

## TREND OF ACUTE HEPATITIS A IN THE STATE OF BAHIA, BRAZIL OVER A 5-YEAR PERIOD

Felicidade Mota Pereira<sup>1</sup>, Maria Conceição Chagas Almeida<sup>2</sup>,  
Monique Lírio<sup>3</sup>, Maria Fernanda Rios Grassi<sup>4</sup>

<sup>1</sup>Corresponding author. MSc in Biotechnology and Investigative Medicine. Pharmaceutical Biochemist and Epidemiological Surveillance Manager at the Gonçalo Moniz Public Health Central Laboratory. Salvador, Bahia, Brazil. felizmp@yahoo.com.br

<sup>2</sup>PhD in Collective Health. Collective Health researcher at the Oswaldo Cruz Foundation and at the Federal University of Bahia. Salvador, Bahia, Brazil. conceicao@bahia.fiocruz.br

<sup>3</sup>ID MD at the São Rafael Hospital and Hospital-acquired Infection Prevention Services Manager at the Evangelical Hospital of Bahia. Salvador, Bahia, Brazil. monique.lirio@yahoo.com.br

<sup>4</sup>PhD in Immunology. Researcher at the Oswaldo Cruz Foundation. Professor at BAHIANA - School of Medicine and Public Health. Salvador, Bahia, Brazil. grassi@bahia.fiocruz.br

**ABSTRACT | Introduction:** Hepatitis A virus (HAV) has a universal distribution. The prevalence of HAV infection varies greatly according to hygiene and sanitary conditions. **Objective:** To determine the proportion of acute infection of HAV in the state of Bahia during a 5-year period. **Methods:** This study was conducted at Central Public Health Laboratory of Bahia (LACEN-BA). All individuals referred for anti-HAV IgM serology from 417 municipalities from January 2009 to December 2013 were included. Percentages of HAV positive cases were presented according to age range for each year of the 5-year study and for each of the nine health districts (RHC) of Bahia. **Results:** 21,175 samples were analyzed. Proportion of HAV infection was 7.2% (1,535 / 21,175) throughout the study period. The highest proportion was in 2009 (17.4%) and the lowest in 2012 (3.8%), demonstrating a decreasing trend ( $r = 0.7$ ). The highest infection rates were found in children up to 10 years old. HAV infection was more frequent among males among all age groups. 52.4% (184/351) of the municipalities had acute HAV cases diagnosed. The North and West regions had the highest number of cases. **Conclusion:** There was a progressive decrease of approximately 70% in the proportion of acute HAV infection in the state of Bahia during a five-year assessment period. However, children up to 10 years old remain at higher risk, therefore the vaccine should be expanded to reach this age range.

**Keywords:** Hepatitis A, IgM, epidemiology, Bahia

## INTRODUCTION

Hepatitis A virus (HAV) has a worldwide distribution. Overall, roughly 1.4 million cases of HAV are reported per year<sup>1</sup>. The virus is transmitted via fecal-oral route by contaminated food and water, or by inter-human contact. Currently, endemic areas for HAV are classified according to the incidence of infection as high endemicity (up to 45 cases / 100,000 inhabitants), intermediate endemicity (between 15 and 45 cases / 100,000 inhabitants) and low endemicity (less than 15 cases / 100,000 inhabitants)<sup>2</sup>. High endemic rates of infection are found mainly in developing countries with very poor sanitary and hygienic conditions such as parts of Africa, Asia and Central and South America<sup>3</sup>. In these regions, HAV infection is usually acquired during childhood mostly as an asymptomatic infection. Developing countries and regions where sanitary conditions are unequal have intermediate levels of HAV infection, while developed countries with good sanitary and hygienic conditions have low levels<sup>1</sup>.

In Brazil, according to a population-based study conducted in the 26 capitals and Federal District from 2004 to 2009, a positive serology for HAV (IgM or IgG) was found in 39.5% (95% CI 36.5% - 42.5%) of individuals aged 5-19 years. This rate corresponds to an intermediate endemicity pattern (4). From 1999 to 2011, the Brazilian Case Registry Database (Sinan, Sistema de Informação de Agravos de Notificação), reported 138,305 confirmed cases of HAV, the majority of them occurring in the Northeast (31.2%) and North (23.3%) regions. In the Northeast, Pernambuco (22.0%), Bahia (18.4%), Ceará (13.9%) and Maranhão (13.2%) states had the highest number of reports. In the same period, the Mortality Information System (SIM, Sistema de Informação de Mortalidade) declared 867 deaths linked to HAV, of which 640 as a primary cause and 227 as an associated cause. The majority of deaths occurred in the Northeast (31.3%) and Southeast (29.3%) regions<sup>5</sup>. The present study aimed to estimate the proportion of HAV infection and the distribution of cases in Bahia, Brazil, over a five-year period.

