Genetic Counseling as a key for Birth Defects & Genetic Disorders Prevention.

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Aim of genetic counselling
To reduce the incidence of genetic disorders in the population

Aim of prenatal diagnosis
- To confirm the normality of the fetus at risk for a genetic or congenital severe disease.
- To alert parents about their affected fetus status.
- Ethical consideration: choice freedom
Genetic counselling

Prenatal screening

Preimplantation diagnosis

Prenatal diagnosis
Evaluate the impact of genetic counseling on population?

Study population behavior through:
- union type choice (consanguinity)
- reproduction attitude
- acceptance/refusal of preimplantation or prenatal diagnosis

Analyze the evolution of genetic disorders epidemiology in the population.
Evaluate Impact of GC among population

• Do people interact with genetic counselling?

• Do genetic counselling reduce the frequency of handicapped severe genetic/congenital disorders?
Population sample: Tunisian families at risk of genetic disorders and birth defects

- Study carried out at Hereditary & congenital disorders department, Charles Nicolle hospital in Tunis.

- Patients, couples and families are referred from different regions of the country.
Cultural and Social Environment

- Arab (mostly), descent of Berbers [10,000,000]
- Muslim (98%)
- Mean marriage age 25.9y (females) and 32.1y (males).
- Population growth rate is about 0.99% with a birth rate of 15.5 births/1,000 population.
- Life expectancy at birth is 74.89 years.
Cultural and Social Environment

- Education is mandatory; 98% of children go to school; literacy in total population is 74.3%.
- Contraception is encouraged
- Mean family size is 1.75
- Pregnancy termination for medical reason is allowed.
- Consanguinity rate is 32%
Population referred during 2005

- Patients and families, referred for the first time in 2005 their medical dossier established during the period January 1\textsuperscript{st} to December 31\textsuperscript{st}.

- 2862 patients/families

- 57 new patient/family per week.

- People are coming from different parts of the country, more than 60% from the north.
Patients/Families referred

- Genetic Counselling
- Investigation of a probable Genetic Disease followed by Genetic Counselling
- Prenatal Diagnosis and Genetic Counselling
Impact of GC among Tunisian population

3 Questions

1-Do people ask for genetic counselling?

2-Do people accept & follow genetic counselling?

3-Do people ask and accept prenatal diagnosis and pregnancy termination?
Do people ask for genetic counselling?

143 Patients/couples, came to clinics with one question: which risk for my children to have a congenital anomaly/ genetic disorder?

Out of pregnancy

Patient/couple: own demand for genetic counselling
Why people ask for genetic counselling?

- Family history
- Personal history (advanced maternal age excluded)
- Genetic disorder / congenital malformation
When do they ask for genetic counselling?

- Out of pregnancy
- 55% before conception,
  - preconception
  - premarital
- 45% after abnormal child (fetus) conception.

Family constitution: children number

0 1 2 3 4
Before conception, they ask about the risk occurrence of genetic disease in their offspring

# family history of genetic (or suspected) disease in family members in 64%

# Consanguinity, in 36%
<table>
<thead>
<tr>
<th>Pathology</th>
<th>GC Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosomal abnormality</td>
<td>consanguinity</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>Cerebral malformation</td>
</tr>
<tr>
<td>Metabolic disorder</td>
<td>CAH</td>
</tr>
<tr>
<td>Dysmorphic syndrome</td>
<td>Hemoglobinopathies</td>
</tr>
<tr>
<td>Deafness</td>
<td>Neonatal death/miscarriages</td>
</tr>
<tr>
<td>Ophtalmologic disease</td>
<td>2 associated diseases</td>
</tr>
<tr>
<td></td>
<td>Other pathology</td>
</tr>
</tbody>
</table>
Population characteristics?

- Mean age of parents/couples
  - Female: 29 y (19-43)
  - Male: 36 y (24-56)

- Socio-economic & Education levels
  - High: 15%
  - Medium: 41%
  - Low: 44%
CONCLUSION (1)

• People ask for genetic counseling

• Before reproduction

• Demand comes from different socio-economic levels

• Percentage remains low
2-Do people accept & follow genetic counselling?
Couples at birth defect risk

• 742 couples:
  – Birth defect history
  – Diagnosis of fetal malformation during pregnancy survey

• Birth defects:
  – Major malformations of genetic origin
  – Major malformations of other origin
  – Chromosomal origin: Down syndrome….
  – Genetic disorders without congenital malformations not included.
• All couples received Genetic Counselling related to disease case.

• **Survey of these couples from 2005 to 2007**
• 60% came again to outclinics at least one time
  – To get further information and more details about genetic counselling
  – To ask for prenatal diagnosis
  – To complete medical investigations for propositus or other family’s members

• 15% did not come again, no pregnancy planned mostly due to advanced parental age.
11% did not return; they didn’t need to do.

14% did not return and we have no valuable information about.

25% do not consider GC as pertinent medical service
Do people follow genetic counselling?

