Rev. Inst. Med. trop. São Paulo
28(6):400-405, *novembro-dezembro,* 1986

EPIDEMIOLOGICAL ASPECTS OF ACUTE VIRAL HEPATITIS IN SÃO PAULO, BRAZIL

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SUMMARY

As few reports on the prevalence of each type of viral hepatitis have been published in our country, we studied 154 patients with acute viral hepatitis consecutively seen at the Liver Unit from November 1980 to November 1984.

The frequency of hepatitis A, B and non-A, non-B was 52.6%, 27.3% and 20.1% respectively. Greater frequency in young people, previous contact with infected patients and ingestion of suspected foods were the predominant epidemiological features in the hepatitis A group. Hepatitis B was characterized by the parenteral, non-transfusional exposure, previous contact and a high occurence in health-care workers. A history of blood transfusion was a significant finding in the hepatitis non-A, non-B group. Finally, the routes of transmission were unknown in 30-40% of the three groups of patients.

KEY WORDS: Viral hepatitis — Epidemiology; Virus A, B, non-A, non-B.

INTRODUCTION

Various markers of hepatitis B virus have proved to be of great value for a correct diagnosis of hepatitis B infection. Thus, detection of hepatitis B surface antigen (HB_sAg) by sensitive methods makes it possible to identify most patients with acute viral hepatitis type B [22]. The possibility of such a diagnosis can be further increased by the detection of antibody to core antigen (anti-HB_c). The development of sensitive serological tests for identifying antibodies to hepatitis A virus (anti-HAV) has provided a valuable tool for the diagnosis of hepatitis A infection [5,8,9]. These diagnosis have permitted recognition of a third etiological form of viral hepatitis, the so-called non-A, non-B viral hepatitis. Its diagnosis, however, is made only by the serological exclusion of hepatitis A and B [3,7,9,15].

In our country, few reports on the prevalence of each type of viral hepatitis have been published [13,18,28].

In this paper we report our experience on 154 patients with acute viral hepatitis consecutively seen in our Liver Unit from November 1980 to November 1984.

MATERIAL AND METHODS

The diagnosis of acute viral hepatitis was based on clinical and laboratorial data. Only patients studied during the first eight weeks were included as serum IgM antibody to hepatitis A virus (anti-HAV) may be short-lived [5,10,19,20].

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In the patients with post-transfusional hepatitis, the diagnosis was based on an elevation of alanine-amino-transferase (ALT) of at least five times the upper normal limit. Patients with a past history of drug ingestion or alcohol abuse were excluded.

Acute-phase sera were routinely tested for HB_sAg by radioimmunoassay (AUSRIA II, Abbott). In HB_sAg-negative patients, the sera were tested for antibody to the hepatitis B core antigen (anti-HB_c) and antibody to the hepatitis B surface antigen (anti-HB_s) by radioimmunoassay (CORAB and AUSAB, respectively).

Antibody to HAV (IgM) was detected by radioimmunoassay. From 1982 on, radioimmunoassay was replaced by the enzyme-linked-immunoabsorvent-assay (ELISA).

Non-A, non-B hepatitis was defined by the absence of IgM anti-HAV, HB_sAg and anti-HB_c [18].

Statistical analysis — Fisher Snedecor's F statistic [12] was used for the comparison of age averages and Tukey's method for multiple comparisons. For homogeneity tests, Pearson's χ^2 statistic [29] was used and when significant, an additive partition was employed.

RESULTS

As show in Table I, 81 out of 154 patients (52.6%) showed positive results for anti-HAV-IgM and were included in the hepatitis A group (AVH group). Forty-two patients (27.3%) were positive for HB_sAg and were included in the hepatitis B group (BVH group). Thirty-one patients (20.1%), without anti-HAV-IgM, HB_sAg or anti-HB_c were included in the non-A, non-B viral group (NANB group). In all three groups there was a predominance of males over females in a proportion of 1.8 : 1.0.

TABLE I

Prevalence of acute A (AVH), B (BVH) and non-A, non-B (NANBVH) viral hepatitis, according to sex and AGE

Groups	AVH	BVH	NANBVH	Total
Sex	81 (52.6%)	42 (27.3%)	31 (20.1%)	154 (100.0%)
Male *	52 (64.2%)	27 (64.3%)	20 (64.5%)	99 (64.3%)
Female	29 (35.8%)	15 (35.7%)	11 (35.5%)	55 (35.7%)
Age ** (years)	21.7 ± 10.7	36.7 ± 16.0	38.3 ± 18.3	

* $p = 0.9994$ (NS)

** $p < 0.05$ According to Tukey's method, age was similar in the groups BVH and NANBVH, but significantly lower in group AVH.