## MATERIALS AND METHODS

### Study population

The present cross-sectional study attempted to assess the proportion of acute HAV infection in samples analyzed at the Central Public Health Laboratory of Bahia (LACEN-BA), located in Salvador, northeastern Brazil. LACEN-BA, the infectious diseases reference laboratory of the State of Bahia, receives samples from individuals followed by the public health system (SUS) who are suspected of diseases requiring mandatory notification. This study included all individuals referred for anti-HAV IgM serology from January 01, 2009 to December 31, 2013. Individuals were received from 9 (nine) Regional Health Centers (RHC) located throughout the state of Bahia with 417 municipalities. RHCs are political designations of the health department of the state of Bahia and are responsible for monitoring health surveillance activities (Figure 1). The Education and Research Commission of LACEN-BA approved the present study.

### Serological diagnosis

All samples were screened for HAV IgM antibodies by chemiluminescence assay (ADVIA Centaur® HAV IgM, Siemens Healthcare Diagnostics Inc., USA) using ADVIA Centaur Immunoassay System XP equipment. Samples with a calculated signal-to-cutoff value greater than or equal to 1.0 were considered reactive for IgM antibodies to HAV. Additionally, some samples were tested for leptospirosis (enzyme immunoassay assay using the EIA kit - IgM Leptospirosis Bio-Manguinhos, Rio de Janeiro, Brazil) and for dengue (Panbio® Dengue IgM Capture ELISA kit, Borahagal-ro, Giheung-gu, Yongin-si Gyeonggi-do, KO). Samples were considered positive when optical density readings were higher than additional test cutoff values.

