Introduction: Osteogenesis imperfecta (OI) is a rare single gene disorder characterized by osteoporosis, increased risk of bone fracture, bone deformities and short stature. About 17 genes responsible for OI have been identified to date. Mutations in the COL1A1 and COL1A2 genes encoding type 1 collagen account for approximately 70-80% of the etiology.

Objective: The aim of this study was to investigate the molecular genetic etiology and to determine the genotype-phenotype relationship with targeted next generation sequencing (NGS) in patients with OI phenotype.

Material and Methods: OI patients followed by Ege University Medicine Faculty Pediatric Endocrinology Department. 42 patient were included:

- Clinical typing (Silence 1979)
- Demographic features
- Auxological measurements

All genes known to be responsible for OI and all genes known to play role in collagen / bone synthesis were studied by NGS-TrusightOne®

RESULTS

<table>
<thead>
<tr>
<th>COL1A1 (n:20)</th>
<th>COL1A2 (n:4)</th>
<th>FKBP10 (n:4)</th>
<th>SERPINF1 (n:4)</th>
<th>P3H1 (n:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>11 girl / 10 boy</td>
<td>2 girl / 2 boy</td>
<td>1 girl / 3 boy</td>
<td>2 girl / 2 boy</td>
<td>Girl</td>
</tr>
<tr>
<td>Admission age (years)</td>
<td>4.5 ± 3.8</td>
<td>2.05 ± 3.03</td>
<td>4.51 ± 3.22</td>
<td>5.76 ± 2</td>
</tr>
<tr>
<td>Consanguinity</td>
<td>2 (10%)</td>
<td>2 (50%)</td>
<td>(-)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Family history</td>
<td>10 (47%)</td>
<td>2 (50%)</td>
<td>4 (100%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Average height SDS</td>
<td>-1.79 ± 1.52</td>
<td>-2.72 ± 0.87</td>
<td>3.06 ± 1.58</td>
<td>-4.26 ± 2.30</td>
</tr>
<tr>
<td>Average weight SDS</td>
<td>-1.03 ± 1.10</td>
<td>-3.35 ± 2.62</td>
<td>-2.14 ± 1.46</td>
<td>-2.86 ± 1.55</td>
</tr>
<tr>
<td>Clinical Type</td>
<td>Type 1: 10 (47.6%)</td>
<td>Type 2: 2 (9.5%)</td>
<td>Type 1: 1 (25%)</td>
<td>Type 2: 2 (50%)</td>
</tr>
<tr>
<td></td>
<td>Type 2: 1 (25%)</td>
<td>Type 3: 1 (25%)</td>
<td>Type 3: 1 (25%)</td>
<td>Type 4: 1 (25%)</td>
</tr>
</tbody>
</table>

Targeted NGS Analysis

- 18 cases without mutation
- 9 cases (6 novel mutations)

Figure 1: Distribution of clinical typing

- Consanguinity: 13 (31%)
- Family History: 21 (50%)
- Admission age: 4.5 ± 3.8 years
- Median body weight SDS (min-max): -1.3 (-6.8-1.2)
- Median height SDS (min-max): -2 (-7.6-0.8)
- Bone deformity: 23 (54.8%)
- Unaided mobilization: 22 (52.4%)
- Blue sclera: 27 (64.3%)
- Scoliosis: 11 (26.2%)
- Dentinogenesis imperfecta: 6 (14.3%)
- Hearing loss: 2 (4.8%)

Table 1: Clinical features of all patients (n:42)

Table 2: Clinical features of patients with mutation (n:33)

Genetic etiology was determined in 33 (78.5%) of 42 cases by targeted sequence analysis. In our study, 13 novel mutations in the OI genes were identified and made significant contributions to the literature.