**Abstract ID: -** 55

**Abstract Topic: -** Epigenetics

**Abstract Title: -** Differentially expressed miRNAs in Diabetic Nephropathy target oxidative stress and mitochondrial dysfunction pathways

**Presenting author name: -** Abhishek Sehrawat

**Presenting author institute: -** Central University of Punjab

**Co-authors name: -** Dr. Jasvinder Singh Bhatti

**Co-authors institute: -** Central University of Punjab

**Aims: -** Diabetic Nephropathy (DN) is a multifactorial metabolic disorder affecting millions worldwide and has become a global healthcare challenge. Emerging evidence indicates the involvement of miRNAs in personalized medicine. This study aimed to identify the specific deregulated miRNAs among people with DN, Type 2 diabetes (T2DM) and healthy controls (HC) and to investigate their targeting pathways.

**Methods: -** The miRNA expression profiles of patients with Diabetic Nephropathy (n=5), Type 2 Diabetes (n=5), and healthy controls (n=5) were investigated by high-throughput sequencing. The differentially expressed miRNAs (DE-miRNAs) were identified by bioinformatics analysis followed by target prediction for the top DE-miRNAs using various miRNA-target gene database: miRTarbase, miRNET, miRTarget Link 2.0 and miRWalk. The predicted DE-miRNA targets that overlapped with the DN-associated genes from the database of gene-disease associations (DisGeNET) were used for further analysis. Afterwards, the gene ontology (GO) and functional enrichment analysis was performed to illustrate the biological functions followed by miRNA-target mRNA network construction to suggest a regulatory role for specific miRNAs in DN pathogenesis.

**Results: -** Sequencing analysis revealed that 66 miRNAs were differentially expressed in DN patients compared with the healthy controls (HC) whereas 184 miRNAs were differentially expressed in DN patients compared with Type 2 diabetes (T2DM). Further pathway enrichment analysis highlighted that these DE-miRNAs were specifically involved in the DN-related biological processes. The pathway analysis highlighted several significant pathways of predicted target genes including TGF-β signaling pathway. FoxO signaling pathway, PI3K/Akt pathway, AGE-RAGE signaling pathway, oxidative damage, focal adhesion, and neovascularization processes are involved in mediating the miRNA-based progression of DN.

**Conclusions: -** The findings from present study demonstrated a specific subset of miRNAs that are dysregulated in DN compared to T2DM and HC. These DN-miRNAs might be used to identify the progression of DN and are significantly linked to the regulation of oxidative stress and mitochondrial dysfunction. Moreover, this study might help to improve our mechanistic understanding of DN specifically, with respect to these serum miRNAs.

**Keywords: -** Sequencing analysis revealed that 66 miRNAs were differentially expressed in DN patients compared with the healthy controls (HC) whereas 184 miRNAs were differentially expressed in DN

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