Abstract Type 2 Diabetes Mellitus (T2DM) is characterized by persistently elevated blood glucose, or an elevation of blood glucose after a meal containing carbohydrate. *IRS1* gene was considered to be susceptible to cause type 2 diabetes in Pakistani population. The current study was aimed to identify the association of genetic variation in *IRS1* gene and diabetes type 2 development. For this purpose blood samples were collected from 31 patients and 19 controls along with their clinical characteristics. Families samples were also collected to evaluate heritability pattern of type 2 diabetes. All patients were clinically diagnosed with diabetes according to WHO criteria. Genomic DNA was isolated from the blood. DNA was amplified by polymerase chain reaction (PCR) followed by using DNA sequencing and Restriction Fragment Length Polymorphism (*sma I*). Moreover genotypic frequencies of two SNPs (rs180278 (0.0024), rs2943641 (0.0045) were higher in patients as compared to controls and were significantly associated with ($P<0.05$) with type 2 diabetes in population of Pakistan. The haplotype analysis indicated that frequencies were higher in patients as compared to controls ($P<0.05$). In conclusion, the polymorphism between *IRS1* was significantly associated with type 2 diabetes. A large scale genetic screening is required to build a set of genetic markers that can be used for genetic study for early diagnosis and prevention.