

## Pretransplant elevated serum ferritin levels are associated with increased risk of invasive fungal pneumonia (IFP) in patients that underwent allogeneic hematopoietic stem cell transplantation (alloHSCT)

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**Objectives and aim:** Invasive fungal pneumonia (IFP) has become increasingly common in patients that previously underwent alloHSCT due to prolonged neutropenia, immunosuppressive therapies to prevent Graft-vs-host disease (GvHD) and widespread use of broad-spectrum antibiotics. The aim of this study was to determine the role of hyperferritinemia in invasive fungal pneumonia in patients that underwent alloHSCT.

**Materials and Methods:** Medical records of 73 patients with pneumonia that underwent alloHSCT were studied retrospectively, whereby a pre-transplantation serum ferritin level measured up to 100 days prior to transplantation of patients with invasive fungal pneumonia (IFP) and non-fungal pneumonia (non-IFP) was compared.

**Results:** Patient records revealed 35 and 38 cases of IFP and non-IFP respectively. All 35 patients diagnosed with IFP also showed signs of probable pneumonia. Isolated causative microorganisms were *Candida* spp in five (14.2 %) of the patients and Aspergillosis in three (8.6 %). In risk evaluation for IFP, age, gender, HLA status, conditioning regimen, CD34+ count, donor gender, GVHD presence, smoking history, and underlying disease were not significantly different among groups ( $p > 0.05$ ). However, performance status (Karnofsky) was significantly lower in patients with IFP ( $p < 0.05$ ), compared to the control group. The median ferritin levels were 1705 ng/ml (41 – 7198) in the IFP group and 845 ng/ml (18 – 7099) in non-IFP group and the difference was found statistically significant ( $p = 0.001$ ).

**Conclusion:** Elevated pretransplant serum ferritin level is associated with IFP in patients that underwent alloHSCT, in particular when values exceed 1550 ng/ml.

**Keywords:** alloHSCT, invasive fungal pneumonia, ferritin, aspergillosis, survival.

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Parameters	N%	Normal ranges
Diagnosis	0	
Proven	35 (100 %)	
Probable		
Serum median (min-max)	0.245 (0.13-1.71)	>0.5;positive 0.5< negative
GM		>80;positive, <60; negative
$\beta$ -D glucan	32.0 (7.0-198.0)	
<b>Serum</b>	positive	>0.5;positive 0.5< negative
	negative	
GM	8 (22.8)	>80;positive, <60; negative
$\beta$ - D glucan	7 (20.0)	
	28 (80.0)	
<b>BAL fluid median (min-max)</b>	0.415 (0.26-4.65)	>0.5;positive 0.5< negative
GM		>80;positive, <60; negative
$\beta$ - D glucan	41.0 (7-339)	
<b>BAL fluid</b>	positive	>0.5; positive negative positive, negative
	negative	
GM	4 (33.4)	>80; positive, <60;
$\beta$ - D glucan	5 (41.7)	7 (58.3)
<b>Isolated microorganism</b>		
Aspergillus spp.	5 (62.5 %)	
Candida spp.	3 (37.5 %)	
<b>Clinic</b>		
Yes	35 (100 %)	
No	0	
<b>CT image</b>		
Yes	31 (88.5 %)	
No	4 (11.5 %)	
<b>Culture positivity</b>		
Yes	8 (22.8 %)	
No	27 (77.2 %)	
<b>Culture origin</b>		
BAL fluid	5 (62.5)	
Blood	0	
Other (sputum)	3 (37.5)	

Variables	IFP group 35 (%)	Non-IFP group 38 (%)	p value	Normal ranges
Ferritin (ng/ml)	1705 (41-7198)	845 (18-7099)	0.001	18.5-306.5
Serum Fe ( $\mu$ g/dL)	143 (11-321)	137 (30-396)	0.930	65-175
TIBC ( $\mu$ g/dL)	256 (122-503)	271 (111-444)	0.728	225-480
TS (%)	52.1 (3.7-96.9)	68.9 (13.8-100.0)	0.996	35-50

TIBC: Total iron binding capacity, TS: Transferrin saturation, Fe: iron