ABSTRACT

Fetal alcohol spectrum disorder (FASD) encompasses a range of conditions induced by prenatal alcohol exposure. Fetal alcohol syndrome (FAS) is the most severe of these conditions. FAS is characterised by discriminating facial features along with growth deficiencies and central nervous system abnormalities.

FASD is a growing concern in South Africa, particularly in the Northern and Western Cape Provinces. In the Northern Cape, astounding prevalence rates of 122 and 73.8 per 1000 school entry children have been established for the towns of De Aar and Upington respectively.

Studies involving twin concordance research and animal models have indicated that there is a genetic influence contributing towards FAS susceptibility in individuals. FAS is considered a complex disease whereby both genetic and environmental factors interact in disease pathogenesis. For this reason a case-control study involving the investigation of appropriate candidate genes was conducted.

The neuronal migration pathway in the developing brain is targeted by prenatal alcohol exposure. The *astrotactin* (*ASTN*) and *reelin* (*RELN*) genes were selected for investigation based on their fundamental role in neuronal migration. A FAS case-control study involving 45 cases and 112 controls was conducted on the Northern Cape Coloured population.

Four single nucleotide polymorphisms (SNPs) including missense and non-coding variants were selected within *ASTN* and four missense SNPs were selected within *RELN*. The study aimed to determine the genotype and allele frequencies of the variants within the case and control groups and to assess whether any association between the gene variants and the predisposition to FAS existed. Statistical analyses indicated a significant genotypic association (P= 0.049) between *RELN's* rs607755 marker; the C/T genotype was more likely to be found amongst controls thus inferring a possible protective effect against FAS. A logistic regression model supported the

above association by indicating the C/T genotype as being independently significant (P= 0.026).

The most limiting factor of this study was the small sample size and consequent lack of power to detect genes with minor effects. It would therefore be suggested that the study be repeated once a larger sample size has been established. A larger sample size would increase the chances of detecting true associations between genes of minor effect and FAS, thus minimising false-positive associations from arising.