Hemophagocytic Syndrome in Adults - Real-World data on Mortality from a tertiary reference center
Category: Hemostasis, transfusion medicine, vascular, laboratory medicine

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Background and Objective
Hemophagocytic Syndrome (HLH) is a rare, life-threatening disorder. Real-world data on HLH in adults are sparse. We analyzed the clinical characteristics and outcomes of HLH adult patients in our hospital.

Methods
The hospital database was searched to identify adult HLH patients diagnosed between January 2014 - June 2021. We used the Saint Antoine score (HScore) (L. Fardet et al. Arthritis & Rheumatology 2014) to evaluate the data. Overall survival (OS) was estimated by Kaplan-Meier method and a logistic regression analysis to predict death including all variables with p value <0.10 at univariate analysis.

Results
We analyzed medical reports of 591,136 patients.
The diagnosis of HLH was mentioned in 79 patients. After the exclusion of 24 duplications, the remaining 55 patients were analyzed using the HScore and 54 patients were included (0.009% of all screened patients).
Patients characteristics are describe in table 1. The OS at 180 days was 58%+6.85, all but one death occurred in the first 30 days after diagnosis.
In univariate analysis, the statistically significant unfavorable predictive factors were: neurological symptoms, cardiovascular complications, requiring platelet transfusion, increased alkaline phosphatase and age >50 years.
A backward stepwise procedure was used to eliminate non-significant variables. Table 2.

Table 1. Patients characteristics – Comparison alive vs dead

Categorical variables	total	alive	dead	P
All	54	32 (59.3%)	22 (40.7%)	
Male	18 (33.3%)	13 (40.6%)	5 (22.7%)	0.170
Female	36 (66.7%)	19 (59.4%)	17 (77.3%)	
Relapse	5 (9.3%)	4 (12.5%)	1 (4.5%)	0.322
Fever	44 (81.5%)	27 (84.4%)	17 (77.3%)	0.509
Cytopenia	53 (98.1%)	31 (96.9%)	22 (100%)	0.403
Neutropenia < 0.5 G/L	15 (27.8%)	11 (34.4%)	4 (18.2%)	0.192
Ferritin	50 (92.6%)	30 (93.8%)	20 (90.9%)	0.695
Splenomegaly	43 (79.6%)	23 (71.9%)	20 (90.9%)	0.088
BMB	18 (33.3%)	10 (31.3%)	8 (36.4%)	0.695
Hypofibrinogen	16 (29.6%)	7 (21.9%)	9 (40.7%)	0.115
CD25	5 (9.3%)	3 (9.4%)	2 (9.1%)	0.972
Hepatomegaly	6 (11.1%)	5 (15.6%)	1 (4.5%)	0.203
Neurological symptoms	21 (38.9%)	8 (25.0%)	13 (59.1%)	0.012
Cardio-pulmonary symptoms	30 (55.6%)	11 (34.4%)	19 (86.4%)	<0.001
Hepatitis	17 (31.5%)	7 (21.9%)	10 (45.5%)	0.067
Skin changes	12 822.659	9 (29%)	3 (13.6%)	0.187
RBC transfusions	29 (53.7%)	14 (43.8%)	15 (68.2%)	0.077
Platelet transfusions	29 (53.7%)	12 (37.5%)	17 (77.3%)	0.004
Hematological malignancies	23 (42.6%)	10 (31.3%)	13 (59.1%)	0.042
Cancer	5 (9.3%)	4 (12.5%)	1 (4.5%)	0.332
Autoimmunity	9 (17.0%)	8 (25.0%)	1 (4.8%)	0.055
Age >50 years	40 (74.1%)	20 (62.5%)	20 (90.9%)	0.019
Ferritin >9999 µg/l	29 (54.7%)	15 (48.4%)	14 (63.6%)	0.272
Calendar year (before 2018)	22 (40.7%)	8 (25%)	14 (63.3%)	
Calendar year since 2018	32 (59.3%)	24 (75%)	8 (36%)	0.005

Continuous variables	total	alive	dead	P
Age at diagnosis	61 (22-83)	52.5 (24-79)	69.6 (22-83)	0.002
Diagnostic criteria	5 (3-7)	5 (3-7)	5 (3-7)	0.997
St Antoine score %	96 (8.8-99.98)	95 (8.8-99.98)	98.1 (25-99.98)	0.246
WBC	4.55 (0.06-53.1)	4.3 (0.53-26.1)	4.7 (0.6-53.1)	0.532
Hb	84 (60-133)	84.5 (60-133)	82.5 (64-111)	0.245
Neutrophils	1.93 (0.09-23.19)	1.97 (0.09-23.2)	1.87 (0.15-9.05)	0.295
Platelet count	51.5 (1-408)	72.5 (7-408)	20.5 (1-236)	0.009
Triglycerides	3.24 (0.60-14)	2.74 (1.0-6.61)	3.57 (0.6-14)	0.274
Fibrinogen	2.07 (0.47-7.94)	2.12 (0.56-6.25)	1.51 (0.47-7.9)	0.567

Overall survival at 180 days – Patients with vs without hematological neoplasms

Without hematological malignancies: 71% ±8.2% (SEM)
With hematological malignancies 40.7% ±11% (SEM)
Log rank p=0.038

Overall survival at 180 days – Comparison after age groups at diagnosis

Aged 50 or lower: 85% ±9.4%
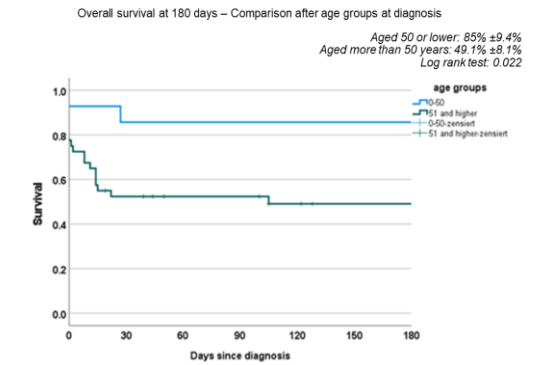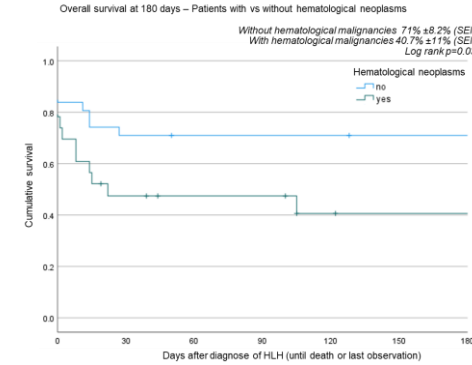Aged more than 50 years: 49.1% ±8.1%
Log rank test: 0.022

Table 2. Multivariate analysis: Relative risk of early mortality after diagnosis of HLH

Parameter	Odds ratio (RR)	95% CI	P value
Age at diagnosis (continuous)	1.175	1.0038 - 1.329	0.011
Increased Triglycerides (ref not increased)	465.68	3.466 - 62572.6	0.014
Cardiopulmonary (ref absent)	254.9	4.649 - 13979.3	0.007
Hepatitis (ref absent)	18.935	0.940- 381.52	0.055
Platelet transfusion (ref absent)	31.011	0.799 - 1203.76	0.066

Conclusions
- These data confirm the rare occurrence and high risk of dying from HLH in adults patients.
- The number of diagnostic criteria and a high HScore were not related with higher death rates.
- The main associated factors with overall mortality were advanced age, the presence of cardiovascular complications, and high triglycerides at diagnosis.
- Further awareness on this entity and multidisciplinary work are essential to improve outcome.

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