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Clinical assessment of damage markers of blood–air barrier in children with acute leukemia

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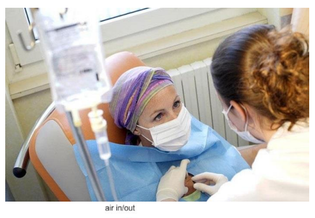
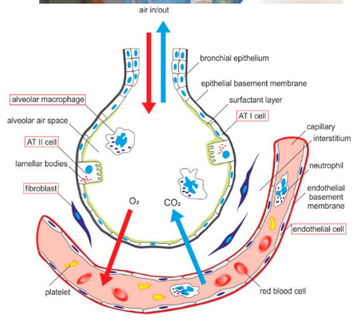
Introduction

- Acute leukemia (AL) is a most common cancer in children.
- The course of the disease itself and the treatment can cause serious complications, including pulmonary ones.

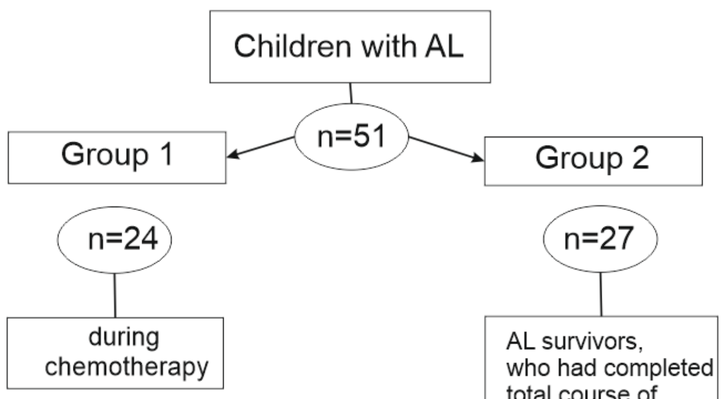




Blood–air barrier (BAB) is a functional part of the lungs with epithelial, interstitial and endothelial components.

The aim of the study is to assess the level and clinical significance of damage markers of epithelial **(IL-6**), interstitial (**TGF-β**) and endothelial (**VEGF**) components of BAB in children with AL.

Materials and methods.



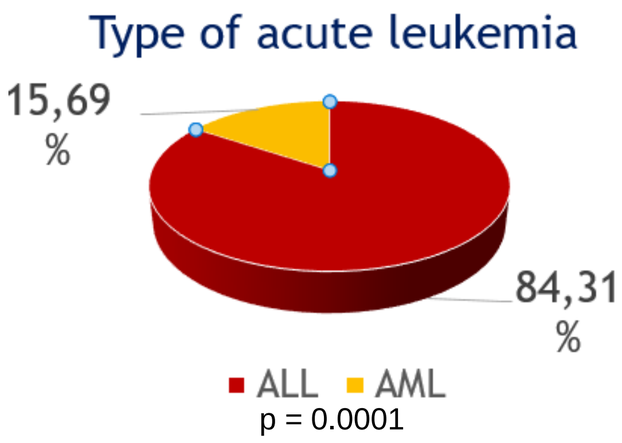
▶Our study included 51 children aged 6-17 years with AL and 15 healthy children for the control group.

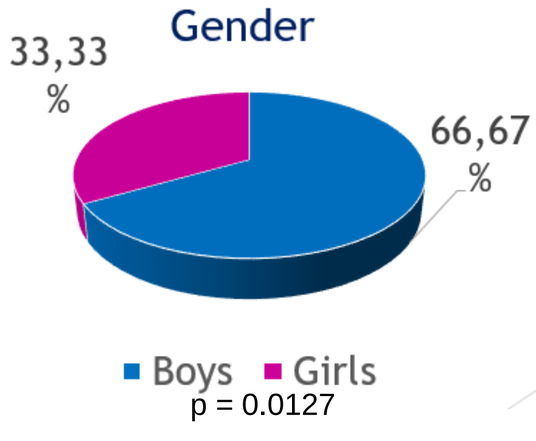
▶Diagnosis and treatment of AL were according to BFM protocols

▶The level of IL-6 and TGF-β in exhaled breath condensate (EBC), VEGF in blood serum were investigated by ELISA.

▶We used STATISTICA 8 and MedCalc 17.2 for data processing.

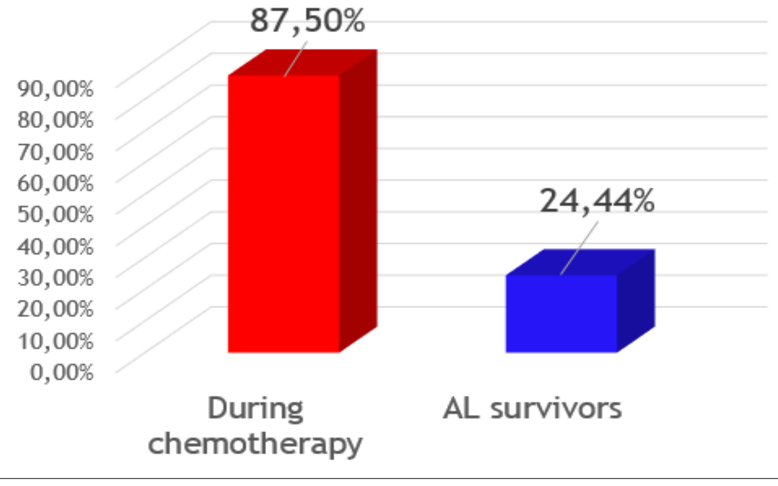
Results





15 of children belonged to a high-risk group (HR)
5 of children had a relapse of acute leukemia

