**Description of Hypereosinophilic syndrome (HES) and subtypes in the literature**

**Aims**

- Hypereosinophilic syndrome (HES) is a group of rare hematologic disorders in which eosinophils are overproduced for prolonged periods of time resulting in organ damage. Different subtypes of HES have been identified but little is known about their similarities or differences. This review aimed to describe clinical characteristics of HES types based on reported cases in the literature.

**Methods**

- A PubMed search focused on different types of HES (idiopathic HES, lymphocyte variant L-HES, myeloproliferative variant M-HES, and eosinophilic leukemia, where otherwise specified CEL-NOS), was performed on March 20th, 2020, from articles only in English. Search strings of HES terms, organ damage, HES types, and HES variants were combined to yield 513 unique hits. From the selected articles (Figure 1) the following information was collected:
  - Author, country and year of publication
  - Age, gender, HES subtype and blood eosinophilic count at diagnosis
  - Organ affected, symptoms/diagnosis at presentation
  - Treatment, malignancy, therapy, follow-up time and mortality
  - Only individual data from 170 publications is presented here.

**Results**

**Figure 1. PRISMA flow chart**

- Included 170 publications from 121 articles
- 41.7% (n=12) of records from individual case data, 28% from publications with aggregate data only

**Figure 2. Organ involvement by HES subtype**

- Percentage of patients affected per organ system

**Table 1. Age, gender and eosinophilic count at diagnosis by subtype**

<table>
<thead>
<tr>
<th>HES Type</th>
<th>Age (n=121)</th>
<th>Gender (n=121)</th>
<th>Male (71.3%)</th>
<th>Female (28.7%)</th>
<th>Male (71.3%)</th>
<th>Female (28.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-HES (n=2)</td>
<td>66.1 (16-99)</td>
<td>91 (94.8%)</td>
<td>6.0 (1.0-30.0)</td>
<td>6.0 (1.0-30.0)</td>
<td>6.0 (1.0-30.0)</td>
<td></td>
</tr>
<tr>
<td>M-HES (n=4)</td>
<td>65.5 (60-70)</td>
<td>150 (80.9%)</td>
<td>6.0 (1.0-30.0)</td>
<td>6.0 (1.0-30.0)</td>
<td>6.0 (1.0-30.0)</td>
<td></td>
</tr>
<tr>
<td>CEL-NOS (n=12)</td>
<td>57.9 (17-94)</td>
<td>56 (46.1%)</td>
<td>6.0 (1.0-30.0)</td>
<td>6.0 (1.0-30.0)</td>
<td>6.0 (1.0-30.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Five most commonly reported signs and/or symptoms**

<table>
<thead>
<tr>
<th>HES Type</th>
<th>Main signs</th>
<th>Fatigue</th>
<th>Pruritus/Itch</th>
<th>Bone marrow involvement</th>
<th>Spleenomegaly</th>
<th>Cardiovascular</th>
<th>Skin lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-HES (n=2)</td>
<td>23%</td>
<td>54%</td>
<td>34%</td>
<td>6%</td>
<td>14%</td>
<td>22%</td>
<td>14%</td>
</tr>
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<td>22%</td>
<td>14%</td>
</tr>
</tbody>
</table>

**Table 3. Main treatment reported**

- M-HES/CEL-NOS: M-HES-CEL-NOS (N=12)
- M-HES: M-HES (N=4)
- CEL-NOS: CEL-NOS (N=12)
- HES: HES (N=121)

**Conclusions**

HES is a rare disease with heterogeneous manifestations involving different medical specialties such as allergy/immunology, dermatology, pulmonology, hematology, oncology and coagulation. Given the heterogeneity of HES, differentiating subtypes is important for optimal management.

**Findings summary**

- The most common type of HES reported is idiopathic.
- There is a male predominance of HES particularly for the M-HES/CEL-NOS subtypes.
- Cases with M-HES/CEL-NOS presented higher AEC compared to the other types.
- Skin is the organ most affected by L-HES patients; spleen is the organ most affected by M-HES patients whereas for HES, heart, lungs and skin are affected in a similar way.
- Mortality was similar between subgroups except for CEL-NOS, which was higher.
- Majority of L-HES, M-HES and CEL-NOS patients received CS, whereas most of M-HES received interferon.

**References**


**Disclosures**

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- PR declares advisory board membership and research funding from GSK, consultancies, advisory board membership, and research funding from GSK and Shamloul, F. PR is director of the Global Medical Affairs Department of a company in the respiratory field of the respiratory care industry and holds intellectual property rights related to respiratory care. The other authors have no disclosures in the past 5 years related to the content of this manuscript.
- Articles included in this review were selected based on title and abstract, and categories are not mutually exclusive in Table 2. The authors declare no competing interests.