The mean age was 21.7 ± 10.7, 36.7 ± 16.0 and 38.3 ± 18.3 years for AVH, BVH and NANBVH groups, respectively. The last two groups showed similar mean ages, which differed significantly from the first group. The distribution according to age was similar in groups BVH and NANBVH (figure 1). However there was a tendency to a greater frequency in the third decade in BVH group.

Epidemiological data could be obtained from all but two patients and are show in Table II. The predominant risk factors for patients with AVH were previous contact with a hepatitis patient (24.7%) and suspected food (17.3%). The most important risk factors for patients with BVH were parenteral (33.3%), particularly non-transfusional (23.8%) and previous contact (30.9%). The incidence of BVH in health-care workers (23.8%) was significantly higher than in the other groups. In the NANBVH group blood transfusion was mentioned in a significantly higher number of patients ($p < 0.0001$).

No exposure was mentioned in 39.5%, 42.9% and 31.0% of patients with hepatitis A, B and non-A, non-B, respectively. These differences were not statistically significant.

DISCUSSION

Our results show that hepatitis A (AVH) is more frequently found when patients of all

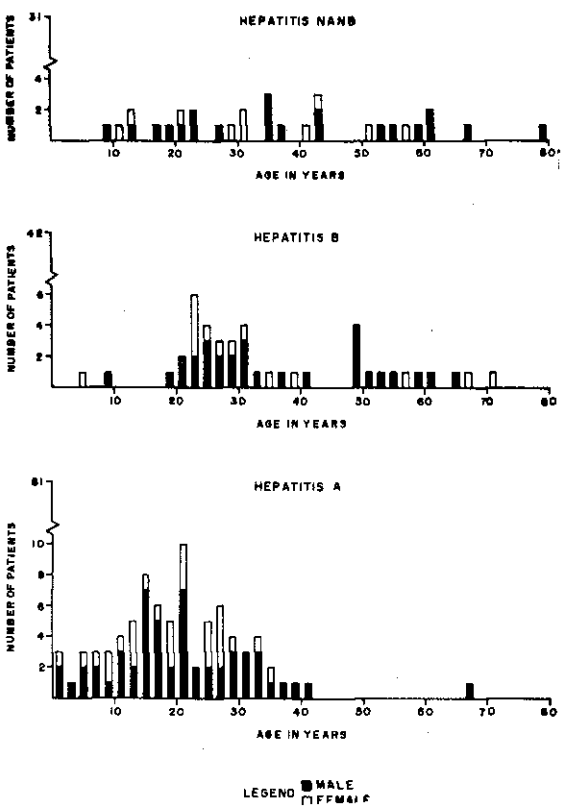

Fig. 1 — Distribution of patients according to age and sex

age groups are studied. However, our data have some limitations, one of which is the possible bias associated with patient selection at Liver Unit. This fact may explain the higher frequency of AVH (82.0%) at a São Paulo's General Hospital (Hospital do Servidor Público Estadual), where 86 out of 150 patients (57.3%) with viral hepatitis were 1 to 10 years old, 33 (22.0%) 11 to 20 years old and 31 (20.7%) were 21 years of age or more [26]. In our 15[6] patients, the distribution according to the same age groups, were respectively, 15 (9.7%), 28 (18.2%) and 111 (72.1%). In both studies, the majority of patients was not hospitalized. These figures show that proportionally less children are attended at the Liver Unit than at the mentioned hospital and suggest that the hospital's statistics are more representative of the relative frequency of hepatitis in the community. Even if we take into account these differences, hepatitis A is the predominant type of acute viral hepatitis found in São Paulo, Brazil.

Our data are closer to another study from the same hospital [18] and to those found in a recent multicenter study of 800 patients in United States of America [14]. In order to compare the frequency and distribution of acute viral hepatitis in different areas of the world, some data were drawn from the literature and are shown in Table III.

