Abstract

Critical impacts of metabolic disorder like Diabetes Mellitus (DM) on diverse pathology of vital organs *viz.* heart, kidney, eye along with macro/micro-vascular complications in retinopathy, nephropathy and neuropathy and their pathobiological studies are crucial in the field of early diagnostic research. Diabetic Retinopathy (DR) is a *sequela* of DM which may even cause blindness but its pathology remains almost asymptomatic until vision loss. Conventional diagnostic practice employing color fundoscopy, Fluorescein Angiography (FA) and Optical Coherence Tomography (OCT) are not always effective in early DR diagnosis. Hence, besides imaging such complex pathobiology may be evaluated using vital attributes of proteomics, lipidomics, metabolomics and biophysical interfaces of the body fluids (*Viz.* Serum and tear) using varied molecular methods as performed in this study involving diabetics with or without DR and normal counterpart. It investigated retinal health of diabetics with correlated fundoscopy, FA and OCT including extraction of image attributes. Subsequently, the serum samples were subjected to quantitative proteomic techniques, Fourier Transform Infrared Spectroscopy, Raman and Nuclear Magnetic Resonance spectroscopy and gas-chromatography coupled high resolution mass spectroscopy for elucidating "Omics" signatures of DR. Novel biophysical properties of serum under the exposure of gold nanoparticles were also explored in terms of fractal dimension analysis. Findings on geometric attributes extracted from fundus and FA images could be correlated with OCT features to differentiate the retinal lesions having neurodegeneration with high sensitivity and specificity. Again, DR serum samples depicted unique gold nano-colloid aggregation pattern and fractal dimension. Expressions of proteins were found to be associated with wound healing and retinal neurodegeneration. FTIR and Raman spectroscopy of serum samples confirmed the differential expressions of lipids and β-sheet containing proteins responsible for neo-angiogenesis, vascular fragility, vascular asymmetry and subsequent neuroretinal degeneration in DR while NMR findings revealed elevated levels of ribitol, glycerophosphocholine, and uridine-diphosphate n-acetyl glucosamine. Lipidomic biomarkers further served as complementary proof towards early detection of neuroretinal degeneration in DR. Thus, this work can be considered as an integrated attempt to delineate multidimensional signatures in DR at early stage and in providing option to correlate structural changes with molecular pathology attributes in body fluids towards finding theragnostic markers for DR.

Keywords: Diabetic Retinopathy, Optical Coherence Tomography, Quantitative Imaging Biomarkers, Fractal Dimensions, Spectral Signatures, Proteomics, Lipidomics, Metabolomics.