ABSTRACT

Hepatitis C is a notifiable disease in South Africa (SA), but there is a lack of surveillance and reporting systems. The availability of routine, reliable and validated methods of hepatitis C virus (HCV) detection and genotyping, together with better surveillance strategies is vital to ensure optimal patient diagnosis, treatment and disease management. This is the first extensive molecular study on the HCV in this country to identify circulating genotypes, host immuno-genetics and patients responses to combination therapy.

HCV genotypes in the patient and blood donor groups were determined by sequencing of the 5'untranslated (5'UTR) and non-structural -5B (NS5B) regions. Three molecular-based tests, line probe assay (LiPA), real-time and palindromic nucleotide substitutions (PNS), were compared to the sequencing method. Molecular sequence analyses of the core, envelope 1(E1), NS4B and NS5B were determined. The inferred amino acid data was used to determine epitope variation across immunodominant regions. Viral load monitoring was performed on patients receiving combination treatment.

A positive HCV polymerase chain reaction (PCR) result is necessary to confirm active infection. A National HCV surveillance database was established to collate patient demographics with results from public health laboratories. Genotype 5a predominates in patients with liver disease. Changing frequencies and introductions of other subtypes were determined. The LiPA (5'UTR) was found to surpass the other genotyping tests, as it was quick and easy. Geographical clustering within the genotype 5a clade was

evident in the E1 and NS4B regions. The branching order of genotype 5a suggests that genotype 5a is older than genotype 3, inferring that patients with genotype 5a may respond better to therapy than those infected with genotype 3. The divergence estimate of genotype 5a was found to be between 100-156 years. Despite the homogeneity of genotypes 1 and 5 epitope sequences, well-published epitopes were predicted to bind sub-optimally to the common human leukocyte antigen (HLA) alleles, making a vaccine less effective in SA. The treatment response for genotype 5a was higher in this study compared to previous global studies.

This new molecular knowledge on HCV genotypes circulating in SA will allow informed decisions when planning preventative and treatment strategies relevant to local viral and host genetics.