Whereas AVH is the most frequent type of hepatitis in Brazil, in some developed countries, the frequency of the different types varies considerably. In a multicenter study in USA, the prevalence of AVH varied from 14 to 56% [14] It was also variable in two close countries as

T A B L E II

Epidemiological data as acknowledged by 152 patients with A (AVH), B (BVH) and non-A, non-B (NANBVH) viral hepatitis

Groups	AVH (81)		BVH (42)		NANBVH (29)		
Exposure	No.	(%)	No.	(%)	No.	(%)	p
Previous contact	20	(24.7)	13	(30.9)	2	(6.9)	0.0214 *
Suspected food	14	(17.3)	1	(2.4)	0	(0.0)	0.0011 **
Parenteral:							
Transfusion	0	(0.0)	4	(9.5)	10	(34.5)	< 0.0001 ***
Ilicit drug use	0	(0.0)	0	(0.0)	2	(6.9)	
Other percutaneous exposure	0	(0.0)	10	(23.8)	1	(3.4)	
Dental care	10	(12.3)	5	(11.9)	3	(10.3)	
Unkown	32	(39.5)	18	(42.9)	9	(31.0)	0.5932
Health-care workers	5/79	(6.3)	10/42	(23.8)	2/31	(6.5)	0.0095 ****

* AVH and BVH groups are similar and differ significantly from group NANBVH ($p = 0.0214$)
** BVH and NANBVH groups are similar and differ significantly from group AVH ($p = 0.0011$)
*** AVH and BVH groups are similar ($p = 0.0609$) and differ significantly from group NANBVH ($p < 0.0001$)
**** AVH and NANBVH groups are similar ($p = 0.9761$) and differ significantly from group BVH ($p = 0.0095$)

TABLE III

Frequency (%) of sporadic acute viral hepatitis in different areas of the world *

Geographic area	Total number	AVH (%)	BVH (%)	NANBVH (%)	Others [a] (%)	Reference No.
Brazil	295	62.0	21.0	17.0	—	18
Brazil	150	82.0	12.0	6.0	—	26
Brazil	154	52.6	27.3	20.1	—	Our data
Costa Rica	103	—— 88.3	——	10.6	1.1	30
Denmark	115	57.4	33.9	6.1	2.6	22
Italy	332	59.6	22.6	15.1	2.7	4
Spain	163[b]	15.3	39.0	35.0	10.7	6
Sweden	148	27.0	57.4	15.5	—	24
Sweden	276	30.4	46.7	22.8	—	31
U.S.A.	800	41.0	32.6	26.4	—	14

* Only papers refering frequency in all age groups were included

[a] Including unclassified cases and those due to Epstein Barr or cytomegalovirus infection

[b] Most patients were adults

Sweden and Denmark: 27 and 57%, respectively [22,24]. It is possible that a lesser inclusion of children under age 15 [14] may explain some differences. However, different epidemiological features of AVH could also be an explanation, as will be shown below. In Latin America, if only children are considered, the prevalence ot AVH will be much higher, varying from 88.7% to 97.5% [26,27,33]. Hepatitis B (BVH) and non-A, non-B (NANBVH) are rare in children, varying from 1 to 4% and 2 to 5%, respectively [26,27].

The prevalence of the three types of viral hepatitis in different areas in non-pediatric population is also difficult to compare. Some authors simply mention "adult" patients whereas others include adolescent patients over 12 to 14 years of age (Table IV). A predominance of BVH is observed in many publications [1,21,25] but in series from our country, from Argentine [11], and from England [2], a predominance of AVH is still seen. In São Paulo, Brazil, such predominance is not always observed after 20 years of age. Thus, in a general hospital's series [26] the frequency of AVH, BVH and NANBVH was 7/31 (22.6%), 17/31 (54.8%) and 7/31 (22.6%), respectively, whereas in our series it was 43/107 (40.2%), 39/107 (36.4%) and 25/107 (23.4%), respectively. These somewhat different results are not unexpected. Patients attended at the Liver Unit belong to a higher socioeconomic level and it is a well-known fact that such individuals are less prone to develop antibodies to hepatitis A virus and so are more susceptible to this infection.

