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Prevalence of Immunity against Infection of Hepatitis A and Hepatitis B in Children Cochabamba, Bolivia

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Abstract

Background: Knowing the immune status against Hepatitis A and Hepatitis B in children Cochabamba, Bolivia and seroepidemiological association.

Study method: A seroepidemiological study (n=424) and HBV (n=436) of HAV in children living in Cochabamba, Bolivia, 2010. A questionnaire was completed by parents for demographics, socioeconomic was performed and housing and blood samples were collected, An ELISA was used to measure antibodies to hepatitis A and B.

Results: As regards Hepatitis A, the overall prevalence 95.4 (95% CI -93.5 to 97.4) were immune. The immunity was higher in children of 5-10 years (97%) and tweens 10-13 years (97.9%), the prevalence of immunity was also higher in subjects whose parents had a low level of education (99, 4 to 99.5%) living in rural areas (98.7%) lived in municipalities with an urban development under (99.1 to 100%), had water delivered home by an oil sisterna (99.4%) and spoke Quechua at home (99.5%).

As to Hepatitis B virus, immunity that presented to the IgG anti-HBs IgG antibodies in the cohort of pre-universal vaccine was 5.8% (95% CI: 3.3 to 8.3%); was higher in men (9.1%), and those living in the suburbs (9.7%). The anti-HBsIgG prevalence among cohort universal post-vaccine was 37.9% (95% CI: 28.5 to 48.1%), and was higher in children who speak Quechua at home (51.0%), those living in the suburbs (53.9%), and those born in 2005 (72.7%). Neither cohort showed differences concerning education of parents. The prevalence of IgG anti-HBc was 1.1% among post universal vaccine cohort and 1.2% among pre-universal vaccine cohorts (p>0.05).

Conclusion: The susceptibility to infection by the hepatitis A child reaches 4.5%. There is a high susceptibility of contracting hepatitis B infection by low immunity was identified.

Keywords: Bolivia; Hepatitis A; Hepatitis B; Immunity; Universal; Hepatitis B vaccination

Introduction

The Infections of hepatitis A and hepatitis B viral are a public health problem worldwide. Hepatitis A virus (HAV) infects 212 million individuals each year, including 55 million symptomatic cases and 35,245 deaths. Lifelong protection is observed after HAV infection, but the disease burden of HAV increases with increasing age [1]. Only 10-50% of infections in children are symptomatic, whereas 70-95% of infections in adults cause jaundice or complications, including liver failure. A dramatic decline in the endemicity of HAV has occurred in many parts of the world over the past few decades due to improvements in socioeconomic status, accessibility to clean water, sanitation, and the introduction of effective immunization programs. This global decline in HAV endemicity has been observed mainly in countries with a human development index (HDI) >0.58 or a water coverage rate >55%. Since 2005, only three Latin American countries (Argentina, Panama, and Uruguay) have introduced [2-4]. HAV vaccinations into their routine immunization programs.

The Plurinational States of Bolivia conducted three studies on HAV epidemiology between 1987 and 2003 in the Southeastern region of Santa Cruz. The observed seroprevalence in 5-year-old children ranged from high-medium to low [Bartoloni et al., 1989, 1999; Gandolfo et al., 2003]. In addition, over the last few decades, Bolivia has experienced improvement in education, health, and income according to the HDI, which increased from 0.596 in 1990 to 0.729 in 2007. In addition, a decrease in social inequality occurred according to the Gini index, which decreased from 0.618 in 2000 to 0.564 in 2007 [5-7]. Few studies have been conducted in Bolivia [8-10], and most have been in the same geographical area. Therefore, insufficient data are available to determine current HAV epidemiological patterns and trends with certainty. The endemicity of HAV may have changed to an intermediate or low level.

