Diabetes mellitus has become a major global health problem. It is therefore critical to elucidate the metabolic alterations during the diabetic progression for better understanding its pathogenesis, and identifying potential biomarkers. Metabolomics is a systems biology approach that provides global metabolic information about biological samples. Here we applied a serum untargeted metabolomics study based on GC-QTOFMS from a cohort study including 48 patients with diabetic kidney disease (DKD), 76 diabetic peripheral neuropathy (DPN), 44 diabetic foot disease (DFD) collected in three hospitals from March 2015 to March 2016. It was shown that the three groups could be separated in PLS-DA scores plot according to the metabolites. Serum levels of beta-alanine, beta-alanine/L-aspartic acid, L-arabinose/L-arabitol, caproic acid were significantly lower in DKD groups than DPN groups, while those of L-arabitol, o-phosphoethanolamine, allantoin, fumaric acid and myoinositol were higher. Serum levels of glycerol 1-octadecanoate, L-glutamic acid/pyroglutamic acid, fructose 6-phosphate, taurine and L-glutamic acid were significantly lower in the DKD group than DFD group, while benzoic acid, erythrose, L-arabitol and fumaric acid were higher. Serum levels of L-glutamic acid/pyroglutamic acid, allantoin, glycerol 1-octadecanoate, L-glutamine, homocysteine and L-arginine were lower in DPN group than DFD group, while beta-alanine, beta-alanine/L-aspartic acid and d-glucose were higher. It is the first time to compare the serum metabolism alterations among different diabetic complications. We hope it could help further understand the mechanism of diabetic complications, and provide new targets and ideas for preventing and treating diseases.