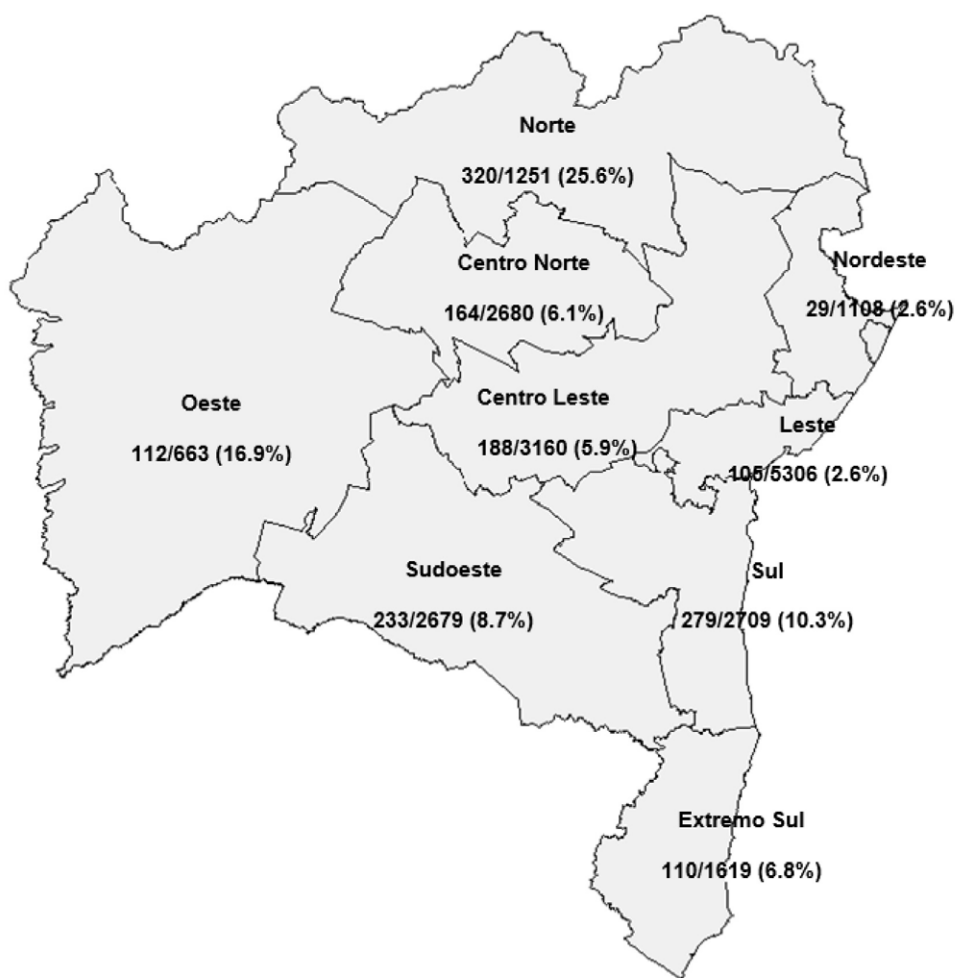
### Statistical Analysis

Data were obtained from SMART LAB software, coded and entered into a database using Microsoft Office Excel 2010. The following variables were analyzed: date of birth, gender, city of origin, serological test results for HAV, leptospirosis and dengue (categorized as reagent or non-reagent),

and serological test dates for each sample. Data were presented as frequencies, median and interquartile range. The number and percentage of individuals diagnosed with hepatitis A were presented for each of the nine health districts (RHC) of Bahia. In addition, total percentages of HAV positive cases were presented according to age range for each year of the 5-year study. The linear trend of the total number of HAV cases was calculated using the least square method using Microsoft Office Excel 2010 software.

## RESULTS

A total of 21,175 samples from 348/417 (83.4%) of the municipalities were analyzed. The largest number (5,306 samples, 21.5%) was sent from RHC-Leste, comprised of the state capital, Salvador, and 47 other cities, followed by RHC-Centro-Leste (3,160 samples, 14.9%) and RHC-Centro-Norte (2,680 samples, 12.7%). The lowest number of samples (663, 3.1%) was sent from RHC-Oeste (Figure 1 and Table 1). Sixty-nine municipalities did not send any samples.



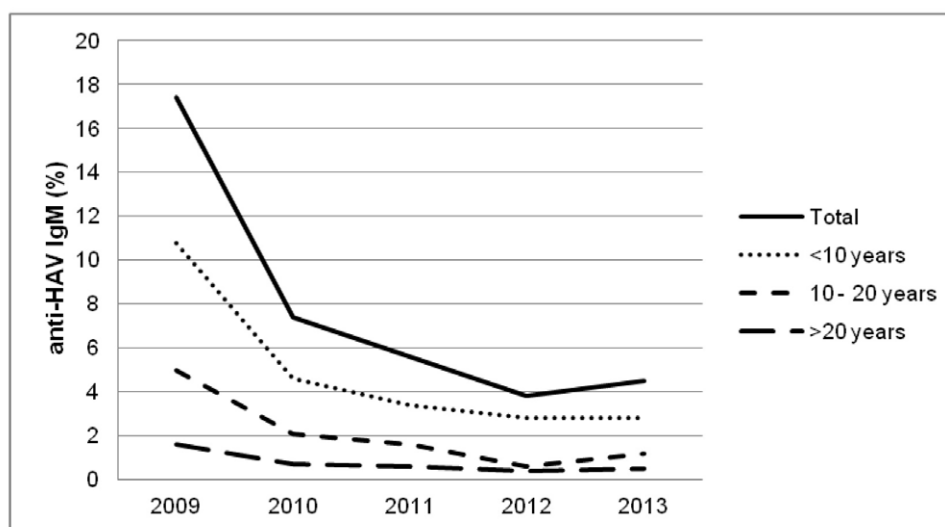
**Figure 1.** Distribution of acute hepatitis A cases diagnosed in LACEN-Bahia according to Regional Health Center in Bahia, Brazil evaluated in the period of 2009 to 2013. Data represent positive anti-HAV-IgM samples/ total of evaluated samples (percentage positive samples).

**Table 1.** The number of individuals tested for hepatitis A virus infection per year, according to Regional Health Centers (RHC) at LACEN-Bahia - Brazil in the period from 2009 to 2013.