The hepatitis B virus (HBV) infects an estimated two billion people worldwide, with 378 million having chronic infections; this large affected population leads to 4.5 million new HBV infections and 620 000 deaths per year. In various South American countries, the carrier rate ranges from low hepatitis B surface antigen [HBsAg] less than 2%) to intermediate endemicity (HBsAg of 2–8%) and HBV infection is probably most commonly transmitted in adulthood through sexual intercourse. Since 1990, all American countries have gradually introduced HBV vaccination [11-13]. The lowest rate of coverage with three doses of the HBV vaccine remains in children, year of age in Andean countries, with Bolivia having the lowest coverage rate (83%) in 2010. Bolivian data about hepatitis B profile were obtained from blood bank records and observed prevalences of HBV infection ranging from 2.0 per 1000 in 1993 to3.8 per 1000 in 2002, or from seroepidemiological studies developed in children in 1990 (0.9% in native children and 4.3% in Japanese children), in1993 (0.35%) and in 2003 (hepatitis B core (HBc), 1.1-3.8%).

The Plurinational State of Bolivia has low HBV endemicity, and introduced universal vaccination against hepatitis B in 2000 as a national wide campaign as part of its Expanded Program on Immunization (EPI). The current protocol involves three doses at 2, 4, and 6 months of age. The vaccine administered as part of the EPI is a pentavalent vaccine against diphtheria-tetanus-pertussis-Hib-hepatitis B (DTP-Hib-HepB) in single-dose vials. Bolivia was the fourth Latin American country to introduce the HBV vaccination into the EPI, after Colombia (1994), Brazil (1998), and Ecuador (1999). In 2009, the World Health Organization recommended lowering the age of administration of the HBV vaccine to at birth, but Bolivia has not yet implemented this vaccination strategy [14-16].

Universal infant vaccination induces protective levels of antibodies to the HBV surface antigen (anti-HBs) in 94–100% of healthy infants, children and adolescents. The high estanti-HB stitres are attained 1–3 months following administration of the primary course of hepatitis B vaccine, and are considered a reliable marker of immediate and long-term protection against infection. These antibody levels rapidly decrease over the 12 months following immunization, and more slowly thereafter; however, vaccine-induced immunological memory is maintained for at least 12 years [17-20]. Data about serological HBV markers and incidence in Bolivia is scarce due to a poor surveillance system and low burden of HBV infection.

This study aimed to determine the state of immunity against hepatitis A and hepatitis B in children in Cochabamba, Bolivia and seroepidemiological association, including age, socio-demographic characteristics and socioeconomic status [21-24].

In this study were considered a total of 436 subjects 5-16 years. In the case of hepatitis A they were evaluated 436 subjects who not received vaccine, in the case of the hepatitis B were evaluated 424 subjects, of the which 329 subjects who not received vaccine and if 95 of them were vaccinated.

Materials and methods

Study design: This population based cross sectional study included a survey of school children aged 5–16 years old in the Cochabamba region of Bolivia. Participation was voluntary, with no financial incentive. This study was conducted according to the guidelines in the Declaration of Helsinki. All procedures involving human subjects were approved by the institutional ethical review board (Universidad Mayor de San Simon/Universitat de Barcelona), various Bolivian ministries (Education, Health, and Sport), and involved school directors [25,26].

Setting: The Cochabamba regional health status survey, entitled Bolkid, was a region-wide, population based, cross sectional study conducted in children in the Cochabamba region of Bolivia from March to April 2010. Cochabamba is an eastern Bolivian province that covers an area of 55.631 km^2 and comprises 1,862,000 inhabitants [Instituto Nacional de Estadı´stica, 2010]. Five municipalities were selected for the study. The defined geographical areas were urban (Cochabamba city), suburban (Tiquipaya and Punata), and rural (Vinto and Parotani) [27-30].

Sampling: The target population consisted of Cochabamba inhabitants aged 5–16 years and was derived from both public and private school registries in the Bolivian Education Ministry's official census. Calculations were performed with 95% confidence intervals (CI). The age groups were children (5.1–10.0 years), pre-adolescents (10.1–13.0 years), and adolescents (13.1–16.0 years). The sampling technique included stratification according to population size, geographical area (rural, urban, or suburban), and type of school (private or public) [31]. The initial sampling units (Cochabamba regional schools) and final sampling units (schoolchildren) were selected randomly. The student was considered a nonparticipant if they did not attend school on the physical examination day [32,33]. Nonparticipants were not replaced by another student because prior parent approval could not be obtained [34].

