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# Outcome of mother to infant acquired GBV-C/HGV infection

G Zuin, B Saccani, S Di Giacomo, E Tanzi, A R Zanetti, N Principi

## Abstract

**Twelve children born to hepatitis C virus antibody GBV-C/HGV RNA positive mothers who acquired GBV-C/HGV infection by the vertical or perinatal route were studied. Most (91%) were persistently GBV-C/HGV RNA positive up to 12 months of age. Four out of six cases who acquired GBV-C/HGV alone had normal alanine amino transferase activities. Long lasting evidence of hepatocellular injury was detected only in children with GBV-C/HGV and hepatitis C virus and HIV coinfection.**

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Keywords: hepatitis virus infection; mother to infant transmission; HIV

The clinical implications of infection with hepatitis GB-C (GB-C) and hepatitis G (G), two closely related isolates of the same virus, are largely unresolved.<sup>1</sup> Mother to infant transmission has been reported,<sup>2</sup> but very little is known about the outcome of GBV-C/HGV infection in children,<sup>3</sup> particularly those who have evidence of infection in the first months of life. This study aimed to assess the outcome of GBV-C/HGV infection in infants infected vertically.

## Methods

Twelve infants born to 12 hepatitis C virus antibody GBV-C/HGV RNA positive mothers (nine coinfecting with HIV) were studied. These subjects represented all putative cases of vertical/perinatal GBV-C/HGV infection retrospectively observed during a study of mother to infant hepatitis C virus (HCV) transmission from January 1993 to January 1996. A blood sample for hepatitis C antibodies (EIA, Abbott Laboratories, Chicago, USA), hepatitis C virus RNA RT-PCR (polymerase chain reaction) with nested primers derived from the 5' non-coding region of the viral genome,<sup>4</sup> GBV-C/HGV RNA, antibodies to anti-E2 glycoprotein (anti-E2) of the GBV-C/HGV (assayed using an ELISA test, reagents kindly supplied by Abbott),<sup>5</sup> HIV DNA (using PCR), and alanine amino transferase (ALT) were collected from each child at birth, and then at 3, 6, 9, 12 and 18 months of age, and thereafter every 3 to 6 months. GBV-C/HGV RNA was detected by nested RT-PCR.

Briefly, viral RNA was extracted from 100 µl of serum and retrotranscribed to cDNA in the presence of random hexamers. Amplification was performed using nested primers derived from the 5' non-coding region of the viral

genome.<sup>6</sup> The presence of GBV-C/HGV RNA was considered indicative of infection. ALT values were considered abnormal when >40 IU/l (normal range 10-40).

Three children with HCV/HIV coinfections underwent percutaneous liver biopsy during follow up. Histological findings were interpreted by the same pathologist according to the scoring system proposed by Desmet *et al.*<sup>7</sup>

## Results

Among the 12 infants, six were GBV-C/HGV RNA positive only whereas the remaining six were coinfecting with HCV and two cases were infected with HIV alone. GBV-C/HGV RNA was detected within three months of life in all cases and persisted in 10 out of 11 (91%) children at 12 months of age; then the cumulative percentage of GBV-C/HGV RNA positivity gradually declined (table 1).

Children who became GBV-C/HGV RNA negative seroconverted to E2 glycoprotein. Seroconversion occurred within 18 months of life in three infected with GBV-C/HGV alone, whereas none of the coinfecting children seroconverted within this period.

Among the six children infected with GBV-C/HGV alone, two had a transient, minor ALT increase (peak of 91 and 115, respectively) coincidentally or just after the first appearance of GBV-C/HGV RNA, at three months; ALT was within the normal range in all further samples obtained. Despite persistence of viral RNA, the remaining four cases always had normal ALT values during follow up. In all coinfecting cases there was a persistent increase in ALT as well as positivity for hepatitis C virus RNA and GBV-C/HGV RNA. None of the patients became jaundiced; infection with hepatitis B virus, cytomegalovirus, and Epstein Barr viruses was excluded in cases with raised ALT.

Histological studies of three coinfecting patients showed mild chronic hepatitis in two with hepatitis C virus coinfection and chronic active hepatitis in the child who was coinfecting with hepatitis C virus and HIV.

Table 1 Persistence of GBV-C/HGV (as cumulative percentage) during follow up

Months	Tested cases n =	GBV-C/HGV RNA positive n (%)
3	12	12 (100)
6	12	11 (92)
12	11	10 (91)
18	8	5 (62)
24	7	4 (57)
36	6	3 (50)
40	6	1 (17)

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### Discussion

Little information exists about the natural history of paediatric GBV-C/HGV infection, especially in children infected by the vertical or perinatal route.<sup>2</sup> Furthermore, even in adults, it is still unclear whether GBV-C/HGV infection causes acute or chronic liver disease.<sup>1</sup> Most infected adults have no biochemical evidence of hepatocellular injury; in the few cases of hepatitis in which GBV-C/HGV is the only agent identified, the ALT increases are quite small and unrelated to viraemia.<sup>8</sup> Our findings are similar: most of GBV-C/HGV RNA positive children have normal ALT values despite persistence of viraemia; minor and transient increases in ALT occurred only in two cases. There was biochemical evidence of liver disease only in children coinfecting with hepatitis C and HIV; the histological features observed in the children who underwent liver biopsy suggest that GBV-C/HGV does not seem to have any effect on the severity of coexisting infection.

These findings support the histological studies reported in adult patients.<sup>8</sup> In most children GBV-C/HGV RNA was persistently positive during the first 12 months and 57% of tested cases had infection at 24 months. Thereafter two out of three viraemic children were HIV positive. We do not know if immunosuppression induced by HIV could be a risk factor for prolonged GBV-C/HGV viraemia; as far as we are aware there are no available data on children so infected.

Prolonged GBV-C/HGV viraemia has been reported in immunocompromised adults such

as patients on haemodialysis and even in those who are immunocompetent.<sup>1 8</sup> Our results also suggest that anti-E2 seroconversion is associated with viral clearance; seroconversion seems to occur later in coinfecting children. Whether these antibodies can give long lasting protection is not yet known.

Long term follow up studies in larger series are required to establish the clinical outcome of this infection; however our findings, although not from a large enough group to be entirely conclusive, suggest that GBV-C/HGV is a benign infection.

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