TABLE IV

Frequency (%) of sporadic acute viral hepatitis in different areas of the world, excluding pediatric patients

Geographic area	Total number	AVH (%)	BVH (%)	NANBVH (%)	Others (%)	Age groups	Reference No.
Argentine	278	43.4	35.3	17.3	4.0	Not children	11
Brazil	133	48.1	30.1	21.8	—	All 14 yrs	our data
England	172	51.2	33.7	12.8	2.3	All 15 yrs	2
Greece	216	10.0	76.0	14.0	—	All 15 yrs	21
Sweden	480	22.3	61.9	13.1	2.7	15 — 68 yrs	25
U.S.A.	295	10.2	48.1	41.7	—	All 12 yrs	1

Non-A, non-B hepatitis is mainly found in patients over 30 years [23]. The actual frequency of NANBVH in our material may be lower. Thus, we cannot discard the possibility of other etiologies in this group as serological tests for citomegalovirus and Epstein-Barr virus were not routinely performed. It must be emphazised, however, that these viruses account for few cases of sporadic acute viral hepatitis [1,11,25].

The frequency of BVH, based on the detection of anti-HB_c of IgM type is presently under investigation in our laboratory.

The predominance of male over female patients (1.8 : 1.0) was observed in all three groups of hepatitis and is in agreement with other reports [6,24,31].

Epidemiological data (Table II) show that previous contact with a hepatitis patient is frequently mentioned by patients with AVH and BVH. These risk factors seem to be less important in NANBVH [13].

Ingestion of suspected foods (raw shellfish) was referred by 17.3% of the patients with AVH and represents a possible vehicle of transmission [17]. This route of transmission did not seem to be important in non-A, non-B hepatitis. Furthermore, we did not observe cases of epidemic non-A, non-B hepatitis transmitted via contaminated water as was described in India [16,32].

Summing-up, acute viral hepatitis in São Paulo, Brazil is mainly due to hepatitis A virus, being followed in frequency by the hepatitis B.

RESUMO

Aspectos epidemiológicos da hepatite viral aguda em São Paulo, Brasil

A necessidade de maior número de dados sobre prevalência das hepatites por vírus em nosso meio levou-nos a estudar a freqüência das hepatites por vírus na Unidade de Fígado de São Paulo.

Foram estudados 154 pacientes atendidos consecutivamente de novembro de 1980 a novembro de 1984. O emprego de marcadores para hepatite A (anti-VHA-IgM), hepatite B ($AgHB_s$, anti-HB_c e anti-HB_e) e a ausência dos mesmos para hepatite não-A, não-B (NANB), permitiu verificar a freqüência das mesmas que foi, respectivamente, de 52,6%, 27,3% e 20,1%. A hepatite A caracterizou-se pela maior freqüência em jovens, contacto prévio com doente ou ingestão de alimento suspeito. Na hepatite B os dados epidemiológicos preponderantes foram transmissão parenteral não-transfusional, contacto prévio e alta incidência em profissionais de saúde. Na hepatite NANB predominaram os casos pós-transfusionais (34,5%). Ausência de antecedentes epidemiológicos foi observada em 30-40% dos pacientes dos três grupos.

ACKNOWLEDGEMENTS

This research was supported by FINEP — Financiadora de Estudos e Projetos (Grant no. 43.83.0862.00). We are indebted to Noriko la Regina for secretarial assistance and to Monica Relvas for reviewing the manuscript.

REFERENCES

1. ALTER, M. J.; GERETY, R. J.; SMALLWOOD, L. A.; SAMPLINER, R. E.; TABOR, E.; DEINHARDT, F.; FORSNER, G. & MATANOSKI, G. M. — Sporadic non-A non-B Hepatitis: frequency and epidemiology in a urban U.S. population. **J. infect. Dis., 145: 886-893, 1982.**

2. BAMBER, M.; THOMAS, H. C.; BANNISTER, B. & SHERLOCK, S. — Acute type A, B, and non-A, non-B hepatitis in a hospital population in London: clinical and epidemiological features. **Gut, 24: 561-564, 1983.**

3. BERNSTEIN, L. M.; KOFF, R. S.; SIEGEL, E. R.; MERITT, R. D. & GOLDSTEIN, C. M. — The hepatitis knowledge base. **Ann. intern. Med., 93 (suppl. 1, part 2): 183-222, 1980.**

4. BORTOLOTTI, F.; CADROBBI, P.; CARRETTA, M.; MENEGHETTI, F.; PORNARO, E. & REALDI, G. — Epidemiological aspects on acute viral hepatitis in Northern Italy. **Scand. J. infect. Dis., 14: 161-164, 1982.**

