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ASSOCIATION OF CXCR3 RECEPTOR CHEMOKINES SERUM LEVELS WITH THE CLINICAL COURSE OF FEBRILE NEUTROPENIA AMONG CHILDREN TREATED FOR CANCER

M. NOWAK, K. BOBEFF, K. WYKA, J. KOŁODRUBIEC, J. WALENCIAK, W. MŁYNARSKI, J. TRELIŃSKA
Department of Pediatrics, Oncology & Hematology Medical University of Lodz, Lodz, Poland

MEDICAL UNIVERSITY OF LODZ

INTRODUCTION

Neutropenia is a major risk factor for infection in patients treated with chemotherapy for cancer. Oligosymptomatic infections during neutropenia prompt the search for new laboratory markers.

AIM

To evaluate the usefulness of chemokine concentrations (CXCL9/MIG, CXCL10/IP-10, CXCL11/I-TAC) in predicting infection during neutropenia in children undergoing oncological treatment.

METHOD

Children treated for cancer with fever during neutropenia (ANC<500/mm^3) were eligible for the study. A physical examination and microbiological tests were performed. Levels of C-reactive protein (CRP); procalcitonin (PCT); and the chemokines MIG, IP-10, and I-TAC were determined at the first fever (point 1) and 12-24 hours later (point 2). Infectious episodes were divided into 2 groups: 1) CDI/MDI - clinically documented infection (CDI) or microbiologically documented infection (MDI) (n=66) or 2) FUO - fever of unknown origin, without clinical and microbiological evidence of infection (n=34).

Table 1. Characteristic of the study group

Parameter	All episodes (n=100) N (%)/ Median (25%, 75%)
Sex: female male	48 (48%) 52 (52%)
Age (years)	9.8 (4.9-13.6)
Underlying disease: Leucaemias and Lymphomas - First line of treatment - after bone marrow transplantation Brain tumors Solid tumors	66 (66%) 58 (87.9%) 8 (12.1%) 8 (12.1%) 26 (26%)
Disease status: - Remission - Relapse/Progression of malignancy	85 (85%) 15 (15%)
Neutrophil count (x10^3/uL)	0.065 (0.02-0.17)
Duration of neutropenia (days)	4 (2-6.5)
Fever at home Inpatient fever	52 (52%) 48 (48%)

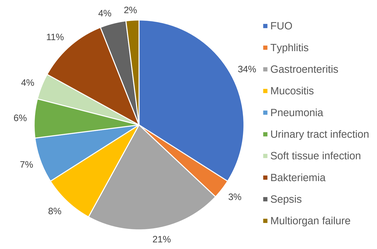


Figure 1. Type of infection episodes in the study group

RESULTS

One hundred consecutive infectious episodes among 62 patients (24 girls, 38 boys) were analyzed, with a median age of 9.8 (4.9-13.6) years - Table 1.

Analysis between CDI/MDI vs FUO groups showed significantly higher I-TAC-1 (p=0.03), IP-10-1 (p=0.04), IP-10-2 (p=0.05) values in the CDI/MDI group (medians, respectively: 70.99 vs 48.64 pg/ml; 96.84 vs 59.95 pg/ml; 149.39 vs 102.40 pg/ml). There were no statistically significant differences between groups in CRP, PCT, or MIG levels at any time point – Table 2.

ROC curves were drawn for the analyzed parameters at the first time point. The best cutoff, accuracy, and AUC were obtained for I-TAC-1 = 33.34 pg/ml, AUC = 0.637 (p = 0.02) – Figure 2.

IP-10 concentration = 63.3 pg/ml identified patients at increased risk of infection (p=0.03 and AUC = 0.624) – Figure 3. Among the tested markers, I-TAC-1 had the highest sensitivity of 87.9%, with a specificity of 41.2%.

Table 2. Comparison of infection markers concentrations at both time points between the FUO group and the CDI/MDI group

Parameter	Group 1 FUO (n=34) Median (25%, 75%)	Group 2 CDI/MDI (n=66) Median (25%, 75%)	p
time point 1			
CRP-1 (mg/l)	16.20 (5.90-39.50)	25.65 (8.10-42.0)	0.25
PCT-1 (ng/ml)	0.16 (0.07-0.22)	0,16 (0.11-0.31)	0.15
MIG-1 (pg/ml)	75,39 (57.77-184.87)	87.06 (52.52-242.99)	0.54
IP-10-1 (pg/ml)	59.95 (46.45-111.80)	96.84 (56.28-246.36)	0.04
I-TAC-1 (pg/ml)	48.63 (30.22-84.38)	70.99 (40.25-132.03)	0.03
time point 2			
CRP-2 (mg/l)	44.60 (10.50-78.90)	39.15 (21.90-85.70)	0.31
PCT-2 (ng/ml)	0.17 (0.08-0.46)	0.22 (0.14-1.10)	0.14
MIG-2 (pg/ml)	81.28 (60.76-132.03)	93.22 (63.53-235.77)	0.56
IP-10-2 (pg/ml)	102.4 (67.52-193.65)	149.38 (92.06-362.81)	0.05
I-TAC-2 (pg/ml)	52.92 (31.38-101.52)	66.15 (40.25-136.26)	0.16

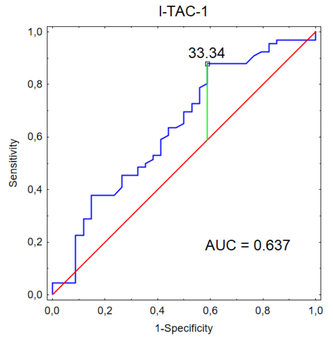


Figure 2. I-TAC-1 threshold values for best identification of fever of unknow origin (FUO) shown by ROC curve.

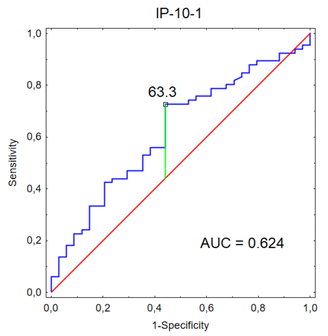


Figure 3. IP-10-1 threshold values for best identification of fever of unknow origin (FUO) shown by ROC curve.

CONCLUSIONS

Selected pro-inflammatory chemokines (I-TAC, IP10) allow for identifying the group with the highest risk of infection in oncology patients with febrile neutropenia.

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CONTACT INFORMATION

Department of Pediatrics, Oncology & Hematology
Medical University of Lodz
Sporna 36/50, 91-738 Lodz, Poland
tel. +4842 6177750
e-mail:m.kruk777@gmail.com