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Natural Immunity to Hemophilus influenza Type b in Children, South of Iran: Need for Vaccination

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Abstract: Hemophilus influenza type b (Hib) infection has a high morbidity and mortality rate especially in children less than 5 years of age. The incidence of Hib disease in Iran is not known and Hib vaccine is not included in the National Immunization Program. The aim of the present study was to investigate the level of antibody to Hib of children five years or younger living in Jahrom, Iran. Three hundred eighty six children 5 years or younger were selected by random sampling method. A blood samples were taken from those children. Anti-Hib IgG antibody (anti-PRP) level was determined in the serum by using anti-Hemophilus influenza IgG EIA kit (IBL, Germany). An anti-PRP antibody levels of 0.15 μg mL^{-1} and over were accepted as the natural immunity. The mean concentration of Hib antibody was 0.94±0.480 μg mL^{-1}. Natural immunity was determined in three hundred and twenty six (84.5%) of the children. The proportion of natural immunity was increased from 64.9% among children = 12 month old to 95.2% in children aged 49-60 month ($p<0.001$). The exposure rate of children with Hib was higher than expected, even in children who were just a few months old. Present data revealed need to be introducing Hib conjugate vaccine in the National Immunization Programs.

Key words: Natural immunity, hemophilus influenza Type b, children, vaccination

INTRODUCTION

Hemophilus influenza type b (Hib) is a common reason of serious diseases such as meningitis, septicemia, pneumonia, respiratory infections, epiglottitis and otitis media in children universal (Ghazvini *et al*., 2007; Watt *et al*., 2009; Tambekar *et al*., 2007; Mashouf *et al*., 2006; Nikakhlagh *et al*., 2011; Rekabi *et al*., 2008). Also, Hib disease is an significant foundation of vaccine-preventable morbidity and death (Peraza *et al*., 2004) in young children in developing countries. Hib caused about 8.13 million severe illnesses and 371,000 deaths in children aged 1-59 months global in 2000 (Cherian *et al*., 2009). In study that was done in Iran among children under 6 years old, Hib organism was isolated from throat of 11% children. A lot of countries have introduced Hib conjugate vaccines into their routine childhood vaccine schedules and the force on insidious Hib disease has been consistently notable (Heath *et al*., 2000; Muganga *et al*., 2007). Wang *et al*. (2008) has regarded that almost 60% of insidious Hib cases in children are preventable, in that they are happening in unimmunized or incompletely immunized children among whom the occurrence of Hib disease is expected to be about 15 times that of fully immunized children. A study conducted by Heath *et al*. (2000) in United Kingdom investigated protection of Hib diseases among children under 6 years old who received three dose of Hib conjugated vaccine. Vaccine protection was reported about 98% (Heath *et al*., 2000). In Cuba the Hib vaccination was introduced in the National Immunization Program in 1999, for all the children born between January 1998 and October 1999 (Peraza *et al*., 2004). After that, the incidence of Hib disease has decreased to 0.1 per 100,000 inhabitants, in 2001. Despite the availability of a protective vaccine, few developing countries are using Hib vaccine in their immunization programs (Peraza *et al*., 2004). The major difficulty to the routine use of Hib conjugate vaccine in most non-industrialized countries is cost (Peraza *et al*., 2004; Lee *et al*., 2008). In addition to capsule of Hib, there is another factor lipopolysaccharide of this microorganism participate in its virulence (Schweda *et al*., 2006). Hib vaccine consists of its capsule (Heath *et al*., 2000). Some researches have been done on DNA vaccine for infectious diseases (Rawat *et al*., 2007) and Plant-Derived Human Vaccines (Aliahmadi *et al*., 2006). The effects of diet supplementations (Jafari *et al*., 2008; Batool *et al*., 2002) and some trace elements

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(Mahmoud *et al*., 2009; Hosseini *et al*., 2011) have been determined on immune response to vaccination and to infectious diseases.

In Iran the Hib vaccination is still not included into the National Immunization Program.

Some studies have been done on Iranian primary school children immune response to BCG vaccination (Sakha and Behbahan, 2008) and Measles vaccination (Zamani and Daneshjou, 2006) but there is no study of immunity to Hib in Iran.

This is the first study about immunity to Hib in Iran. The intention of this study was to calculate the natural acquired immunity to Hib in a group of well children 5 years or younger in Jahrom, Iran.

MATERIALS AND METHODS

This study was performed between February and May 2008, in Jahrom, Iran. Three hundred and eighty seven well children attending urban health care centers were selected randomly. No child had previously received Hib vaccine or had received any immunoglobulin preparation or blood product. Demographic and medical data were obtained through a personal interview with the mothers. Blood samples were drawn from children and the serum was stored at -20°C until further analysis. Serum capsular polysaccharide specific IgG antibody concentration was measured by an ELISA kit (IBL, Germany). Results are expressed as μg mL^{-1}. Subjects who had Hib antibody level ≥1.0 μg mL^{-1} as long term protection, between 0.15 to <1.0 μg mL^{-1} as short term protection and <0.15 μg mL^{-1} as no protection (Peraza *et al*., 2004; Kayhty *et al*., 1983). Also anti-PRP antibody levels of 0.15 μg mL^{-1} and over were accepted as the natural immunity or protective level (Ocaktan *et al*., 2006).