Pulmonary complications



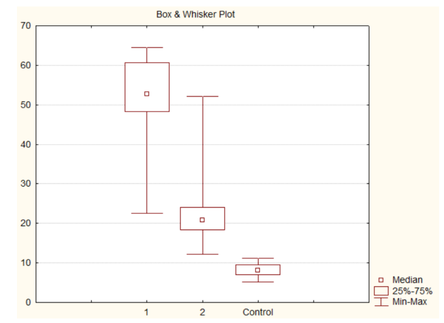
In general in 86.27% (n=51)

Pulmonary complications in children with AL (n=51)

Complication	During chemotherapy	After complete course of chemotherapy
Acute bronchitis	23	-
Recurrent episodes of acute bronchitis	3	3
Wheezing	11	1
Asthma	-	3
Pneumonia	25	2
Interstitial pneumonia	1	-
Pleurisy	2	-
Pneumothorax	3	-
Lung fibrosis	-	3
Blast infiltration of lungs	1	-
Respiratory failure	6	-
Total	44	11

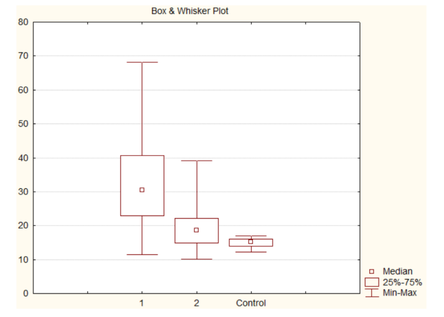
IL-6, pg/ml

Group 1: 52,71 (48,28; 60,71)
Group 2: 20.74 (18.34; 24.08)
Control: 8.12 (7.02; 9.45)
Kruskal-Wallis H= 52,36248; p =0,0000
Mann–Whitney U-test: p_{1-C}=0.000000; p_{2-C}=0.000000; p_{1-2}= 0,000007



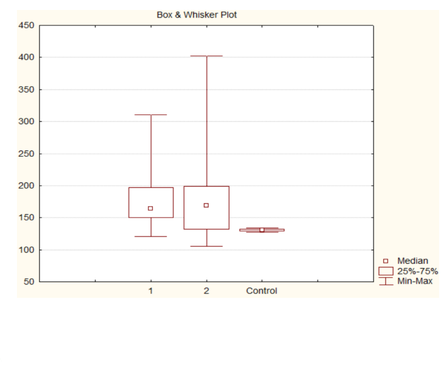
TGF-β, pg/ml

Group 1: 30.46 (22.90; 40.65)
Group 2: 18.55 (14.91; 22.14)
Control: 15.22 (13.88; 16.00)
Kruskal-Wallis H=31,92150; p =0,0000
Mann–Whitney U-test: p_{1-C}= 0,000002; p_{2-C}= 0,011302; p_{1-2}= 0,000013.



VEGF, pg/ml

Group 1: 164.12 (150.18; 197.08)
Group 2: 169.11 (132.15; 198.66)
Control: 130.65 (129.45; 132.15)
Kruskal-Wallis H=16,90223; p =0,0002
Mann–Whitney U-test: p_{1-C}=0,000041; p_{2-C}= 0,001184; p_{1-2}=0,623648.



ROC-analysis

Marker	Pulmonary complications	AUC	Cut off point	Sensitivity	Specificity
Markers collected at the beginning of chemotherapy					
IL-6	Acute	0,952	>47,64	85,71%	100%
	Pneumonia	0,843	>52,08	100%	78,57%
Markers collected after completed course of chemotherapy					
IL-6	Persistent complications in AL survivors	0,891	>25,19	80%	95,45%
TGF-β		0,904	>22,14	71,43%	95%
VEGF		0,900	>196,28	85,71%;	95%

Conclusions:

1. Level of IL-6 in EBC collected at the beginning of chemotherapy >47,64 pg/ml can be predictive for acute pulmonary complications with sensitivity 85,71%; specificity 100%); >52,08 pg/ml can be indicative for pneumonia with sensitivity 100%; specificity 78,57%.
2. Level of IL-6 in EBC >25.19 pg/ml after total course of chemotherapy can be predictive for pulmonary complication in long-term remission with sensitivity 80%; specificity 95,45%.
3. Level of TGF-β >22,14 in EBC after completed course of chemotherapy can be predictive for pulmonary complication in AL survivors sensitivity 71,43 %; specificity 95%.
4. Serum VEGF >196,28 pg/ml after total course of chemotherapy can be prognostic for pulmonary complication in AL survivors with sensitivity 85,71%; specificity 95%.