5. BRADLEY, D. W.; MAYNARD, J. E.; HINDMAN, S. H.; HORNEBECK, C. L.; FIELDS, H. A.; McCAUSTLAND, K. A. & COOK, E. F. N. — Serodiagnosis of viral hepatitis A: detection of acute phase immunoglobulin M anti-hepatitis A virus by radioimmunoassay. **J. clin. Microbiol., 5: 521-530, 1977.**

6. BRUGUERA, M.; SÁNCHEZ-TAPIAS, J. M.; CABALLERIA, J. & RODÉS, J. — Hepatitis vírica aguda. Características epidemiológicas de la hepatitis A, B y no A no B. **Gastroent. Hepat., 5: 237-242, 1982.**

7. BURREL, C. J. — Serological markers of hepatitis B infection. **Clin. Gastroent., 9: 47-63, 1980.**

8. DIENSTAG, J. L. — Viral hepatitis type A: virology and course. **Clin. Gastroent., 9: 135-150, 1980.**

9. DIENSTAG, J. L.; STEVENS, C. E. & SZMUNESS, W. — The epidemiology of non-A, non-B hepatitis: emerging patterns. **In:** GERETY, R. J., ed. — **Non-A Non-B hepatitis.** New York, Academic Press, 1981. p. 119-138.

10. DUERMEYER, W. & VAN DER VEEN, J. — Specific detection of IgM-antibodies by ELISA, applied in hepatitis A. **Lancet, 2: 684-685, 1978.**

11. FINDOR, J. A.; IGARTUA, E. B.; DOMEQ, P.; LAFAGE, M. & DOMEQ, R. — Epidemiologia de la hepatitis viral en Buenos Aires. **In:** JORNADAS LATINOAMERICANA DE HEPATOLOGIA, 8., Lima, 1983 **Anales.** Lima, 1983. p. 25.

12. FLEISS, J. L. — **Statistical methods for rates and proportions.** 2nd. ed. New York, John Wiley & Sons, 1980.

13. FOCACCIA, R. — Etio-epidemiologia das hepatites virais tipo A e B. Contribuição ao estudo da prevalência e risco de contágio em funcionários hospitalares. São Paulo, 1982 (Dissertação de Mestrado — Faculdade de Medicina da USP).

14. FRANCIS, D. P.; HADLER, S. C.; PRENDERGAST, T. J.; PETERSON, E.; GINSBERG, M. M.; LOOKABAUCH, C.; HOLMES, J. R. & MAYNARD, J. E. — Occurrence of hepatitis A, B, and non-A, non-B in the United States. CDC Sentinel Country Hepatitis Study I. **Amer. J. Med.**, 76: 69-74, 1984.

15. HOOFNAGLE, J. H. — Acute non-A, non-B hepatitis: clinical course and diagnosis. **In:** GERETY, R. J., ed. **Non-A, Non-B hepatitis.** New York, Academic Press, 1981. p. 23-38.

16. KHUROO, M. S. — Study of an epidemic of non-A, non-B hepatitis: possibility of another human hepatitis virus distinct from post-transfusion non-A, non-B type. **Amer. J. Med.**, 68: 818-824, 1980.

17. KOFF, R. S. & GALAMBOS, J. — Viral Hepatitis. **In:** SCHIFF, L. & SCHIFF, E. R., ed. — **Diseases of the liver.** 5th. ed. New York, J.B. Lippincott, 1982. p. 461-610.

18. KOFF, R. S.; PANNUTI, C. S.; PEREIRA, M. L. G.; HANSSON, B. G.; DIENSTAG, J. L.; AMATO NETO, V.; WONG, D. C. & PURCELL, R. H. — Hepatitis A and non-A, non-B viral hepatitis in São Paulo, Brazil. Epidemiological, clinical and laboratory comparisons in hospitalized patients. **Hepatology**, 2: 445-448, 1982.

19. KRUGMAN, S. & GOEKE, D. — **Viral hepatitis.** Philadelphia, W.B. Saunders, 1978. p. 30-47.

20. LOCARNINI, S. A.; COULEPIS, A. G.; STRATTON, A. M.; KALDOR, J. & GUST, I. D. — Solid-phase enzyme linked immunosorbent assay for detection of hepatitis A specific immunoglobulin M. **J. clin. Microbiol.**, 9: 459-465, 1979.

