Effects of immigration on the incidence of congenital hypothyroidism

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Abstract

Objective: The incidence of congenital hypothyroidism (CH) has been shown to vary among different parts of the world. This could result from environmental or hereditary factors. Studies of other congenital diseases have shown that immigrants tend to retain the incidence of their country of origin while their children acquire the incidence of their new homeland, suggesting an environmental influence. This study aimed to assess the differences in the incidence of CH among immigrants from different parts of the world and to study the effects of immigration on its occurrence.

Methods: During the 9-year period between 1979 and 1987, 196 Jewish infants with primary CH were born in Israel; this constitutes an incidence of 1:3354 live births. We collected data from hospitals, endocrine pediatric clinics and the children’s parents regarding the birth place of the parents and grandparents of those infants. These data were compared with the birth place of the parents and grandparents of all infants born in Israel during that period in order to learn about the incidence of CH among infants of different origins and to compare the incidence between children of parents born in Israel and those of immigrants of the same grandparental origin.

Results: CH incidence was lower among offspring of mothers and fathers of Israeli origin (1:4717 and 1:4255 live births respectively) and higher among those of African mothers (1:2950) and Asian fathers (1:2941). Parents of Asian or African origin, born in Israel have a lower incidence of CH-affected children compared with parents of the same origin born in their own continent. This trend is reversed for European and American parents, for whom being born in Israel is related to an increase in the CH incidence in their children. The difference in CH incidence between offspring of parents born in Israel and those of parents born in their original country was statistically significant (P<0.05). In the different origin groups the gender of the parent did not influence significantly the incidence of CH.

Conclusions: Environmental changes resulting from immigration can influence the incidence of congenital hypothyroidism.

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Introduction

Primary congenital hypothyroidism (CH) is one of the common endocrine diseases which affect neonates and can lead to growth and mental retardation. Although extensively studied, its etiology has not yet been clarified. Excluding the cases of dyshormonogenesis, the occurrence of primary CH is sporadic. The incidence of CH has been shown to vary among different parts of the world. While being around 1:3000–1:4000 in Europe (1) and 1:4429 in Northwest USA (2), it can be as low as 1:6874 in Slovakia (3), 1:5632 in Hungary (4) and 1:32 377 in the black population in Georgia (5). It can also be as high as 1:2096 in Saudi-Arabia (6) and 1:918 in Asian families in England (7).

The incidence of other congenital diseases, such as neural tube defects (NTD), has also been shown to vary significantly among different parts of the world. Some studies have shown that immigrants tend to retain the NTD incidence of their country of origin while their children acquire the incidence of their new homeland (8). This might imply an environmental etiology. Previous studies have also shown some clues for environmental influence on the incidence of CH, such as seasonal variations (9, 10) and regional influences (11).

The Jewish population of Israel consists of a high proportion of immigrants and their first generation descendants. This provides a unique opportunity for the epidemiological study of diseases.

This study aimed to assess the differences in the incidence of CH among Jewish immigrants from different parts of the world and to study the effects of the immigration on its occurrence. We were especially interested in the difference in CH incidence between children of parents born in Israel and those of immigrant parents of the same origin.
Table 1: The number of CH infants (born between 1979 and 1987) and the incidence of CH among offspring of parents of different origins.

<table>
<thead>
<tr>
<th>Birth place of the parent</th>
<th>No. of CH infants</th>
<th>No. of live births</th>
<th>CH incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Israel</td>
<td>89</td>
<td>419 027</td>
<td>1:4717</td>
</tr>
<tr>
<td>Asia</td>
<td>11</td>
<td>43 613</td>
<td>1:3968</td>
</tr>
<tr>
<td>Africa</td>
<td>32</td>
<td>94 405</td>
<td>1:2950</td>
</tr>
<tr>
<td>Europe/America</td>
<td>28</td>
<td>100 418</td>
<td>1:3584</td>
</tr>
<tr>
<td>All origins</td>
<td>160</td>
<td>657 463</td>
<td>1:4115</td>
</tr>
<tr>
<td>The father</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Israel</td>
<td>86</td>
<td>365 805</td>
<td>1:4255</td>
</tr>
<tr>
<td>Asia</td>
<td>21</td>
<td>61 725</td>
<td>1:2941</td>
</tr>
<tr>
<td>Africa</td>
<td>31</td>
<td>108 463</td>
<td>1:3497</td>
</tr>
<tr>
<td>Europe/America</td>
<td>24</td>
<td>104 464</td>
<td>1:4348</td>
</tr>
<tr>
<td>All origins</td>
<td>162</td>
<td>640 457</td>
<td>1:3953</td>
</tr>
</tbody>
</table>

