Description of Hypereosinophilic syndrome (HES) and subtypes in North America

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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[1]. Different subtypes of HES have been identified but little is known about their similarities or differences[2]. This review aimed to describe clinical characteristics of HES subtypes based on reported cases in the literature.

Methods

- A Pubmed targeted literature search from January 2000 to March 2020 was conducted to identify publications, in English, of the following HES subtypes: idiopathic (I-HES), myeloproliferative (M-HES), lymphocytic variant (L-HES) and chronic eosinophilic leukemia, not otherwise specified, (CEL-NOS). Information from 170 publications with individual case data worldwide was reviewed. Among them, 78 individual cases (31 I-HES; 25 M-HES; 21 L-HES; 1 CEL-NOS) were reported in North America (Canada and USA) and have been summarized here.
- 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, maintenance therapy, follow-up time and mortality

Key inclusion criteria

- I-HES: persistently elevated eosinophil counts without any underlying causes and with presence of end-organ damage
- L-HES: with abnormal T-cell immunophenotype and clonal T-cell receptor gene rearrangement
- M-HES: myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2
- CEL-NOS: with clonal cytogenetic/molecular abnormalities and/or increase marrow blasts (5-19%)

Key exclusion criteria

- Animal studies
- Pre-clinical studies
- Secondary HES
- Associated / reactive HES
- Overlap / single organ HES
- Familial HES
- No relevant data
- No specific data by HES subtype
- Duplicate data
- Full text article not available
- Article not written in English

Results

Figure 1. PRISMA flow chart

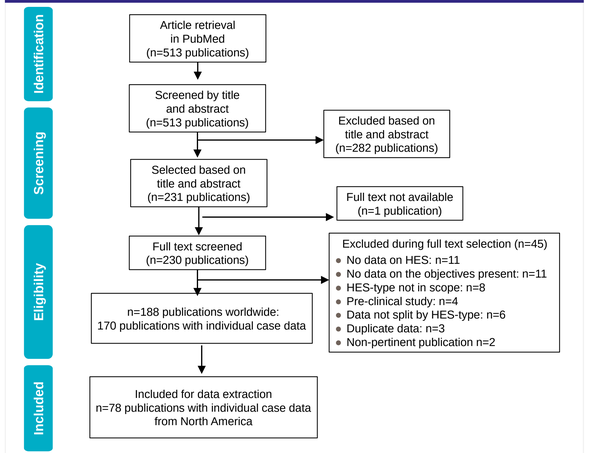
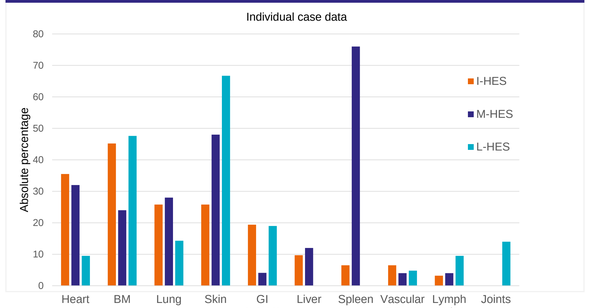


Table 1. Age, gender and eosinophilic count at diagnosis by HES subtype

HES subtype	Age, years mean (range)	Male n (%)	AEC, cells/µL Median (range)
I-HES (N=31)	48.6 (4 – 88)	20 (64.5)	6700 (726 – 215700)
M-HES (N=25)	42.7 (15 – 67)	24 (96.0)	9900 (55.5 – 200000)
L-HES (N=21)	55.3 (22 – 81)	14 (66.7)	3000 (1040 – 23300)
CEL-NOS (N=1)	45 (n=1)	1 (100.0)	5200 (n=1)

*AEC=Absolute Eosinophil Count; I-HES- idiopathic HES; M-HES- myeloproliferative HES; L-HES-lymphocyte variant; CEL, NOS-chronic eosinophilic leukaemia, not otherwise specified

Figure 2. Organ involvement by HES subtype



BM=Bone marrow; GI=Gastrointestinal
* The only CEL-NOS case presented heart, liver, spleen, lung and lymph nodes involvement

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

I-HES (N=31)	M-HES (N=25)	L-HES (N=21)	CEL-NOS (N=1)
Cardiac#: **26%**	Splenomegaly: **60%**	Pruritus/Itch: **38%**	Hepatosplenomegaly: **100%**
Dyspnea: **26%**	Skin lesions: **40%**	Fever: **29%**	Lymphadenopathy: **100%**
Bone marrow involvement: **23%**	Cardiac#: **24%**	Skin lesions: **29%**	
Fatigue/tiredness/ lethargy: **19%**	Lung and pulmonary abnormalities: **24%**	Bone marrow involvement: **24%**	
Abdominal pain/swelling: **16%**	Anemia/ thrombocytopenia: **20%**	Myalgia: **19%**	

*Signs and/or symptoms are presented as reported in the articles, and categories are not mutually exclusive
#Left ventricular abnormalities, murmur, thrombus

Conclusions

Differences in clinical manifestations and treatment between subtypes were observed. For optimal management of HES patients it is important to differentiate these sub-types and provide an early treatment in an effort to limit the end-organ damage observed[3].

Table 3. Main treatment reported

	I-HES (N=31)	M-HES (N=25)	L-HES (N=21)	CEL-NOS (N=1)
Any corticosteroid (CS)	77%	56%	81%	100%
Hydroxyurea / hydroxycarbamide	45%	56%	5%	-
Imatinib	42%	96%	5%	100%
Interferon alpha	26%	16%	10%	100%
Cyclosporine	10%	8%	-	-
Vincristine	7%	4%	5%	-
Methotrexate	3%	-	24%	-
Mepolizumab / Alemtuzumab	10%	-	-	-

Standard medication to reduce eosinophils levels
Treatments indicated for HES

Findings summary

- The most common subtype of HES reported was idiopathic.
- There was a male predominance of HES particularly for the M-HES/CEL-NOS subtypes.
- Cases with M-HES presented higher AEC compared to the other subtypes.
- Skin and bone marrow were the organs most affected in L-HES patients; spleen and skin were the organs most affected in M-HES patients; whereas for I-HES, bone marrow, heart, lungs and skin were the organs most commonly affected.
- Mortality rate was 10% among I-HES patients over a median follow up of 14 months (range 3-96), and 12% among M-HES patients over a median follow up of 47 months (range 1-60).
- Majority of I-HES and L-HES patients received CS, whereas most of M-HES received imatinib.

References

1. Kahn JE, Groh M & Lefevre G. (A Critical Appraisal of) Classification of Hypereosinophilic Disorders. *Front Med (Lausanne)* 2017;4:216, doi:10.3389/fmed.2017.00216.
2. Shomali W & Gotlib J. World Health Organization-defined eosinophilic disorders: 2019 update on diagnosis, risk stratification, and management. *American journal of hematology* 2019;94:1149–1167. doi:10.1002/ajh.25617.
3. Klion, A.D. Eosinophilia: a pragmatic approach to diagnosis and treatment. *Hematology. American Society of Hematology. Education Program* 2015, 92-97, doi:10.1182/asheducation-2015.1.92.

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