Patterns and Consanguinity

This study has also highlighted the high prevalence of consanguinity, and in particular first cousin marriage in this community and the higher consanguinity rate among the families of the blind in comparison with the rest of the population, this is in line with findings in other countries and in particular other Arab countries including neighbouring Jordan<sup>32, 33</sup>. This difference is noticeable between sibships of the genetic cases and the non-genetic cases (Table 22-15 and 22-16). This disparity becomes wider in the <16 cohort reading 74% in the genetic cohort versus 47% in the non-hereditary cohort in the WB and 83.6% versus 66.6% in the corresponding cohorts in the GS (Table 20 -2).

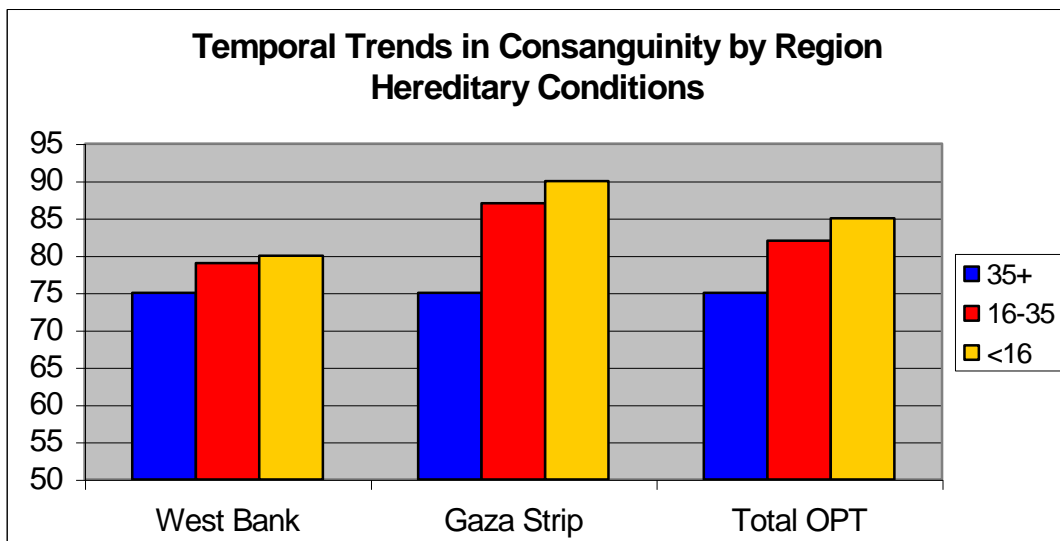
Again, this is line with the bulk of evidence that higher consanguinity causes an increase in genetic disorders<sup>49, 60, 50, 51, 105, 108, 110</sup>. In addition, the higher prenatal and postnatal mortality rates in the genetic series than in the acquired cases (Table 21-3) reflects other reports that show the increase in pre-reproductive mortality with inbreeding and the higher under 5 mortality in first cousin marriage<sup>53, 54, 109</sup>.

This high consanguinity rate is reflected in the high prevalence of recessive conditions seen in the study which parallels the rate of inbreeding in the community. This is found both in communities where cousin marriage is not the custom as well as in those who practise cousin marriages<sup>19, 20, 21, 23</sup>.