Materials and methods

The Israeli national screening program for congenital hypothyroidism was initiated in April 1978. During the 9-year period between 1979 and 1987, 657,463 Jewish infants were born in Israel (based on the monthly report of the Israeli Central Bureau of Statistics (ICBS)). All the newborns’ blood samples spotted on filter paper on the second or third day of life were processed at the central laboratory (the Israeli CH center) at the Sheba Medical Center, Tel-Hashomer, Israel. Initially, thyroxine (T4) was measured using the neonatal T4 RIA kit (DPC, Los Angeles, CA, USA) and this was followed by thyrotropin (TSH) measurements (neonatal TSH RIA kit; DPC) in those samples with T4 less than 70 μg/l.

From the list of all Jewish infants born during this period with T4 levels less than 70 μg/l (n=243) we excluded from this study those infants known to have thyroid binding globulin deficiency, premature infants with low T4 and low TSH, transient CH, secondary CH and tertiary CH. The remaining 196 infants were diagnosed as having primary CH. This constitutes an incidence of 1:3354 live births. A drug interruption trial at the age of about 1 year verified that all the 196 infants were indeed primary and not transient CH.

We visited the archives in maternity wards, hospitals and endocrine pediatric clinics in Israel to trace these 196 children, gather as much information as possible about them, and search for other cases of CH which were not detected by the national screening. We sent questionnaires to all the parents of CH children whose files were not found and, furthermore, we attempted to phone all families for which information about the parents’ and grandparents’ birth places was missing.

We calculated the CH incidence based on the number of Jewish CH infants born during the 9-year period to parents from a specific grandparental origin and the total number of live births during that period from the same grandparental origin (as reported by the ICBS).

For the statistical analysis we classified the parents’ and grandparents’ country of birth into four main origin groups according to the ICBS classification (Israel, Asia, Africa and Europe-America). For the grandparents’ origin we used the place of birth of the grandfather since only those data were available from the ICBS. We used the grandfather’s birth place as a marker for the original ‘genetic’ background of the parents and we compared the CH incidence among offspring of parents born in Israel and parents born abroad from the same grandparental origin.

For the statistical analysis we used χ² statistics, Student’s t-tests and one-way analysis of variance.

Results

Out of the total of 196 Jewish primary CH infants born during the 9-year period between 1.1.1979 and 31.12.1987, the parents’ country of birth was known for 82% of the infants (160 mothers and 162 fathers). Table 1 presents the number of CH infants born during these 9 years, classified according to the mother’s and father’s origin. It also includes the total number of live births from each origin during that period and the calculated CH incidence.

As can be seen in Table 1, the CH incidence was lowest among offspring of mothers and fathers of Israeli origin (1:4717 and 1:4255 respectively) and highest among those of African mothers (1:2950) and Asian fathers (1:2941). We compared the number of CH infants from each origin to the number we expected to find assuming the incidence of CH to be similar in all groups (1:4115 and 1:3953 for mothers and fathers respectively). In spite of the noticed differences in CH incidence among the different origins, the comparison between the observed and expected number of CH infants was not statistically significant for the mothers’ origin ($\chi^2=5.84$, degrees of freedom (DF)=3, $P>0.05$) or for the fathers’ origin ($\chi^2=2.83$, DF=3, $P>0.05$).

In order to examine the influence of the parent’s sex on the CH incidence we compared the CH incidence among children of mothers of different origins to the incidence among offspring of fathers of the same origin (Table 1). This difference was not statistically significant (paired $t$-test=0.07, DF=3 $P=0.95$ and one-way analysis of variance: $F[1,6]=0.004$, $P=0.95$).