21. MATHIESEN, L. R.; PAPAEVANGELOU, G.; PURCELL, R. H.; GRAMMATIKOPOULOS, D.; CONTOYANNIS, P. & WONG, D. — Etiological characterization of hepatitis B surface antigen-negative hepatitis among adult patients in Athens, Greece. **J. clin. Microbiol.**, 11: 297-300, 1980.

22. MATHIESEN, L. R.; SKINHO J., P.; HARDT, F.; NIELSEN, J. O.; SCOTH, K.; ZOFFMANN, H.; MOLLER, A. M.; WONG, D.; PURCELL, R. H. & Copenhagen Hepatitis Acuta Programme. Epidemiology and clinical characteristics of acute hepatitis types A, B, and non-A, non-B. **Scand. J. Gastroent.**, 14: 849-856, 1979.

23. MILICUA, J. M.; DOMINGUES, A.; BUENO, R.; FARO, M. V.; IÑIGUEZ, F. I.; HERNANDEZ RANZ, F.; MOREIRA, V.; RUIZ DEL ARBOL, L.; CELMA, M. L. & BOIXEDA, D. — Hepatitis viral aguda: estudio epidemiológico, virológico y evolutivo de cien casos. **Gastroent. Hepat.**, 4: 221-228, 1981.

24. NORKRANS, G.; FROSNER, G.; HERMODSON, S.; NENONEN, N. & IWARSON, S. — The epidemiological pattern of hepatitis A, B, and non-A, non-B in Sweden. **Scand. J. Gastroent.**, 13: 873-877, 1978.

25. NORKRANS, G.; FROSNER, G.; HERMODSON, S. & IWARSON, S. — Clinical, epidemiological and prognostic aspects of hepatitis non-A non-B. A comparison with hepatitis A and B. **Scand. J. infect. Dis.**, 11: 259-264, 1979.

26. PANNUTI, C. S.; MENDONÇA, J. S.; PEREIRA, M. L. G.; CARVALHO, M. J. M. & AMATO NETO, V. — Sporadic acute viral hepatitis A, B, and non-A, non-B. A prospective study of 150 consecutive cases in São Paulo. **Trop. geogr. Med.**, 37: 136-138, 1985.

27. RAMONET, M.; ARUSA, O.; PLANES, N.; NUÑEZ, M.; AFAZANI, A. & CIOCCA, M. — Etiologia de la hepatitis viral aguda en una problación pediátrica. In: JORNADAS LATINOAMERICANA DE HEPATOLOGIA, 8., Lima, 1982. **Anales.** Lima, 1982. p. 27.

28. SILVA, L. C.; SETTE Jr., H.; MORAES, C. R.; SÁEZ-ALQUÉZAR, A.; TAKEDA, A. & RAIA, S. — Marcadores imunológicos das hepatites por vírus A e B. Estudo de 52 paicentes. In: JORNADA CIENTÍFICA DO INSTITUTO DE MEDICINA TROPICAL DE SÃO PAULO, 1., São Paulo, 1981. **Resumos.** São Paulo, Byk-Procienx, 1981. p. 64.

29. SNEDECOR, G. W.& COCHRAN, W. G. — **Statistical methods.** 7th. ed. Ames, The Iowa State University Press, 1980.

30. VILLAREJOS, V. M.; VISONA, K. A.; EDUARTE, C. A.; PROVOST, P. T. & HILLEMAN, M. R. — Evidence for viral hepatitis other than type A or type B among persons in Costa Rica. **New Engl. J. Med.**, 293: 1350-1352, 1975.

31. WEILAND, O.; BERG, J. V. R.; FLEHMIG, B.; LINDH, G. & LUNDBERGH, P. — Acute viral hepatitis types A, B and non-A, non-B: a prospective study of the epidemiological laboratory and prognostic aspects in 280 consecutive cases. **Scand. J. infec. Dis.**, 13: 247-255, 1981.

32. WONG, D. C.; PURCELL, R. H.; SREENIVASAN, M. A.; PRASAD, S. R. & PAVRI, K. M. — Epidemic and endemic hepatitis in India: evidence for a non-A, non-B hepatitis virus aetiology. **Lancet**, 2: 876-879, 1980.

33. ZACARIAS, J.; RAKELA, J.; RIVEROS, J. & BRUNCK, P. — Anticuerpos de hepatitis A. Prevalência en niños aparentemente sanos y con hepatitis aguda. **Rev. med Chile**, 109: 833-836, 1981.

Recebido para publicação em 13/1/1986.