BACKGROUND

- Renal impairments (RI) pharmacokinetic (PK) studies are recommended for most type 2 diabetes mellitus (T2DM) and obesity, other common comorbidities such as non-alcoholic fatty liver disease (NAFLD) and the more severe, non-alcoholic steatohepatitis (NASH) are typically exclusionary.

- NASH is strongly associated with RI and obesity, and since three of those metabolic diseases are on the rise [1], it is anticipated that many CKD patients may also have NASH-related liver fibrosis.

Figure 1. Chronic Metabolic Disease Triad in relation to Renal Impairment Study Inclusion Criteria

OBJECTIVE

- The aim of the present study was to determine the predicted screen failure rate in CKD patients with signs of liver fibrosis in RI PK studies. Two prognostic, non-invasive composite biomarkers, FIB4 and APRI, commonly used for NASH screening were examined in a CKD population.

METHODS

- The dataset for this exploratory analysis was created using screening clinical laboratory results from Celerion's proprietary database.

RESULTS

- Fifty-six subjects were included in this pilot study, and stratified based on CKD stages, age, BMI and clinical values were similar to control subjects, except for Stage II CKD patients who were older than controls.

Figure 2. Creatinine and eGFR Values

- The majority of subjects were males (80%) and between 46-77 years old. Across all CKD stages, age, BMI and clinical values were similar to control subjects, except for Stage II CKD patients who were older than controls.

Table 1. CKD Patient Anthropometric and Clinical Data

- Nearly one third of CKD patients had T2DM (34%). Fasting plasma glucose was increased in Stage II and Stage III CKD patients compared to the control group and glucose levels were significantly associated with eGFR.

Figure 3. Fasting Plasma Glucose Concentrations

- While mean FIB4 and APRI scores were similar among CKD patient and control subjects, more patients were above the NASH cut-off with FIB4 versus the APRI biomarker. Seven control subjects and 25 CKD patients were predicted NASH-positive with FIB4 compared to one control subject and two CKD patients who were predicted NASH-positive with APRI. By CKD stage, Stage II and Stage III patients demonstrated the highest rates of predicted NASH by FIB4 (60% and 62%, respectively) compared to controls (41%). For all CKD patients, half were predicted to display NASH.

Figure 4. CKD Patients Categorized by FIB4 and APRI Cutoffs

- While mean FIB4 and APRI scores were similar among CKD patient and control subjects, more patients were above the NASH cut-off with FIB4 versus the APRI biomarker. Seven control subjects and 25 CKD patients were predicted NASH-positive with FIB4 compared to one control subject and two CKD patients who were predicted NASH-positive with APRI. By CKD stage, Stage II and Stage III patients demonstrated the highest rates of predicted NASH by FIB4 (60% and 62%, respectively) compared to controls (41%). For all CKD patients, half were predicted to display NASH.

- The presence of liver fibrosis was determined with two non-invasive biomarkers, FIB4 or APRI formulas; cutoff values of FIB4 > 1.3 or APRI > 0.5 are predictive of NASH.

REFERENCES

4. FIB4 index = (Age [years] x AST [u/L]) / (Platelet count [109/L] x √ALT [u/L])
5. APRI = (AST [u/L] / 40 u/L) / (Platelet count [109/L]

CONCLUSION

- In the present study, we examined the potential for liver fibrosis and the NASH rate in a CKD population. Using a well-established NASH cutoff of FIB4 >1.3, we identified 46% (50/110) of RI patients with a high likelihood of having NASH (NFS >0.676) had a 5.1-fold increased risk of having CKD [5].

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