Examining the CH incidence in each of the 9 years of the study we noticed substantial variations in the CH incidence from year to year in each of the origin groups. However, a one-way analysis of variance comparing the
second-generation Israeli.

incidence (1:7576) among infants of mothers who are

significant \( (P < 0.05) \) both for the mothers and the fathers.

<table>
<thead>
<tr>
<th>Grandfather's birth place</th>
<th>Mother born in the country of origin*</th>
<th>Father born in Israel</th>
<th>Father born in the country of origin*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>1:4425 (25)</td>
<td>1:4202 (22)</td>
<td>1:2941 (21)</td>
</tr>
<tr>
<td>Africa</td>
<td>1:4464 (23)</td>
<td>1:4854 (14)</td>
<td>1:3497 (31)</td>
</tr>
<tr>
<td>Europe and America</td>
<td>1:3367 (38)</td>
<td>1:3597 (40)</td>
<td>1:4349 (24)</td>
</tr>
<tr>
<td>Israel</td>
<td>1:7576 (6)</td>
<td>1:3745 (10)</td>
<td>1:4629 (24)</td>
</tr>
<tr>
<td>All origins</td>
<td>1:4184 (99)</td>
<td>1:3898 (86)</td>
<td>1:3676 (76)</td>
</tr>
</tbody>
</table>

* Difference between the CH incidence among infants of parents born in the country of origin compared with parents born in Israel is significant \( (P < 0.05) \) both for the mothers and the fathers.

four different parental origin groups resulted in non-
significant differences among the origins, both for the
mother’s origin \( (F[3,32]=0.91, P=0.44) \) and the
father’s \( (F[3,32]=0.88, P=0.46) \).

Table 2 compares the CH incidence between offspring
of parents born in Israel and those of parents born
abroad of the same origin. (the same grandfather’s birth
place).

As can be seen, in the ‘all origins’ group both mothers
and fathers born in Israel have a lower incidence of CH-
affected infants compared with parents born abroad.
While this is true for both mothers and fathers of Asian
and African origin, this trend is reversed for European
and American parents, for whom being born in Israel is
related to an increase in the incidence of CH in their
children. A comparison of CH incidence between infants
of Israeli-born parents and infants of non-Israeli-born
parents showed a significant difference both for mothers
\( (\chi^2=6.31, DF=2 P<0.05) \) and fathers \( (\chi^2=8.3, DF=2, P<0.02) \). It is interesting to note the very low CH
incidence (1:7576) among infants of mothers who are
second-generation Israeli.

Discussion

One of the methods used to differentiate hereditary from
environmental etiologies is to analyze the disease’s
incidence among immigrants. While immigration is
related to an environmental change, it has no effect on
genetic traits.

This study has shown a different (albeit not
statistically significant) incidence of CH among infants
of parents of different origins (different continents). The
parental gender had no significant influence upon the
incidence of CH.

In order to analyze the effects of immigration on the
incidence of CH we compared the CH incidence between
offspring of parents born abroad and those of parents
born in Israel of the same origin. Matching them for
origin should have reduced the hereditary effects.

We have shown that for both mothers and fathers of
African and Asian origin being born in Israel is related
to a lower CH incidence in their children, while for
European and American parents the opposite is true. A
similar influence of immigration was shown in children
suffering from NTD. Children of immigrants from Iran,
Iraq and Yemen had a higher incidence of NTD than
those of immigrants from Europe. However, children of
mothers born in Israel of a similar Asian or African
origin had a much lower NTD incidence (8).

These findings suggest an influence of environmental
factors on the occurrence of CH. For example, changes
in socio-economic status due to immigration might play
a role. It is well known that many Jews of Asian or
African origin have experienced a rise in their standard
of living after immigrating to Israel while European and
American Jews might have suffered some decrease.

On the other hand, immigration (causing cultural
changes) might affect the percentage of consanguineous
marriages and thus influence the expression of
some genetic factors.

In conclusion, this study points to the effect of
environmental factors on the incidence of primary CH.
Until these factors can be isolated, the similar incidence
of CH among infants of all origins emphasizes the need
to screen newborns of all origins for the occurrence of
the disease. Further studies comparing the incidence of
CH among children of different origins might help
clarify the environmental factors affecting its
occurrence.

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