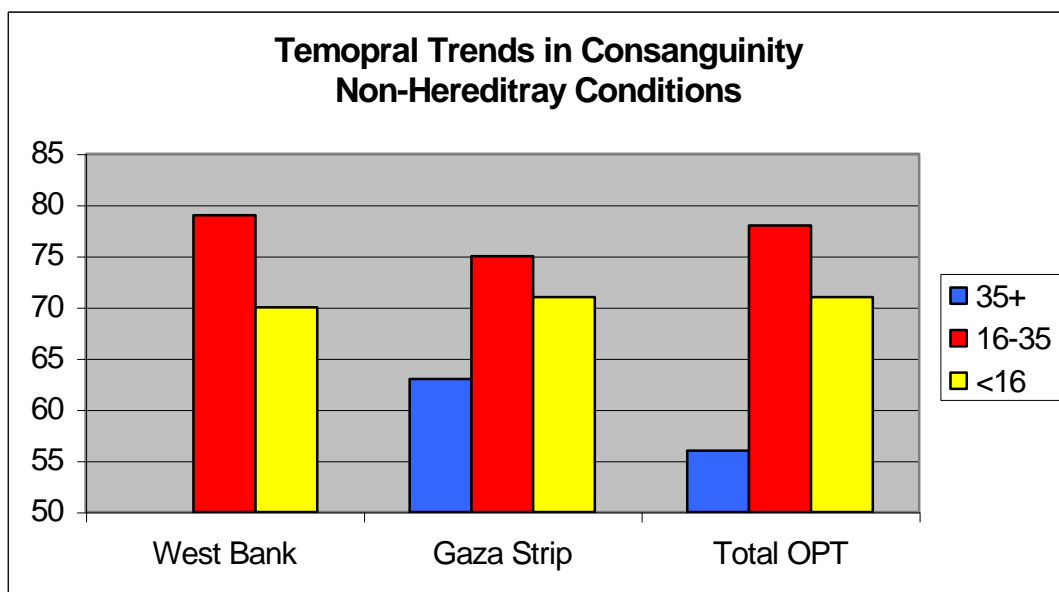
Like the rest of the Arab and Muslim world, first cousin marriages are the commonest type of consanguinity in both regions, although it is higher in the GS, with Type A (son and daughter of two brothers) being the commonest followed by Type B (son and daughter of two sister). Such information is important in any educational campaign especially in view of the common misconception that maternal cousins marriage is not a relative marriage and does not influence the outcome. Regional variations exist in the pattern of cousin marriage between the WB and GS with a higher percentage of marriages from the paternal side in the Gaza Strip (46.7%) than the WB

(41.5%). Conversely, marriage from the mother's side of the family was more common in the WB (23%) than the GS (14.3%).

The study has also shown a temporal increase in consanguinity in the 35 years in the preceding 3 decades on both Palestinian regions (Figure 20-2). In the non-hereditary cohorts, however, there is decline in the consanguinity rate perhaps in line with a decline in the consanguinity in general population.



**Figure 20-2: Percentage of consanguinity per age cohort**



**Figure 20-23: Temporal trend in consanguinity in the non-hereditary cohort**

The possibility that the rate of consanguinity, and consequently the prevalence of recessive conditions, is different between the refugees and original town and village settlers could not be concluded in this survey as there was lack of clarity in the definition of the status of refugees in the collected data.

It was also noted by the author that the presence of blindness in sibships can stigmatise these families, especially when several members are affected, and lead to their isolation, as was the case with the pedigree with CRDAI. In this pedigree, individuals descended from the mutant person (who has been identified by the members of the pedigree) are avoided by the remaining extended family. These siblings find no alternative other than taking the risk of marrying from within the family instead of marrying from the extended family or rest of the village. This can be described as double inbreeding or consanguinity fait accompli. ([click for Gaza A family chart](#))

<b>Comparison of Marriage Patterns</b>				
	<b>Cousins</b>	<b>Family total</b>	<b>Same Locality</b>	<b>Unrelated</b>
<b>Genetic Cases</b>				
West Bank	74.2	82.0	6.7	11.2
Gaza Strip	83.6	95.1	4.9	0.0
OPT Total	77.8	87.6	5.9	6.5
Jordan <sup>33</sup>	79	79	-	-
Uzbekistan <sup>43</sup>	33	33	-	-
Bradford <sup>94</sup>	62	62	-	-
<b>Non-Genetic Cases</b>				
West Bank	47.4	68.4	10.3	10.5
Gaza Strip	66.7	77.8	11.1	11.1
OPT Total	54.8	71.0	19.4	9.7
Jordan <sup>33</sup>	33	33	-	-
Uzbekistan <sup>43</sup>	-	-	-	-

**Table 22-16: Marriage patterns in the OPT, other Arab and Muslim communities**