RHC	YEAR					TOTAL
	2009	2010	2011	2012	2013	
EAST CENTER	326	476	562	577	1219	3160
NORTH CENTER	271	490	704	544	671	2680
EXTREME SOUTH	345	224	299	290	461	1619
EAST	882	1189	990	1067	1178	5306
NORTHEAST	137	316	364	214	77	1108
NORTH	232	260	246	289	224	1251
WEST	96	101	196	171	99	663
SOUTHEAST	644	603	520	527	385	2679
SOUTH	562	487	442	637	581	2709
<b>TOTAL</b>	<b>3,495</b>	<b>4,146</b>	<b>4,323</b>	<b>4,316</b>	<b>4,895</b>	<b>21,175</b>

RHC: Regional Health Center

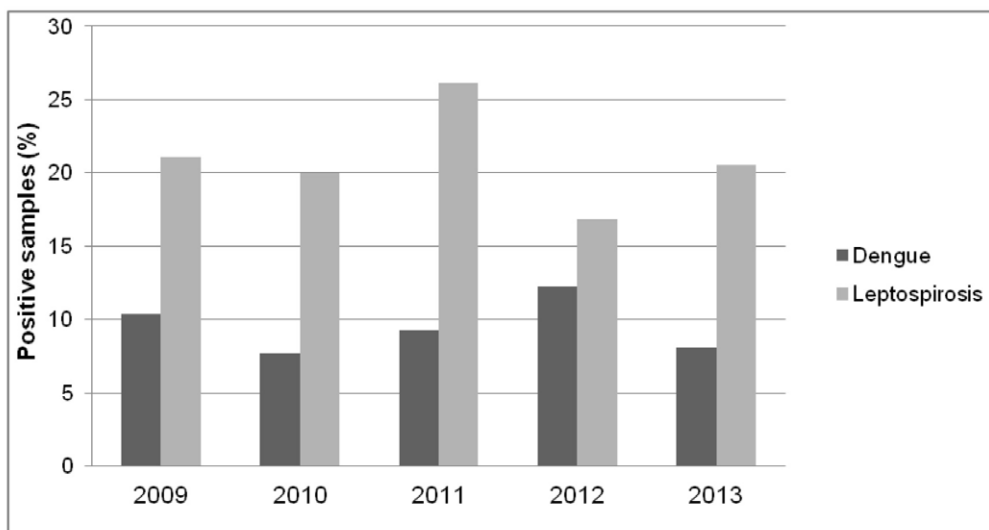
The median age of the studied population was 28 years (interquartile range 19-42) and 61.7% (13,065 / 21,175) were women. Acute HAV infection was diagnosed in 7.2% (1535 / 21,175) of suspected individuals. When HAV proportion was analyzed according to the year of serology sampling, a decreasing trend ( $r = 0.7$ ) in the acute infection rate was observed between 2009 (17.4%) and 2012 (3.8%) (Figure 2). Individuals under 10 years had the highest proportion of infection throughout the study period (Figure 2). Acute HAV infection was more frequent among males, with a male:female ratio varying from 1.2:1 to 1.5:1 among all age groups.



**Figure 2.** Percentage of acute hepatitis A cases diagnosed at LACEN-Bahia according to age group and year in Bahia, Brazil in the period of 2009 to 2013. Trend  $R^2 = 0.7$ , (least square method).

Cases of acute HAV were found in 52.9% (184/348) of the assessed municipalities. RHC-Norte (18/28) and RHC-Oeste (15/37) had the highest proportion of municipalities with diagnosed HAV cases.

Serology for leptospirosis and dengue was requested by local doctors for differential diagnosis purposes in 10.7% (2,273 / 21,175) of the samples evaluated for HAV. Of these, all were negative for HAV, while 21% (478 / 2,273) were positive for leptospirosis and 9.4% (213 / 2,273) were reactive for dengue. The highest proportion of leptospirosis was seen in 2009 and 2011, while the highest number of dengue cases was observed in 2012 (Figure 3).



**Figure 3.** Percentage of positive serologies for dengue and leptospirosis by year among 2,273 samples analyzed for anti-HAV IgM antibody at Lacen-Bahia, Brazil in the period of 2009 to 2013.

## DISCUSSION

The data presented herein indicate a progressive decrease of approximately 70% in the proportion of acute HAV infection in the state of Bahia during a five-year assessment period: from 17.4% in 2009 to 4.5% in 2013. Children under 10 years of age presented the greatest reduction, yet remain the age group most affected by acute HAV infection.

Throughout Brazil, the prevalence of HAV varies according to age, socioeconomic characteristics, and region<sup>6</sup>. In the Brazilian Northeast, one of the country's poorest regions, the highest prevalence is found in children under 5 years<sup>6,7</sup>. Other studies conducted in poor areas from wealthier municipalities around the country, such as the city of Santos, São Paulo in 2007<sup>8</sup> and the metropolitan region of Curitiba, Paraná in 2006<sup>9</sup> found similar results to those obtained in the Northeast, with a higher frequency of HAV infection observed in children under 5 years.