Ethics: The study was approved by the ethics committee of Jahrom University of Mmedical Sciences.

RESULTS

The mean concentration of anti-PRP specific IgG antibody and the proportions of children with an antibody groups at different ages in Iramian children aged 5 years or younger are shown in Table 1.

The mean concentration of Hib antibody was 0.94±0.480 μg mL^{-1}. This amount was 0.982±0.462 μg mL^{-1} for girls and 0.898±0.496 μg mL^{-1} for boys. But the mean concentration of antibody was not different between two sex ($p>0.05$).

A significant increase in mean concentration of antibody was found between children aged ≤12 months with 49-60 months (2.05 fold increase, $p<0.001$) and between children aged ≤12 months with 37-48 (1.83 fold, $p<0.001$). The mean concentration of Hib antibody increased by advancing of age groups ($p<0.001$) be expecting between aged ≤12 months with 13-24 months which was small and no significant.

Three hundred and twenty six children (84.5%) had natural immunity against Hib microorganism. The greatest percentage of children (69.2%) corresponded to protective titers of antibodies as long term protection, correspondingly. Titers expected to be protective for immediate but short-term periods were observed in 59 children (15.3%). One hundred and forty five girls (74.2%) had long term protective antibody level that it was not contrasting to boys (44.9% $p>0.05$). The proportion of long term protective level was increase from 45.9% among children ≤12 months old to 86.7% in children aged 49-60 months ($p<0.001$). Forty five (18.6%) children aged over 24 months had anti-PRP IgG titers under the level associated with long term protection (1.0 μg mL^{-1}).

DISCUSSION

In this study, about 85% children had the Hib antibody concentrations above 0.15 μg mL^{-1} (a defending threshold). Also, the percent of protective level increase with advance age group. This might suggest due to more contact to Hib microorganism during advancing age.

In this study, about 85 and 69% children five years old or younger had natural immunity level and long-term protective level of Hib antibody. Kayhty *et al.* (1983) in Finland has shown that 79% of children 4 to 5 years of age had protective concentrations of antibody and 32 had titers greater than 1 μg mL^{-1} (Kayhty *et al.*, 1983). Also in India, demonstrating high pre-vaccination

Table 1: Serum concentration of Hib antibody among Iranian children

Age (month) (No.)	Mean concentration (μg mL^{-1}) (95%CI)	Concentration <0.15 μg mL^{-1} (%)	Concentration 0.15-<1.0 μg mL^{-1} (%)	Concentration >1.0 μg mL^{-1} (%)
≤12 (74)	0.61±0.48	35.2	18.9	45.9
13-24 (70)	0.71±0.43	22.9	25.7	51.4
25-36 (84)	0.97±0.38	09.5	14.3	76.2
37-48 (75)	1.11±0.43	08.0	10.7	81.3
49-60 (83)	1.24±0.40	04.9	08.4	86.7
Total (386)	0.94±0.48	15.5	15.3	69.2

anti-PRP titers in over 80% of children over 4 years of age (Acharya *et al*., 1997). In a study conducted by Arvas *et al.* (2008) 68.2% unvaccinated children 19-36 month aged had natural immunity. In Turkey, 65.3% children 6-60 month of age living in the Ankara had natural immunity to Hib (Ocaktan *et al*., 2006). In a study conducted by Berrington *et al.* (2006) 51% of term infants have anti-PRP antibody above 1.0 μg mL^{-1}. In England, 10% of children had Hib antibody concentration less than 0.15 μg mL^{-1} and only 10% had Hib antibody 1.0 μg mL^{-1} and over at 2 month old and pre-vaccination (Heath *et al*., 2000).

The mean concentration of Hib antibody in both studies (0.48 μg mL^{-1} in Finland and 0.94 μg mL^{-1}in India) (Kayhty *et al*., 1983; Acharya *et al*., 1997) were lower than mean concentration obtained in this research (2.71 μg mL^{-1}).

In our study, the percent of natural immunity increase with advancing age. Also the rate of natural immunity gradually increases with age among Japanese children (Ishiwada *et al*., 2007). In Egypt, 95.5% of the children under five years old had a protective level (Redwanel and Elsawy, 2005).

This study and others shows that the Iranian children and others had high anti-PRP concentrations and provides strong evidence that children in some developing countries acquired natural active immunity to Hib at an early age (Heath *et al*., 2000; Clemens *et al*., 2003; Tastan *et al*., 2000; Puliyel *et al*., 2001). Immunogenicity and safety protein-polysaccharide conjugate Hib vaccines reported in several studies (Berrington *et al*., 2006; Goldblatt *et al*., 1996). Lagos *et al.* (2009) was shown that Hib vaccines were highly immunogenic and safe in children infants. They have almost completely eliminated Hib disease in both developed and developing countries in which they are routinely used (Watt *et al*., 2009). Muganga *et al.* (2007) reported that vaccine effectiveness of two or three doses of Hib vaccine against purulent meningitis was 52% (95% confidence interval, 5-75%) in Rwanda. Also, Lee *et al.* (2008) reported about 92% vaccine effectiveness in Uganda. These results support the recommendation of the World Health Organization about a strategy for administration of Hib vaccination to all children under 5 years old in IRAN. Further studies on this matter with bigger samples in various areas of IRAN are recommended.

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