**P16**

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**The evaluation of GDF-15 and FGF-21 as potential diagnostic biomarkers for Mitochondrial Disorders**

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**ABSTRACT**

Mitochondrial Disorders (MD) are among the most frequent inherited neurological disorders, caused by mutations in mitochondrial or nuclear DNA, which occur around 1 in 5000 live births. Currently, muscle biopsy is the gold standard for diagnosis of MD due to the lack of sensitive biomarkers. Plasma growth and differentiation factor-15 (GDF-15) and fibroblast growth factor-21 (FGF-21) have been proposed as potential plasma biomarkers for detection of MD. The aim of this study is to evaluate the usefulness of these two factors as promising biomarkers among suspected patients with MD. Plasma samples were obtained from 3 groups of individuals. 41 plasma samples from patients showing neurological symptom of MD (group 1), 104 samples from children with no symptoms but showed positive screening tests (group 2) and 45 samples from healthy control (group 3). Samples were analysed for GDF-15 and FGF-21 using ELISA kit (R&D Systems). The levels of GDF-15 and FGF-21 in healthy controls were 257.33 pg/ml ± 14.03 SEM and 42.02 pg/ml ± 4.47 SEM. The levels in group 1 were significantly higher compared to the healthy control (mean 84,560 pg/ml ± 24808 SEM and 33,086 pg/ml ± 25,845 SEM respectively, p<0.05), while level in group 2, GDF-15 and FGF-21 were elevated 4 – 34 times (mean 1017 pg/ml ± 167 SEM and 1467 pg/ml ± 15 SEM respectively, p<0.05). The area under receiver-operating-characteristic curve for GDF-15 was 0.7187±0.0556 SE indicating that it has a good discriminatory power in group 1 compared to FGF-21 (0.6301±0.0603 SE). The overall sensitivity and specificity of GDF-15 for cut-off value of 300 pg/ml was 90.24% and 75.56% (p<0.05). However, we found no significant correlation between GDF-15 and FGF-21 (p value 0.465). Our study showed GDF-15 is a potential biomarker in comparison to FGF-21 in diagnosing of MD.