The decreasing proportion of HAV observed over the five-year study period could be associated with decreased exposure to the virus during the first years of life, which may be partially attributed to an expansion in the National Family Health Program (Programa da Saúde da Família) and improving living conditions, especially in the Northeast. In fact, in 2013 the number of municipalities in the Brazilian Northeast covered by the National Family Health Program was 1,789 out of 1,793<sup>10</sup>. In addition, in 2003 a conditional cash transfer program named

“Bolsa Família” was implemented nationwide. In January 2005, 26.4 million people received this benefit, by the end of 2006 this number surpassed 44 million<sup>11</sup>. This program resulted in a reduction of 46.3% in the infant mortality rate, mainly due to diarrhea, in children under 5 years in the period from 2004 to 2009<sup>12</sup>. The reduction in infant mortality was attributed to the decrease of households with inadequate sanitary conditions and increased average monthly income per individual<sup>12</sup>. In the present study, it was not possible to assess directly the impact of the “Bolsa Família” or coverage of family health program on the frequency of HAV. However, the Human Development Index (HDI) in the state of Bahia presented an increase over the last ten years going from 0.512 in 2000 to 0.660 in 2010<sup>13</sup>. The increase in HDI indicates improvement in health, education, and income, which are directly related to the advances in health conditions, resulting in greater control of HAV transmission.

HAV vaccine was included in the Brazilian immunization public program for children aged one to under two years since 2014. Seroprevalence studies showed an increase in the number of susceptible individuals in Brazilian regions, including the Southeast and the South<sup>6,14,15</sup>, which have wider water treatment and sewage system coverage<sup>16</sup>. Adults susceptible to HAV have a higher risk of symptomatic infection including acute liver failure and more rarely death<sup>6,14,15</sup>.

One of the limitations of the present study was

the non-probabilistic sampling. However, only 16.5% (69/417) municipalities did not send samples to LACEN-BA in the study period, which corresponds to a population of 101,322 inhabitants (0.7%) out of 15,025,049 inhabitants of the state of Bahia<sup>17</sup>. Corroborating the results obtained herein, from 2,216 suspected cases of HAV infection reported to SINAN in Bahia, in the period from 2009 to 2013, LACEN-BA diagnosed 1,535 cases of HAV. That rate corresponds to 69.3% of all reported suspected cases. It is possible that the remaining 681 cases were diagnosed in other laboratories or alternatively were not confirmed or are awaiting diagnosis. Serology for leptospirosis and dengue, which was requested by local doctors for 2,273 individuals (10.7% of total samples) were negative for HAV. Moreover, the highest number of HAV suspected cases in SINAN occurred in 2009 with 912 cases<sup>5</sup>, which coincided with the highest proportion of HAV infection found in the present study.

In conclusion, the results obtained herein show that the proportion of HAV infection in Bahia has been declining in recent years. However, the under-10 age group has the highest proportion compared with other age groups. Thus, the vaccine for HAV in Brazil should be expanded to reach this age range, in order to reduce the morbidity of this disease in adulthood.

#### COMPETING INTERESTS

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) Were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

#### REFERENCES

1. World Health Organization. Hepatitis A [Internet]. Media centre: World Health Organization; 2016 [updated 2016 July 15; cited 2016 Nov 5]. Available from: <http://www.who.int/mediacentre/factsheets/fs328/en/>.
2. Mitre HP, Mendonça JS. Hepatites Virais. In: Lopes AC. Clínica Médica – Diagnóstico e Tratamento. São Paulo: Manole; 2006. p. 1115-1146.

