Immunity to diphtheria among refugees in southern Italy

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Abstract
This study assessed the immune status against diphtheria of a sample of refugees (mainly Kosovars and Kurds) in southern Italy (Puglia). The 54.8% of 1128 subjects showed full protection against diphtheria, 30.1% had basic protection and 15.1% resulted seronegative for antitoxin antibody. Only from 45.9 to 73.9% of 0–10 years old refugees were fully protected while from 12.3 to 24.2% were seronegative to diphtheria with the poorest protection rate among Kurdish children from Turkey. Kosovars showed the highest protection rate to diphtheria whereas data suggest a probable endemic level of diphtheria in Iraq. The screening of refugees revealed a low coverage rate for diphtheria, especially in children, probably due to deterioration of the health service infrastructure or intermittent basic health care in the country of provenience. In terms of public health measures, there is the need of administering booster doses to all refugees coming into Italy and into other host countries to increase the coverage rate against diphtheria. The implementation of the immunization programs against diphtheria in the countries of provenience is also strongly recommended.

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1. Introduction

Before the introduction of universal vaccination, diphtheria was a major cause of death, especially in children. Following extensive childhood immunization the morbidity and mortality decreased dramatically in all industrialized countries [1].

In Italy only four cases of diphtheria were registered between 1990 and 1995, one of which was imported [2]. Since then, no other confirmed cases have been reported.

For many years it was thought that diphtheria was under control in Europe and that the elimination of indigenous cases of the disease was a target achievable by the year 2000 [3].

The re-emergence of diphtheria in Eastern countries raised global awareness of the potential for a resurgence of the disease also in countries with long-standing immunization programs. Therefore, many seroepidemiological surveys have been conducted to assess if immunity rates of 90% in European countries have been achieved in compliance with recommendations by WHO [4].

In 1999, as a result of the armed conflict in the Kosovo province of the Federal Republic of Yugoslavia, about from 500,000 to 850,000 of ethnic Albanians from Kosovo were forced to leave their homes and their land [5]. As a result of these massive movements, many Kosovar people reached the coast of Puglia principally via Montenegro and Albania. Upon arrival, the refugees, mainly children, were housed in refugee camps. In December 1999 and through the first 3 months of 2000 about 8000 Kurdish refugees reached the coast of Puglia together with immigrants from Pakistan, Afghanistan and other Middle East countries. The experience achieved in the field of public health during previous emergencies in Puglia [6–9] had permitted the planning of adequate preventive measures for this more recent exodus of Kosovar and Kurdish refugees.

Little is known on the seroimmunity levels against vaccine preventable diseases in some population of former Yugoslavia and other regions characterized by ethnic conflicts such as Kurdistan. For this purpose, a seroepidemiological study was carried out to evaluate the immunity status against diphtheria in a sample of refugees mainly coming from Kosovo and from Kurdistan area.
2. Materials and methods

2.1. Study population

Between March and April 1999 about 21,000 Kosovar refugees arrived in Puglia in an uninterrupted flow. After identification controls, the refugees were housed in eight refugee camps. However, the number of refugees in the camps varied daily due to the fact that they quickly moved to other camps in different areas of Italy. For the purpose of this study, a team of physicians and nurses went to the refugee camps. Every subject present in the camps on that day was asked to participate to the seroepidemiological survey. After obtaining informed consent, a blood sample was taken on a voluntary basis. The consent to take a blood sample from the children was obtained from their parents or legal guardians. More than 90% of the refugees gave their consent. A total of 633 refugees from Kosovo were recruited for sampling. Between December 1999 and March 2000, about 8000 refugees, mainly from Kurdistan, arrived in Puglia and were housed in the same refugee camps. The practice for the enrollment of subjects was the same used during the previous influx of Kosovars.

A total of 463 refugees from Kurdistan (261 from Iraq and 202 from Turkey) were recruited. In addition, serum samples from 32 refugees from Afghanistan were also collected. The main personal data, such as age, sex, and origin, were obtained from each subject. Detail information on the individual vaccination status was not available. The blood samples were taken to the laboratory, centrifuged and stored at $-20\,^\circ\mathrm{C}$ before being analyzed.

2.2. Serology

The samples were tested for diphtheria antitoxin IgG antibodies by a commercial quantitative ELISA kit (Novum Diagnostica, GMBH, Germany) in accordance with the instructions provided in the package insert. Previous studies indicated a good correlation between ELISA and in vitro neutralization assay and the suitability of ELISA method for screening purposes [10].

