Partial cDNA encoding major histocompatibility complex class I alpha (MHC class Iα) gene was obtained from a cDNA library of Nile tilapia (*Oreochromis niloticus*) spleen. 5' RACE was then conducted to get the full-length of MHC class Iα cDNA. Sequence analysis revealed that this cDNA consisted of 2,131 bp including a 871 bp open reading frame with 5' untranslated and 3' untranslated regions (UTR) of 128 bp and 932 bp respectively. Highly polymorphic characteristic of MHC class Iα in 6 different strains of Nile tilapia (ST1-ST6) was evident. At least 15 different alleles were observed when the specific primers were used to amplify nucleotide sequences of α1 and α2 domains. Additionally, resistance against streptococcosis of these strains was compared by intraperitoneal injection with viable *Streptococcus agalactiae*. The result revealed that ST1 strain showed significantly higher survival rate than the other five strains (ST2-ST6) with 100% survival after 7 days of injection (P<0.05). While the others were 86.67±5.77, 73.33±5.77, 70.00±0.00, 60.00±0.00 and 43.43±5.77%, respectively. Some haematological and immunological parameters were also compared. This study provides valid information for further investigation to select the *S. agalactiae* resistant strain of Nile tilapia using MHC class Iα (*Orni*a allele) as the molecular marker for the strain selection and breeding program.