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.
was measured using the neonatal T \textsubscript{4} RIA kit (DPC, Los

with low T4 and low TSH, transient CH, secondary CH
third day of life were processed at the central
laboratory (the Israeli CH center) at the Sheba Medical
Center, Tel-Hashomer, Israel. Initially, thyroxine (T\textsubscript{4})
was measured using the neonatal T\textsubscript{4} RIA kit (DPC, Los

Angeleno, CA, USA) and this was followed by thyrotropin
(TSH) measurements (neonatal TSH RIA kit; DPC) in

From the list of all Jewish infants born during this
period with T\textsubscript{4} levels less than 70 \textmu g/l (n=243) we
excluded from this study those infants known to have
thyroid binding globulin deficiency, premature infants
with low T\textsubscript{4} 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

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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 ($\chi^2=5.84, \text{degrees of freedom (DF}=3, P>0.05$) or
for the fathers’ origin ($\chi^2=2.83, \text{DF}=3, P>0.05$).

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

<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>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>
</tbody>
</table>

Table 1 The number of CH infants (born between 1979 and 1987) and the incidence of CH among offspring of parents of different origins (birth places).
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 (χ²=6.31, DF=2, P<0.05) and fathers (χ²=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.

**References**


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