Questionnaire

The Bolkid survey consisted of a questionnaire, a physical examination, and a blood draw to determine the child's health status. Only the analysis regarding HAV seroprevalence y HBV seroprevalence and its relationship with sociodemographic variables, parental education levels, and housing Conditions. The questionnaire was tested initially on a pilot group of several parents and then amended for clarity and coherence. An anthropological approach was considered. Some probing questions were introduced to estimate the consistency of responses.

Parents or guardians completed the questionnaires at home, independent of the child's age. However, when parents or guardians were unable to read or understand the survey on their own (<5% of the sample), the questionnaires were completed on the same day as the blood draw and they received assistance in their native language from the teachers at the school.

The questionnaire gathered demographic data (personal information and family structure) and information on housing conditions, crowding (number of family members in the household), socio-economic status, and geographic location, HAV antibody test and HBV antibody test, A qualified nurse obtained the peripheral blood sample. The blood was centrifuged in the field at 3,000 rpm for 10 min to separate the serum from the fibrin clot, and the serum was stored at -20 C in Bolivia. Frozen samples were transported to Barcelona on dry ice and then stored at 70°C.

For the hepatitis A, the study focused on HAV serology. A serological analysis was performed using the ARCHITECT HAV antibody IgG assay (Abbott, Chicago, IL), a chemiluminescent microparticle immunoassay (CMIA), which provides qualitative detection of IgG antibodies that react to HAV (anti-HAVIgG) in human serum and plasma. Statistical Analysis A descriptive analysis was performed of the demographic and socio-economic data, household structure, housing conditions, geographic location, and HAV seroprevalence. Normally distributed quantitative variables

(Kolmogorov–Smirnov test, p>0.05) were expressed as means and standard deviations, central and dispersion measures, and percentages. The overall prevalence and prevalence stratified by gender and age was estimated with corresponding 95% CI. Qualitative comparisons were performed using the chi-square test or Fisher's test when required. The means of continuous variables were compared using the Student's t-test according to normality criteria. In all cases, p<0.05 was accepted as significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Chicago, IL) version 17.0 for Windows (SPSS).

Serological analysis for hepatitis B was performed by chemi luminescent microparticle immunoassay (CMIA) using the ARCHITECT HIV p24, HIV-1, HIV-2, Anti-HCV, HBsAg, Anti-HBs and Anti-HBc assay system (Abbott). y to the HIV (anti-HIV positive or negative), tothe hepatitis C (anti-HCV positive or negative), and hepatitis B core antigen (HBsAg positive or negative, anti-HBcIgG, 1.00 or ≥ 1.00) and quantitative determination of the antibody to the hepatitis B surface antigen (anti-HBsIgG) in human serum and plasma. The IgG anti-HBs titres were defined as positive if ≥ 10 mIUL21 and negative if, 10 mIUL21. We have performed descriptive analyses of hepatitis B seroprevalence and socio-demographic and parental education levels. Quantitative variables with a normal distribution (Kolmogorov–Smirnovtest, p.0.05) were expressed as means and SDs, central and dispersion measures, and percentages. Overall prevalence and prevalence stratified by gender and birth cohort were estimated with corresponding 95% CI. Qualitative comparisons were performed with the x^2 test or Fisher's test as required. The means of continuous variables were compared with Student's t-test according to normality criteria. In all cases, a p value of 0.05 was accepted as statistically significant. Statistical analyses were performed with the statistical package SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA, 2011).

