Summary:

- Frequency of mutations in podocyte coding genes \textit{NPHS1} and \textit{NPHS2} and polymorphisms analysis of \textit{ACE} and \textit{MDRI} and its association with the pathogenesis of NS in South Indian children were analyzed.

- The project enrolled three groups of study subjects: Group I healthy controls, (n=100) Group II children with SSNS (n=100) and Group III children with SRNS (n=100).

- The genomic DNA was isolated from whole blood sample and subjected to mutation analysis using specific primers by PCR, followed by Sanger sequencing.

- A mutational frequency of 9% in the \textit{NPHS1} was observed in SRNS patients. Six mutations (9%) and three SNPs observed in the study population are novel. The TT genotype of SNP, rs866537732 was observed significantly more associated with cases (SSNS (15%) and SRNS (18%)) when compared with control group (5%), suggesting an association of this SNP with an increased risk for NS.

- A mutational frequency of 18% (12 mutations) and two SNPs was observed in SRNS patients, of which 7 mutations were found to be novel.

- The frequency of I/D in \textit{ACE} did not show any significant difference between the three groups (control, SSNS and SRNS). The genotypes TT, GT and GA of G2677T/A of \textit{MDRI} gene showed a significant association in SRNS patients when compared with that of a SSNS and control group (p < 0.05).
Conclusion:

Our knowledge about the etiology of NS is still limited, due to the complexity and heterogeneity of the genetic mutations and other factors or mechanisms involved. This thesis contributes to the unraveling of the etiology of NS within the context of South Indian children. The results unequivocally demonstrate that the mutations and SNP of *NPHS1*, *NPHS2* and *MDRI* genes contributes to the pathogenesis of NS. These variations are promising and would possibly be considered as probable genetic risk factors or biomarkers with implications in the development and progression of disease. These molecular defects would provide a starting point for future studies to not only clarify the etiology of clinical heterogeneity but also improve the early detection of the disease, identify the patients with steroid-unresponsive NS and prevent acute and long-term complications.