3. Brasil. Ministério da Saúde. Hepatites Virais. 3rd.ed. Brasília: Ministério da Saúde; 2008.
4. Brasil. Ministério da Saúde. Departamento de Vigilância, Prevenção e Controle das IST, do HIV/Aids e das Hepatites Virais. Estudo de prevalência de base populacional das infecções pelos vírus das hepatites a, b e c nas capitais do Brasil 2010 [Internet]. 2010 [updated 2016 July 28; cited 2016 Nov 5]. Available from: [http://www.aids.gov.br/publicacao/2010/estudo\\_de\\_prevalencia\\_de\\_base\\_populacional\\_das\\_infeccoes\\_pelos\\_virus\\_das\\_hepatites\\_b](http://www.aids.gov.br/publicacao/2010/estudo_de_prevalencia_de_base_populacional_das_infeccoes_pelos_virus_das_hepatites_b)
5. Brasil. Ministério da Saúde. DATASUS /TABNET. Sinanet Hepatites virais. [Internet]. [updated 2015 October 02; cited 2014 March 1]. Available from: <http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sinanet/cnv/hepaBA.def>
6. Ximenes RAA, Martelli CMT, Merchán-Hamann E, Montarroyos UR, Braga MC, de Lima MLC et al. Multilevel analysis of hepatitis A infection in children and adolescents: a household survey in the Northeast and Central-west regions of Brazil. *Int J Epidemiol* 2008;37(4):852-61. doi: [10.1093/ije/dyn114](https://doi.org/10.1093/ije/dyn114)
7. Gomes MAC, Ferreira ASP, da Silva AAM, de Souza ER. Hepatitis A: seroprevalence and associated factors among schoolchildren of São Luís (MA), Brazil. *Rev bras epidemiol.* 2011;14(4):548-55. doi: [10.1590/S1415-790X2011000400002](https://doi.org/10.1590/S1415-790X2011000400002)
8. Ciaccia MCC, Moreira RC, Ferraro AA, Lemos MF, Oba IT, Porta G. Epidemiological and serological aspects of hepatitis A among children and teenagers in the city of Santos : a cross-sectional study. *Sao Paulo Med J.* 2012;130(4):230-235. doi: [10.1590/S1516-31802012000400005](https://doi.org/10.1590/S1516-31802012000400005)
9. Markus JR, Cruz CR, Maluf EMCP, Tahan TT, Hoffmann MM. Seroprevalence of hepatitis A in children and adolescents. *J Pediatr.* 2011;87(5):419-24. doi: [10.1590/S0021-75572011000500009](https://doi.org/10.1590/S0021-75572011000500009)
10. Brasil. Ministério da Saúde. DATASUS. Histórico de Cobertura da Saúde da Família. [Internet]. [updated 2017 March 31; cited 2016 October 26]. Available from: [http://dab.saude.gov.br/portaldab/historico\\_cobertura\\_sf.php](http://dab.saude.gov.br/portaldab/historico_cobertura_sf.php).
11. Lindert K. Brazil: Bolsa Familia Program—Scaling-up Cash Transfers for the Poor [Internet]; 2005 [updated Jan 2005 cited 10 Dez 2016]. Available from: <http://www.mfdr.org/sourcebook/6-1brazil-bolsafamilia.pdf>
12. Rasella D, Aquino R, Santos CAT, Paes-Sousa R, Barreto ML. Effect of a conditional cash transfer programme on childhood mortality: A nationwide analysis of Brazilian municipalities. *Lancet.* 2013;382(9886):57-64. doi: [10.1016/S0140-6736\(13\)60715-1](https://doi.org/10.1016/S0140-6736(13)60715-1)
13. Programa das Nações Unidas para o Desenvolvimento no Brasil. Ranking IDHM Municípios 2010 [Internet].

[cited 2015 December 08]. Available from: <http://www.br.undp.org/content/brazil/pt/home/idh0/rankings/idhm-municipios-2010.html>

14. Vitral CL, Ospina FLN, Artimos S, Melgaço JG, Cruz OG, de Paula VS et al. Declining prevalence of hepatitis A virus antibodies among children from low socioeconomic groups reinforces the need for the implementation of hepatitis A vaccination in Brazil. *Mem Inst Oswaldo Cruz*. 2012;107(5):652-8.

15. Ciocca M. Clinical course and consequences of hepatitis A infection. *Vaccine* 2000;18(1):71-4.

16. Brasil. Instituto Brasileiro de Geografia e Estatística. População. Pesquisa Nacional de Saneamento Básico 2008 [Internet]. [cited 2015 December 08]. Available from: [http://www.ibge.gov.br/home/estatistica/populacao/condicaodevida/pnsb2008/defaulttabzip\\_abast\\_agua.shtm](http://www.ibge.gov.br/home/estatistica/populacao/condicaodevida/pnsb2008/defaulttabzip_abast_agua.shtm)

17. Bahia. Secretaria de Saúde. Mapa Bahia. Regiões de Saúde do Estado da Bahia. [Internet]. [updated 2016 May 12; cited 2015 October 26]. Available from: [http://www1.saude.ba.gov.br/mapa\\_bahia/indexch.asp](http://www1.saude.ba.gov.br/mapa_bahia/indexch.asp)