Results

In the study of hepatitis A, a total of 436 subjects aged 5-16 years were tested for the presence of anti-HAV IgG; the participation rate was 93.8%. None of the children were infected with human immunodeficiency virus [HIV] or other immunosuppressive illnesses. None of the children had received immunosuppressive therapy, immunoglobulin administration, or other blood products within the 3-month period prior to the study. The overall prevalence of anti-HAV antibodies was 95.4% (95% CI 93.3-97.4). The prevalence of anti- HAV IgG (Table I) was significantly higher in children with parents who had low education levels (99.5% for fathers and 99.6% for mothers with the lowest education levels). Anti-HAV IgG prevalence was also significantly higher than average among participants whose first language was Quechua (99.5%; 95% CI 98.5-100.0) and among participants who reported tanker-delivered water as the main source of water in the household (99.4%; 95% CI 98.2–100.0).The peak infection risk was found mainly in early childhood (97.0%) rather than adolescence (93.3%), but the difference was not significant. No significant differences were observed in HAV epidemiology according to gender. The prevalence of HAV infection differed among different municipalities. Cochabamba city had the highest HDI and lowest HAV prevalence (P ¼ 0.030). In contrast, Punata and Parotani had the lowest HDI and highest HAV prevalence (P ¼ 0.070). Cochabamba city had the greatest crowding conditions and the lowest prevalence, and Parotani had the lowest crowding conditions and the highest HAV prevalence.

	n/M	Prevalence (95% CI)	p-value
Gender Male Famale	179/185 242/251	96.8 (94.2-99.3) 96.4 (94.11-98.7)	0.830
Age (years) 5.1-10.0 10.1-13.0 > 13.0	96/99 228/233 97/104	97.0 (93.6-100.0) 97.9 (96.0-99.7) 93.3 (88.5-98.1)	0.144
Living area Sub/urban Rural	268/281 153/155	95.4 (92.9-97.8) (96.9-100.0)	0.070
Municipality Cochabamba Punata Parotani Tiquipaya Vinto	166/176 61/61 107/108 43/45 45/46	94.3 (90.9-97.7) 100 % 99.1% (97.3-100.0) 95.6% (89.5-100.0) 97.8% (93.6-100.0)	0.066
Father's education None or basic Intermediate University	206/207 158/159 59/70	99.51 (98.57-100.00) 99.37 (98.14-100.00) 84.29 (75.76-92.81)	<0.001
Mother's education None or basic Intermediate University	264/265 111/114 48/57	99.62 (98.88-100.00) 97.37 (94.43-100.00) 84.21 (74.74-93.68)	<0.001
First language Spanish Quechua	232/243 192/193	95.5 (92.9-98.1) 99.5 (98.5-100.)	0.047
Siblings No Yes	91/93 333/343	97.9 (94.9-100.0) 97.1 (95.3-98.9)	1.000
Tap water No Yes	272/276 230/240	98.6 (97.1-99.9) 95.8 (93.3-98.4)	0.195
Tanker delivers water No Yes	258/271 164/165	95.2 (92.7-97.8) 99.4 (98.2-100.0)	0.015
p-values are based on the Chi-squared test n/N, number of positives out of the number tested.			

Table 1: Epidemiological Characteristics of Individuals Positive for Hepatitis A (n = 436) and Association with Housing Conditions.

In the study of Hepatitis B, Anti-HBc IgG-positive results were found in 0.9% (4/424, 95% CI: 0.2-1.9) of participants, including 0.9% (40/424, 95% CI: 0.1-1.9) of post-universal vaccine cohort and 1.2% (5/424, 95% CI: 0.9-3.1) of pre-universal vaccine cohort, with no significant between-group difference (p.0.05). Only one child in the post-universal vaccine cohort was anti-HBs IgG-negative and anti-

HBc IgG-positive, indicating a 0.2% (1/424, 95% CI: 0.0-0.9) prevalence of anti-HBc alone before the implementation of universal vaccination and 0% over ten years. The overall prevalence of anti-HBs IgG antibodies was 13.0% (95% CI: 9.8-16.2), ranging from 1.0% (1/95) in children born in 1994–1997 to 72.7% (16/22) in children born in 2005, and showing an approximately seven-fold higher prevalence in pre-universal vaccine cohort (37.9%) than post-universal vaccine cohort (5.8%). None of the studied children were HBsAg positive. In the pre-universal vaccine cohort (Table 2) the overall prevalence of anti-HBsIgG was 5.8% (19/329, 95% CI: 3.3-8.3); prevalence was three times higher in boys than girls and tended to be higher in children from urban or suburban areas than rural (p ¼ 0.158). Additionally, 52.6% (10/19) of responders in the post-universal vaccine cohort were hyporesponsive (anti-HBstitres100IU L21), possibly due to progressive loss of measurable anti-HBs. In the pre-universal vaccine cohort (Table 2), the overall prevalence of anti-HBsIgG was 37.9% (36/95, 95% CI: 28.5-48.1).