• Genetic counseling provided to families at risk for a defined genetic disorder
  – **Down syndrome** (DS)
  – Congenital adrenal hyperplasia (CAH)
  – Spinal muscular atrophy (SMA)

• Genetic counseling provided to families at risk for a non defined genetic disorder
Down Syndrome

**Group 1:** 82 patients
DS confirmed for patients born on 2005 and referred to the department.

**POST NATAL DIAGNOSIS**

**Group 2:** 29 Affected Fœtus
Confirmed T21 by fetal karyotyping

**PRENATAL DIAGNOSIS**
Questions

• Did parents of group 1 receive genetic counselling?

• Is there socio-economic difference between group 1 and group 2?
### Characteristics compared between group 1 and group 2

<table>
<thead>
<tr>
<th>Socio-economic level</th>
<th>Group 1 (n=82)</th>
<th>Group 2 (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>low</td>
<td>45 %</td>
<td>35%</td>
</tr>
<tr>
<td>Medium</td>
<td>41%</td>
<td>30%</td>
</tr>
<tr>
<td>High</td>
<td>14%</td>
<td>35%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Residence place</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grand Tunis</td>
<td>52%</td>
<td>77%</td>
</tr>
<tr>
<td>North</td>
<td>48%</td>
<td>23%</td>
</tr>
</tbody>
</table>
Characteristics of group 1 and group 2

<table>
<thead>
<tr>
<th>Reference Centre</th>
<th>Group 1 (%)</th>
<th>Group 2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>University hospital</td>
<td>8</td>
<td>65</td>
</tr>
<tr>
<td>Regional hospital</td>
<td>46</td>
<td>13</td>
</tr>
<tr>
<td>PHCC</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>Private Clinics</td>
<td>37</td>
<td>22</td>
</tr>
<tr>
<td>Not followed</td>
<td>9</td>
<td>-</td>
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<table>
<thead>
<tr>
<th>Maternal Age</th>
<th>Group 1 (%)</th>
<th>Group 2 (%)</th>
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</thead>
<tbody>
<tr>
<td>&lt; 35 years</td>
<td>40</td>
<td>23</td>
</tr>
<tr>
<td>≥ 35 years</td>
<td>60</td>
<td>77</td>
</tr>
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</table>
## Genetic counseling provided & PND proposed?

<table>
<thead>
<tr>
<th>Genetic Counselling &amp; PND</th>
<th>Group 1</th>
<th>Group 1 based on maternal age risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC not provided &amp; PND not proposed</td>
<td>77</td>
<td>94 %</td>
</tr>
<tr>
<td>GC provided &amp; PND refused</td>
<td>5</td>
<td>6 %</td>
</tr>
</tbody>
</table>
CONCLUSION (2)

• Genetic counseling is less provided in PHCC than in university hospital

• Genetic counseling seems underestimated by practitioners

• When genetic counseling is provided people have the choice to accept or refuse PND

• The percentage of people who refuse PND is low
3-Do people ask and accept prenatal diagnosis and pregnancy termination?
Attitude of couples at risk of an autosomal recessive disease

Spinal Muscular Atrophy (SMA)
- severe disease Type I & II
- no treatment available

Congenital Adrenal Hyperplasia (HCS)
- severe disease: SW type
  Ambiguous genitalia
- treatment available at postnatal and prenatal period
Attitude of couples at risk of an autosomal recessive disease

- Group of 63 families with at least one SMA affected member for whom
  - genetic counselling provided and
  - prenatal diagnosis proposed for further pregnancies
Attitude of couples at risk of an autosomal recessive disease

PND was performed for 78 pregnancies (2002-2007)

- **One time** for the same couple: 68
- **Two times** for the same couple: 8
- **Three times** for the same couple: 3

-Affected fetuses 20 cases

- All pregnancies were terminated except one case because of the result delay.
Attitude of couples at risk of an autosomal recessive disease

• Group of 56 couples, parents of affected CAH patients for whom

• genetic counselling delivered and
• prenatal diagnosis combined with prenatal treatment proposed for further pregnancies.
Attitude of couples at risk of an autosomal recessive disease

- PND performed for 31 pregnancies (1999-2007)
- PND performed 2 times for the same couple: 3 cases

- 8 affected fetuses: 4 males & 4 females
- Treatment maintained for females fetuses.
- All pregnancies were maintained
CONCLUSION 3

• Genetic counseling diffuse to other family members in case of severe disease

• PND is more needed by parents in case of severe, lethal, uncurable disease (SMA vs. CAH).

• Parents ask for PND more than one time when necessary.
GENERAL CONCLUSION

• Genetic counselling remains the best and the most efficient action for genetic diseases prevention.

• Success based on people education and practitioners training.

• Followed by prenatal or preimplantation diagnosis, genetic counseling is relevant by reducing the incidence of hereditary and congenital disorders.

• Guidelines have to be defined for genetic counseling practice.

• Legislation for pregnancy termination in countries where it is accepted has to be established considering the community culture.