Introduction: Advancements in sequencing technology have dramatically improved our understanding of genetic kidney diseases such as polycystic kidney disease (PKD) and focal segmental glomerulosclerosis (FSGS). These tests have broad impacts on clinical care including prognostication, family planning, and transplant status; however, access remains difficult for many patients. Often the bottleneck to testing is the time to be seen by a member of the medical genetics team prior to testing. Our study used a multidisciplinary team of nephrologists, clinical geneticists, and genetic counselors to create a mainstreamed pathway to accelerate genetic testing for PKD and FSGS, and to determine if these pathways impact patient satisfaction and clinical care.

Methods: Mainstreamed pathways for genetic testing of patients with PKD and FSGS were developed and studied in a prospective cohort to assess time to return of genetic diagnosis and relevant clinical outcomes, and included survey data to assess patient perceptions. These pathways utilize gene panel testing, driven by patient phenotype. PKD patients received either a 2 or 8 gene panel, while FSGS patients receive a 45 gene panel. This was compared to a retrospective review of genetic testing under the standard system. We prospectively recruited 57 patients, 48 with PKD and 9 with FSGS, of which 35 have been consented to genetic testing through the mainstreamed pathway. 18 have had samples collected, and final genetic results have been returned to 11 patients, 8 with PKD and 3 with FSGS. Our retrospective control cohort who received the standard of care pathway contained 63 subjects, 56 with PKD and 7 with FSGS, with 58 having return of results data available.

Results: We successfully developed mainstreamed pathways for PKD and FSGS and have returned final genetic results to 11 patients within our publically funded healthcare system. The time from referral to return of genetic results in the mainstreamed prospective cohort was 114 days (95% Confidence Interval [CI]: 72-155 days), which is significantly shorter than the 387 days (95% CI: 328-446 days) in the retrospective control cohort (P<0.0001). In the 8 PKD patients we identified 3 positive variants in PKD1 and 1 in PKD2 giving a diagnostic rate of 30%, along with 4 variants of unknown significance (VUS) in PKD1. Within the FSGS cohort we have yet to identify a positive result given the low recruitment. Within the retrospective cohort of PKD patients, 29 of 56 had positive results in PKD1, PKD2, or GANAB with a diagnostic rate of 51% which was not different from the prospective cohort (P=1.0), with an additional 18 VUS identified.

Conclusions: The mainstreamed pathways led to a significantly faster time to return of genetic results compared to the standard system, and patients felt comfortable with these pathways. The panels used had diagnostic yields that were lower than expected in the PKD population and higher rates of VUS identification, but in line with our historic control. This may be due to the known difficulties in sequencing PKD1 due to its closely related pseudogenes.

No conflict of interest

Table 1. Ancestry proportions by country of grandparent origin

<table>
<thead>
<tr>
<th>Country of grandparent origin</th>
<th>Guatemala (n=231)</th>
<th>Honduras (n=296)</th>
<th>El Salvador (n=104)</th>
<th>Nicaragua (n=413)</th>
<th>Costa Rica (n=22)</th>
<th>Panama (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancestry proportions</td>
<td>AFR</td>
<td>0.07</td>
<td>0.21</td>
<td>0.09</td>
<td>0.12</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>EUR</td>
<td>0.40</td>
<td>0.40</td>
<td>0.39</td>
<td>0.44</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>NAM</td>
<td>0.55</td>
<td>0.39</td>
<td>0.52</td>
<td>0.44</td>
<td>0.31</td>
</tr>
</tbody>
</table>

POS-424

RECURRENT EPISODES OF FEVER IN A PATIENT WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE AND CAROLI DISEASE

GEMBILLO, G1, Scolari, P2, IZZI, C2, Siligato, R3, Minutoli, F4, Mazzotti, S1, Santoro, M4
1Policlinico G. Martino- University of Messina- Italy, Department of Biomedical- Dental- Morphological and Functional Imaging Sciences., Messina, Italy; 2University of Brescia- Italy, Nephrology Unit- Spedali Civili Hospital., Brescia, Italy; 3Policlinico G. Martino- University of Messina- Italy, Department of Clinical and Experimental Medicine- Unit of Nephrology and Dialysis., Messina, Italy.

Introduction: Caroli’s disease (CD) is a very rare autosomal-recessive inherited disorder due to a saccular or fusiform dilation and ectasia of the biliary ducts, it is often accompanied by cholelithiasis and subsequent cholangitis and frequently associated with congenital hepatic fibrosis (CHF).

The etiopathogenesis is still unclear but occasional familiar clustering suggests a possible hereditary disease, in particular when occurring in association with polycystic kidney disease and germline PKD1 gene mutations.

Results: Here we describe a rare case of a 55 years old woman with a history of autosomal dominant polycystic kidney disease (ADPKD), autoimmune thrombocytopenia, Helicobacter Pylori infection and with recurrent episodes of fever of unknown origin often causing hospital admissions.

Methods: We describe a rare case of a 55 years old woman with a history of autosomal dominant polycystic kidney disease (ADPKD), autoimmune thrombocytopenia, Helicobacter Pylori infection and with recurrent episodes of fever of unknown origin often causing hospital admissions.

Results: During an episode of fever the patient underwent a Positron Emission Tomography (PET), which revealed an hypercapitation in hepatic hilum correspondence. Based on this finding, he underwent magnetic resonance cholangiography (MRC) that showed multiple cystic dilations of bile ducts, ectasia of the common bile duct of 12 mm and also an anatomical variant of the biliary carreفور caused by a bifurcation of the branches of the right posterior bile duct. These morphological findings led to the diagnosis of CD (Figure 1,2).