According to the WHO standard, antibody titer were classified as no protection (<0.010 IU/ml), basic protection (0.010–0.099 IU/ml) and full protection (≥0.100 IU/ml) [11].

2.3. Statistical analysis

Differences in proportions were evaluated by Chi-square test. A P-value <0.05 was considered significant. In addition, 95% confidence intervals were calculated and the Chi-square test for linear trend was used to evaluate differences in antibody coverage with increasing age. Data analyses were carried out using EPIINFO 6.02 software (CDC, Atlanta, GA, USA).

3. Results

Diphtheria antitoxin antibodies were assessed on 1128 subjects (66.5% males and 33.5% females). The mean age of refugees was 16 years (S.D. ± 12, range 11 months–72 years). Table 1 shows the distribution of diphtheria antitoxin levels of all refugees according to provenience. Overall, 15.1% of refugees were susceptible to diphtheria, 30.1% had basic protection and 54.8% resulted protected.

A significant difference in the prevalence of full protection was found among refugees (P < 0.001) with the lowest rates of full protection in the Kurdish population coming from Turkey (37.6%) and from Afghanistan (37.5%).

Table 2 shows in more detail the immunity levels of refugees from Kurdistan and Kosovo according to age groups. A relevant finding was the lack of adequate protection rate among children 0–10 years of age. In fact, only 69.5% was fully protected whereas 30.5% showed uncertain or no protection against diphtheria.

Among Kosovars, the prevalence rate of full protection in the 0–10 years age group was 73.9%, while 12.3 and 13.8% of the children resulted in susceptible and basic immunization, respectively. The age group with the lowest immunity levels against diphtheria was the 21–30 years with a prevalence of susceptible subjects of 21.7%. In the Kurdish population coming from Turkey the 24.2% of children up to 10 years of age showed no protection against diphtheria, the 18.2% showed a basic immunization and the 57.6% resulted in full protection. In Kurdish refugee children up to 10 years...
Table 2
Age-specific prevalence of diphtheria antitoxin antibody levels in the refugees by provenience

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Antitoxin antibody concentration (IU/ml)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;0.01</td>
<td>0.01–0.09</td>
</tr>
<tr>
<td>0–10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kosovo</td>
<td>51</td>
<td>12.3</td>
</tr>
<tr>
<td>Turkey</td>
<td>8</td>
<td>24.2</td>
</tr>
<tr>
<td>Iraq</td>
<td>11</td>
<td>18.0</td>
</tr>
<tr>
<td>11–20</td>
<td>34</td>
<td>13.3</td>
</tr>
<tr>
<td>Kosovo</td>
<td>16</td>
<td>13.3</td>
</tr>
<tr>
<td>Turkey</td>
<td>13</td>
<td>15.7</td>
</tr>
<tr>
<td>Iraq</td>
<td>5</td>
<td>9.4</td>
</tr>
<tr>
<td>21–30</td>
<td>44</td>
<td>20.8</td>
</tr>
<tr>
<td>Kosovo</td>
<td>13</td>
<td>21.7</td>
</tr>
<tr>
<td>Turkey</td>
<td>13</td>
<td>25.0</td>
</tr>
<tr>
<td>Iraq</td>
<td>18</td>
<td>18.2</td>
</tr>
<tr>
<td>&gt;30</td>
<td>12</td>
<td>9.9</td>
</tr>
<tr>
<td>Kosovo</td>
<td>3</td>
<td>7.7</td>
</tr>
<tr>
<td>Turkey</td>
<td>5</td>
<td>14.7</td>
</tr>
<tr>
<td>Iraq</td>
<td>4</td>
<td>8.3</td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>14.6</td>
</tr>
<tr>
<td>Kosovo</td>
<td>83</td>
<td>13.1</td>
</tr>
<tr>
<td>Turkey</td>
<td>39</td>
<td>19.3</td>
</tr>
<tr>
<td>Iraq</td>
<td>38</td>
<td>14.6</td>
</tr>
</tbody>
</table>

Chi-square test for linear trend (≥0.100 titre vs. <0.09 titre) = 112.264, P < 0.0001.

of age coming from Iraq the prevalence of subjects with antitoxin antibodies titer ≥0.100 IU/ml was 45.9%. In the age group 11–20 years, the rate of full protection against diphtheria raised to 56.6%. In the other older age groups a higher rate of fully protected subjects was found in comparison to Kurdish people from Turkey. A decrease of immunity with increasing age was observed in Kosovars and Kurds from Turkey (P < 0.001) but Iraqi (P = 0.886).

The immunity levels against diphtheria did not show gender dependent differences in all age groups and according to provenience.