Prevalence was over two-fold higher in children speaking Quechua at home and born in 2005, and showed some tendency to be higher in children from urban or suburban areas than rural (p ¼ 0.468). Prevalences did not significantly differ according to gender and parental educational level, although few parents of children in this cohort had a high educational level.

		Vaccinees a (n=95)			Non-vaccinees b (n=329)		
		Rate	Prevalence (95% CI)	p-value	Rate	Prevalence (95% CI)	p-value
Gender	Male	5/48	31.3 (18.1-44.4)	NS	12/132	9.1 (4.2-14.0)	0.034
	Female	21/47	44.7 (30.5-58.9)		7/197	3.6 (1.0-6.1)	
Living area	Urban	3/9	33.3 (2.6-64.1)	NS	7/155	4.5 (1.2-7.8)	NS
	Suburban	7/13	53.9 (26.7-80.9)		9/93	9.7 (3.7-15.7)	
	Rural	26/73	35.6 (24.6-46.6)		3/81	3.7 (0.4-7.8)	
Father's education	None or basic	27/68	39.7 (28.1-51.3)	NS	5/136	3.7 (0.5-6.8)	NS
	Intermediate	7/23	30.4 (11.6-49.2)		8/129	6.2 (2.0-10.4)	
	University	2/4	50.0 (1.0-99.0)		6/64	9.4 (2.2-16.5)	
Mother's education	None or basic	28/75	37.3 (26.4-48.3)	NS	12/182	6.8 (3.1-10.4)	NS
	Intermediate	7/16	50.0 (19.4-68.1)		2/96	2.2 (0.8-5.1)	
	University	1/4	25.0 (0.2-67.4)		5/51	10.2 (1.9-18.5)	
First language	Spanish	10/43	23.3 (10.6-35.9)	0.012	14/193	7.3 (3.6-10.9)	NS
	Quechua	26/52	51.0 (37.4-64.6)		5/136	3.7 (0.5-6.8)	

Data are number of participants, unless stated otherwise: p-values obtained by x^2 or linear trend test.

NS: Not significant.

a Only the subjects seronegative for the hepatitis B surface antigen (HBsAg) and the hepatitis B core antibody (anti-HBc) were included.

b Only the subjects seronegative for HBsAg were included, independent of serostatus for anti-HBc.

Table 2: Hepatitis B seroprotection rate by period birth cohort, and its association with epidemiological characteristics of study participants (n=424).

Discussion

Prior to the present study, the most recent information about the epidemiology of hepatitis A in Bolivia was from 2003 [Gandolfo et al., 2003], before the last decade of national economic improvement. Moreover, that information did not include HAV prevalence in the Cochabamba region after economic improvement, the prevalence of anti-HAV antibodies in the study population exceeded 90% by the age of 10 years. Thus, Cochabamba has high HAV endemicity, and a national trend or shift in the epidemiological pattern did not occur in this region.

The results indicate a high seroprevalence of HAV and a low proportion of adults at risk of infection or severe infection and that the subjects have antibodies against hepatitis A despite not having been vaccinated. Our findings shows low long term humoral immunity against HBV infection. This may be due to departure from a low endemic status, with no HBV carriers observed before or after immunization, such a decrease is much more difficult to detect in just 10 years of inmunization.

Conclusion

In conclusion the results indicate: A high seroprevalence of HAV, The susceptibility to infection by the hepatitis A child reaches 4.5% and a low level of parental education contributes to the maintenance of high HAV endemicity in children from Cochabamba, Bolivia, regardless of sanitation and household conditions. Appropriate vaccination programs should be implemented to target children from high socioeconomic groups. Children show persistent low seroprevalence of hepatitis B infection, and low long-term humoral immunity against HBV infection and there is a high susceptibility of contracting hepatitis B infection by low immunity was identified. The clinical implications of the anti-HBs decrease with time and isolated anti-HBc, namely, a risk of subsequent HBV infection and possible indication for booster doses, are incompletely characterized and merit further studies.

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