4. Discussion

Diphtheria seroimmunity levels were evaluated in a sample of refugees, mainly young people, coming into Puglia during 1999­–2000. The results of the present study show that the immunity levels against diphtheria may vary widely among refugees according to the origin and the different socio-economic conditions of the country of provenience. When considering the fact that the sample of refugees tested was mainly represented by young people, the immunity rates against diphtheria found seemed not to be satisfactory. In previous surveys in Italy from 77.0 to 85.5% of the children of the same age group resulted in full protection and only from 1.0 to 7.2% completely lacked diphtheria antitoxin antibodies [12,13]. In Italy the recommended vaccination schedule is 3, 5 and 11 months, with a booster dose at the age of 5–6 years. In Turkey diphtheria–pertussis–tetanus (DPT) vaccine is used as a primary series of four doses with a booster dose at the age of 6–7 years. Recently, a serosurvey reported a prevalence of more than 79% with full protection against diphtheria in Izmir (Turkey) with the highest rate of protection in the 5–9 years age group [14]. In contrast, our data regarding Kurdish from Turkey evidenced that only the 37.6% of all refugees were fully protected and that only 57.6% of children were fully protected. Hence, it may be supposed that there is an inadequate vaccination of Kurdish children from Turkey. Also adults show a significantly lower protection rate in respect to adults of the latter survey. Such a finding needs more confirmation and efforts by Turkish health authorities to improve the immunization of ethnic Kurdish.

Kurdish refugees coming from Iraq show a different pattern of immunity against diphtheria. The phenomenon of decreasing immunity to diphtheria among adults observed in other refugee populations studied was not observed in Kurds from Iraq. In fact, although low, the immunity levels among adults more than 20 years were significantly higher than those found among Kosovars and Kurds from Turkey. Probably this pattern of immunity reflects an endemic level of diphtheria in Iraq. However, in Iraq infants receive only routine primary vaccination with three doses of DPT (at 2, 4 and 6 months) without booster doses [15]. Therefore, the unsatisfactory protection rate among children could be
due to a lack of basic immunization and of booster doses. In addition, particularly during the last decade, a deterioration of the health service infrastructure or intermittent basic health care in Iraq, due to the recent armed conflict and the following embargo, could have led to a decline in the immunization rates of the population and in particular of Kurds.

A previous study on Kosovar refugees who arrived in Ireland in 1999 estimated the coverage rate for DTP vaccine to be 54% [16]. Nevertheless, taking into consideration that more than 50% of the Kosovar refugees tested were children 0–10 years of age, the results of serosurvey showed a sub-optimal coverage levels for diphtheria. Several factors raised concerns that the coverage level against vaccine preventable diseases might have been inadequate among Kosovar refugees, especially younger people. First, many refugee children were reported to be incompletely vaccinated because of the ethnic conflict in the region since 1990 [17,18]. Second, the poliomylitis outbreak that occurred in 1996 in Kosovo involved several unvaccinated children [19]. These data seem to confirm that during recent years, before the crisis in the Balkan area, a decrease in the immunization levels might have occurred in Kosovo. Regarding Kosovar adults, the decreasing immunity to diphtheria in elderly subjects shows a trend similar to that observed in other European countries [12,20–22].

WHO has outlined that to achieve sufficient herd immunity a minimum immunity rate of 90% in children and 75% in adults is required [23]. The epidemic of diphtheria, that recently occurred in Russia and in the NIS of former Soviet Union has emphasized the importance of maintaining adequate immunity levels both in children and in adults.

The results of our serosurvey show that neither children nor adult refugees have a satisfying degree of protection against diphtheria. Although this study was conducted on a sample of refugees who may be considered biased in respect to the general population, the results highlight the need for improving the vaccination coverage against diphtheria in the refugee population.

In addition, the continuous turnover of immigrants and refugees coming from endemic developing countries may represent a possible risk for a reintroduction of C. diphtheriae in the local population considering that, as previously reported, a large proportion of adult population has no longer diphtheria antitoxin at protective levels [12,13].

In terms of public health measures, there is the need of administering booster doses to all refugees coming into Italy to increase the coverage rate against diphtheria. Moreover, the findings of the present study seem to endorse the vaccination policy for immigrants and refugees of host countries, which provide for immunization measures to refugees at arrival or shortly after. International guidance has stated that there are no particular risks associated with the immunization of previously vaccinated people for the vaccines that were offered [16]. Finally, the implementation of the immunization programs against diphtheria in the countries of provenience of the refugees is also strongly recommended.

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References


